BEFORE THE VETERINARY MEDICAL BOARD DEPARTMENT OF CONSUMER AFFAIRS STATE OF CALIFORNIA

IN THE MATTER OF THE PETITION FOR REINSTATEMENT RE HONG RAK PARK

Agency Case No. 4602023000452 Office of Administrative Hearings Case No. 2022110128

TAB #	DOCUMENT		I.D.	ADMIT
1	•	Notice of Hearing (Redacted).		
2	•	Certification of License History (Redacted).		
3	•	Veterinary Medical Board Case No. 1002460829: Decision and Order re: Stipulated Surrender of License and Order (Effective July 25, 2019); Stipulated Surrender; Decision and Order re: Stipulated Settlement and Disciplinary Order (Effective May 24, 2018); Stipulated Settlement, and; Accusation.		
4	•	Petition for Reinstatement (Redacted).		
5	•	Petitioner's Statement.		
6	•	Petitioner's CV/Resume (Redacted).		
7	•	Petitioner's Continuing Education.		
8	•	Petitioner's Letters of Reference.		
9	•	Petitioner's Live Scan Request (Redacted).		

EXHIBIT 1



 BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY
 GAVIN NEWSOM, GOVERNOR

 DEPARTMENT OF CONSUMER AFFAIRS
 VETERINARY MEDICAL BOARD

 1747 North Market Blvd., Suite 230, Sacramento, CA 95834-2987

 P (916) 515-5520
 Toll-Free (866) 229-6849
 www.vmb.ca.gov



VIA ELECTRONIC MAIL, CERTIFIED MAIL AND REGULAR MAIL

September 30, 2022

Hong Rak Park

Hong Rak Park 3101 Flintridge Dr Fullerton, CA 92835

Klinedinst 2 Park Plaza Suite 1250 Irvine, CA 92614 nfreitas@klinedinstlaw.com

RE: HEARING NOTICE OAH Case No. TBD Petition for Reinstatement or Modification of Penalty – Hong Rak Park

Dear Dr. Park:

You are hereby notified that a hearing will be held before the Veterinary Medical Board, Department of Consumer Affairs:

Date:	Thursday, January 26, 2023	
Time:	1:00 PM Pacific Time	
Location:	Department of Consumer Affairs	
	Hearing Room	
	1625 N. Market Blvd	
	Sacramento, CA 95834	

Alternatively, in lieu of attending in-person at this hearing in the Sacramento office, you may attend and participate virtually via Webex:

Event address: https://dca-meetings.webex.com/dcameetings/j.php?MTID=mcb5e4bac76e07dd089c63e3238adff16

Event number:	2494 114 9694
Event password:	VMB1262023
Phone audio conference:	(415) 655-0001
Access code:	249 441 49694
Passcode:	86212620

The hearing will be conducted before the Veterinary Medical Board, Department of Consumer Affairs and an administrative law judge of the Office of Administrative Hearings, who will preside over the Petition for Reinstatement or Modification of Penalty.

You may be present at the hearing. You have the right to be represented by an attorney at your own expense. You are not entitled to the appointment of an attorney to represent you at public expense. You are entitled to represent yourself without legal counsel. You may present any relevant evidence and will be given full opportunity to cross-examine all witnesses testifying against you. You are entitled to the issuance of subpoenas to compel the attendance of witnesses and the production of books, documents, or other things by applying to:

Office of Administrative Hearings Attn: General Jurisdiction 2349 Gateway Oaks, Suite 200 Sacramento CA 95833

INTREPRETER: Pursuant to section 11435.20 of the Government Code, the hearing shall be conducted in English language. If a party or party's witness does not proficiently speak or understand the English language and before commencement of the hearing requests language assistance, an agency subject to the language assistance requirement in section 11435.15 of the Government Code shall provide a certified interpreter or an interpreter approved by the administrative law judge conducting the proceedings. The cost of providing the interpreter shall be paid by the agency having jurisdiction over the matter if the administrative law judge or hearing officer so directs, otherwise by the party for whom the interpreter is provided. If you or a witness requires the assistance of an interpreter, ample advance notice of this fact should be given to the Office of Administrative Hearings so that appropriate arrangements can be made.

CONTINUANCES: Under section 11524 of the Government Code, the agency may grant a continuance, but when an administrative law judge of the Office of Administrative Hearings has been assigned to the hearing, no continuance may be granted except by him or her or by the presiding judge for good cause. When seeking a continuance, a party shall apply for the continuance within 10 working days following the time the party discovered or reasonably should have discovered the event or occurrence which establishes good cause for the continuance. A continuance may be granted for good cause after the 10 working days have lapsed only if the party seeking the continuance is not responsible for and has made a good faith effort to prevent the condition or even establishing the good cause.

Please visit the Board's website at <u>www.vmb.ca.gov</u> to view a copy of the agenda or you may contact me at (916) 282-6911 or via email at <u>jeffrey.weiler@dca.ca.gov</u>

Sincerely,

10

Jeffrey Weiler Probation Monitor Veterinary Medical Board

cc: Jeff Stone, Deputy Attorney General



BUSINESS, CONSUMER SERVICES AND HOUSING AGENCYGAVIN NEWSOM. GOVERNORDEPARTMENT OF CONSUMER AFFAIRS• VETERINARY MEDICAL BOARD1747 North Market Blvd., Suite 230, Sacramento, CA 95834-2987P (916) 515-5520| • Toll-Free (866) 229-0170| www.vmb.ca.gov



DECLARATION OF SERVICE BY CERTIFIED MAIL

RE: Notice of Hearing

LICENSE NO: 6707

I, the undersigned declare that I am over 18 years of age; my business address is 1747 N. Market Boulevard, Suite 230, Sacramento, CA 95834. I served a true copy of the attached letter by Certified Mail on the following, by placing same in an envelope addressed as follows:

NAME AND ADDRESS

CERTIFIED NUMBER:

7022 0410 0001 3242 7533

Hong Rak Park 3101 Flintridge Dr Fullerton, CA 92835

Said envelope was then, on **September 30**, **2022**, sealed and deposited in the United States Mail at 1747 N. Market Boulevard, Suite 230, Sacramento, CA 95834, the county in which I am employed, as certified mail with postage thereon fully prepaid, return receipt requested.

Executed on September 30, 2022, at Sacramento, California.

I DECLARE UNDER PENALTY OF PERJURY UNDER THE LAWS OF THE STATE OF CALIFORNIA THAT THE FOREGOING IS TRUE AND CORRECT.

DECLARANT:

Jeffrey Weiler Probation Monitor Veterinary Medical Board

533	U.S. Postal Service [™] CERTIFIED MAIL [®] REC Domestic Mail Only	EIPT at www.usps.com®.
~	OFFICIAL	USE
2h2E T000 0Th0	Certified Mail Fee	Postmark Here
П		
	3101 Flintri	age Dr
1-	Fullerton, CA	A 92835



BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY · GAVIN NEWSOM, GOVERNORDEPARTMENT OF CONSUMER AFFAIRS · VETERINARY MEDICAL BOARD1747 North Market Blvd., Suite 230, Sacramento, CA 95834-2987P (916) 515-5520| Toll-Free (866) 229-0170| www.vmb.ca.gov



DECLARATION OF SERVICE BY CERTIFIED MAIL

RE: Notice of Hearing

LICENSE NO: 6707

I, the undersigned declare that I am over 18 years of age; my business address is 1747 N. Market Boulevard, Suite 230, Sacramento, CA 95834. I served a true copy of the attached letter by Certified Mail on the following, by placing same in an envelope addressed as follows:

NAME AND ADDRESS

CERTIFIED NUMBER:

7022 0410 0001 3242 7540

Klinedinst 2 Park Plaza Suite 1250 Irvine, CA 92614

Said envelope was then, on **September 30, 2022**, sealed and deposited in the United States Mail at 1747 N. Market Boulevard, Suite 230, Sacramento, CA 95834, the county in which I am employed, as certified mail with postage thereon fully prepaid, return receipt requested.

Executed on September 30, 2022, at Sacramento, California.

I DECLARE UNDER PENALTY OF PERJURY UNDER THE LAWS OF THE STATE OF CALIFORNIA THAT THE FOREGOING IS TRUE AND CORRECT.

DECLARANT:

Jeffrey Weiler Probation Monitor Veterinary Medical Board

DHD	U.S. Postal Service [™] CERTIFIED MAIL [®] REC Domestic Mail Only	EIPT	
For delivery information, visit our website at www.usps.com [®] .			
3242	OFFICIAL Certified Mail Fee \$	USE	
1000	Extra Services & Fees (check box, add fee as appropriate) Return Receipt (inardcopy) Return Receipt (electronic) Certified Mail Restricted Delivery Certified Mail Restricted Delivery Adult Signature Required	Postmark Here	
DTHD	Adult Signature Restricted Delivery \$ Postage		
2022	Klinedinst 2 Park Plaza Suite 1250 Irvine, CA 92614		



 BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY
 GAVIN NEWSOM, GOVERNOR

 DEPARTMENT OF CONSUMER AFFAIRS
 VETERINARY MEDICAL BOARD

 1747 North Market Blvd., Suite 230, Sacramento, CA 95834-2987

 P (916) 515-5520
 Toll-Free (866) 229-0170

 www.vmb.ca.gov



DECLARATION OF SERVICE BY CERTIFIED MAIL

RE: Notice of Hearing

LICENSE NO: 6707

I, the undersigned declare that I am over 18 years of age; my business address is 1747 N. Market Boulevard, Suite 230, Sacramento, CA 95834. I served a true copy of the attached letter by Certified Mail on the following, by placing same in an envelope addressed as follows:

NAME AND ADDRESS

Hong Rak Park

CERTIFIED NUMBER:

7022 0410 0001 3242 7526

Said envelope was then, on **September 30, 2022**, sealed and deposited in the United States Mail at 1747 N. Market Boulevard, Suite 230, Sacramento, CA 95834, the county in which I am employed, as certified mail with postage thereon fully prepaid, return receipt requested.

Executed on September 30, 2022, at Sacramento, California.

I DECLARE UNDER PENALTY OF PERJURY UNDER THE LAWS OF THE STATE OF CALIFORNIA THAT THE FOREGOING IS TRUE AND CORRECT.

DECLARANT:

Jeffrey Weiler Probation Monitor Veterinary Medical Board

7526	U.S. Postal Service [™] CERTIFIED MAIL [®] RECEIPT Domestic Mail Only For delivery information, visit our website at www.usps.com ⁹ .	
001. 3242	Certified Mail Fee	Postmark Here
D DTHD	Adult Signature Required Adult Signature Restricted Delivery Postage	
7022	Hong Rak	Park
		=XHIBIT 1 - 005

EXHIBIT 2



BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY · GAVIN NEWSOM, GOVERNORDEPARTMENT OF CONSUMER AFFAIRS · VETERINARY MEDICAL BOARD1747 North Market Blvd., Suite 230, Sacramento, CA 95834-2978P (916) 515-5220Toll-Free (866) 229-0170Www.vmb.ca.gov



CERTIFICATION OF LICENSE HISTORY

This is to certify that I, Matthew McKinney, Enforcement Manager of the Veterinary Medical Board (Board), Department of Consumer Affairs, State of California, share the responsibility of maintaining control and custody of the official records of the Board. I made or caused to be made a diligent search of the files and records concerning the license history of Hong Rak Park. I have determined that the official records prepared by Board employees, acting within the scope of their duties, show the dates and time periods listed herein for the issuance, expiration, periods of invalidity, and renewals of the license, as well as citations issued and periods of formal Board discipline:

VET No. 6707:

Hong Rak Park

First Issued:	July 24, 1978
Expiration:	May 31, 2020
Status:	Voluntarily Surrendered
Secondary Status:	None

Discipline:

On August 9, 2017, an Accusation was filed against Hong Rak Park (VET 6707), and Sunnymead Veterinary Clinic (HSP 3440) in case 1002460829.

On May 24, 2018, a Decision and Order became effective in the matter of the Accusation against Hong Rak Park and Sunnymead Veterinary Clinic in case 1002460829. The Order revoked Hong Rak Park's license (VET 6707) and Sunnymead Veterinary Clinic's permit (HSP 3440), stayed the revocations, and placed each on probation for four (4) years with terms and conditions.

On July 25, 2019, a Decision and Order became effective in the matter of the Stipulated Surrender of License and Order against Hong Rak Park (VET 6707) and Sunnymead Veterinary Clinic (HSP 3440). The effective date of the Decision as to Sunnymead Veterinary Clinic only was stayed until September 30, 2019, at which time the premises was to be sold or closed.

Given under my hand at Sacramento, California, this 9th day of September 2022.

orcement Manager

EXHIBIT 3

BEFORE THE VETERINARY MEDICAL BOARD DEPARTMENT OF CONSUMER AFFAIRS STATE OF CALIFORNIA

In the Matter of the Stipulated Surrender Pursuant to Condition 22 of Probation:

HONG RAK PARK Sunnymead Veterinary Clinic 24588 Sunnymead Blvd. Moreno Valley, CA 92553

Veterinarian License No. VET 6707,

and

SUNNYMEAD VETERINARY CLINIC, INC. 24588 Sunnymead Blvd., Moreno Valley, CA 92553

Veterinary Premises Permit No. HSP 3440

Respondents.

DECISION AND ORDER

The attached Stipulated Surrender of License and Order is hereby adopted by the

Veterinary Medical Board, Department of Consumer Affairs, as its Decision in this matter.

This Decision shall become effective on July 25, 2019

It is so ORDERED June 25, 2019

Inoladoval

FOR THE VETERINARY MEDICAL BOARD DEPARTMENT OF CONSUMER AFFAIRS

Case No. 4602019001023

1	XAVIER BECERRA		
2	Attorney General of California GREGORY J. SALUTE		
3	Supervising Deputy Attorney General DIONNE MOCHON Deputy Attorney General State Bar No. 203092 600 West Broadway, Suite 1800 San Diego, CA 92101 P.O. Box 85266 San Diego, CA 92186-5266 Telephone: (619) 738-9012 Facsimile: (619) 645-2061		
4			
5			
6			
7			
8	Attorneys for Complainant		
9	BEFORE THE		
10	VETERINARY MEDICAL BOARD DEPARTMENT OF CONSUMER AFFAIRS		
11	STATE OF C.	ALIFORNIA	
12		1	
13	In the Matter of the Stipulated Surrender Pursuant to Condition 22 of Probation:	Case No. 1002460829	
14	HONG RAK PARK	CTIDUL ATEN CUDDENDED OF	
15 16	Sunnymead Veterinary Clinic 24588 Sunnymead Blvd. Moreno Valley, CA 92553	LICENSE AND ORDER	
17	Veterinarian License No. VET 6707,		
18	and		
19	SUNNYMEAD VETERINARY CLINIC,		
20	24588 Sunnymead Blvd., Moreno Valley, CA 92553		
21	Veterinary Premises Permit No. HSP 3440		
22	Respondents.		
23		FED by and between the newtice to the charge	
24			
25 26	entitied proceedings that the following matters are		
20	PARTIES		
21	Reard (Board) She brought this action solaly in the	e Executive Officer of the veterinary Medical	
20	board (board). She brought this action solely in I	her ormeral capacity and is represented in this	

1	matter by Xavier Becerra, Attorney General of the State of California, by Dionne Mochon,		
2	Deputy Attorney General.		
3	Veterinary Medicine License		
4	2. Hong Rak Park (Respondent) is represented by attorney, Bonnie Lutz, whose address		
5	is 5 Hutton Centre Drive, Ste. 1000, Santa Ana, CA 92707.		
6	3. On or about July 24, 1978, the Board issued Veterinarian License No. DVM 6707 to		
7	Respondent. The Veterinarian License was in full force and effect at all times relevant to the		
8	charges and will expire on May 31, 2020, unless renewed.		
9	Premises Registration		
10	4. On or about September 30, 1981, the Veterinary Medical Board issued Premises		
11	Permit No. HSP 3440 to Respondent Hong Rak Park, as managing licensee of Sunnymead		
12	Veterinary Clinic. The Premises Permit was in full force and effect at all times relevant to the		
13	charges and will expire on May 31, 2020, unless renewed.		
14	JURISDICTION		
15	5. In a disciplinary action entitled <i>In the Matter of the Accusation Against Hong Rak</i>		
16	Park, DVM, and Sunnymead Veterinary Clinic, Case No. 1002460829, the Board issued a		
17	Decision effective May 23, 2018, in which Respondent's Veterinarian license and Premises		
18	Permit were revoked. However, the revocation as to each was stayed and Respondent's		
19	Veterinarian license and Premises Permit were placed on probation for a period of four (4) years		
20	with certain terms and conditions. Condition 22 permits the surrender of Respondent's		
21	Veterinary License and Premises Permit at any time Respondent is otherwise unable to satisfy the		
22	terms and conditions of probation. A copy of that Decision is attached as Exhibit A and is		
23	incorporated by reference.		
24	ADVISEMENT AND WAIVERS		
25	6. Respondent has carefully read, fully discussed with counsel, and understands the		
26	effects of this Stipulated Surrender of License and Order.		
27	7. Respondent is fully aware of his legal rights in this matter, including the right to a		
28	hearing on any charges and allegations of probation violations; the right to confront and cross-		
	2		
	Stimulated Summarian of License (Case Nie 4(02010001022)		

Stipulated Surrender of License (Ease) B (#0301 005023)

examine the witnesses against him; the right to present evidence and to testify on his own behalf;
 the right to the issuance of subpoenas to compel the attendance of witnesses and the production of
 documents; the right to reconsideration and court review of an adverse decision; and all other
 rights accorded by the California Administrative Procedure Act and other applicable laws.

8. Respondent voluntarily, knowingly, and intelligently waives and gives up each and every right set forth above.

CULPABILITY

8 9. For the purpose of resolving the terms of Respondent's probation without the expense
9 and uncertainty of further proceedings, Respondent agrees that the surrender of his Veterinary
10 License and Premises Permit constitute cause for discipline.

11 10. Respondent understands that by signing this stipulation he enables the Board to issue
12 an order accepting the surrender of his Veterinarian License and Premises Permit without further
13 process.

14

5

6

7

CONTINGENCY

11. This stipulation shall be subject to approval by the Board. Respondent understands 15 and agrees that counsel for Complainant and the staff of the Board may communicate directly 16 with the Board regarding this stipulation and surrender, without notice to or participation by 17 Respondent or his counsel. By signing the stipulation, Respondent understands and agrees that he 18 may not withdraw his agreement or seek to rescind the stipulation prior to the time the Board 19 considers and acts upon it. If the Board fails to adopt this stipulation as its Decision and Order, 20the Stipulated Surrender and Disciplinary Order shall be of no force or effect, except for this 21 paragraph, it shall be inadmissible in any legal action between the parties, and the Board shall not 22 be disqualified from further action by having considered this matter. 23

24

25

26

12. The parties understand and agree that Portable Document Format (PDF) and facsimile copies of this Stipulated Surrender of License and Order, including PDF and facsimile signatures thereto, shall have the same force and effect as the originals.

- 27
- 28

13. This Stipulated Surrender of License and Order is intended by the parties to be an integrated writing representing the complete, final, and exclusive embodiment of their agreement.

It supersedes any and all prior or contemporaneous agreements, understandings, discussions, 1 negotiations, and commitments (written or oral). This Stipulated Surrender of License and Order 2 may not be altered, amended, modified, supplemented, or otherwise changed except by a writing 3 executed by an authorized representative of each of the parties. 4 In consideration of the foregoing admissions and stipulations, the parties agree that 5 14. the Board may, without further notice or formal proceeding, issue and enter the following Order: 6 ORDER 7 IT IS HEREBY ORDERED that Veterinarian License No.VET 6707 and managing 8 licensee of a premises certificate registration issued to Respondent Hong Rak Park, and Premises 9 Permit Number HSP 3440 issued to Sunnymead Veterinary Clinic, Hong Rak Park DVM, 10 managing licensee is surrendered and accepted by the Board. The effective date of the Decision 11 as to Respondent Sunnymead only, shall be stayed until September 30, 2019, at which time the 12 premises shall be sold or closed. 13 1. The surrender of Respondent's Veterinary License and Premises Permit and the 14 acceptance of the surrendered license and permit by the Board shall constitute the imposition of 15 discipline against Respondent. This stipulation constitutes a record of the discipline and shall 16 become a part of Respondent's license history with the Board. 17 Respondent shall lose all rights and privileges as a Veterinarian and Managing 2. 18 Licensee of a premises certificate registration in California as of the effective date of the Board's 19 Decision and Order. 20Respondent shall cause to be delivered to the Board his pocket license and, if one was 3. 21 issued, his wall certificate on or before the effective date of the Decision and Order. 22 4. If Respondent ever files an application for licensure or a petition for reinstatement in 23 24 the State of California, the Board shall treat it as a petition for reinstatement. Respondent must comply with all the laws, regulations and procedures for reinstatement of a revoked or 25 surrendered license in effect at the time the petition is filed. 26 The Board may, upon a showing of good cause, allow Respondent to petition the 5. 27 Board for reinstatement after three years. 28

ACCEPTANCE 1 2 I have carefully read the above Stipulated Surrender of License and Order and have fully discussed it with my attorney, Bonnie Lutz. I understand the stipulation and the effect it will have 3 on my Veterinarian License and Premises Permit. I enter into this Stipulated Surrender of 4 License and Order voluntarily, knowingly, and intelligently, and agree to be bound by the 5 Decision and Order of the Veterinary Medical Board. 6 7 6/3//19 DATED: 8 RAK PARK 9 As an Individual and as the Managing Licensee of Sunnymead Veterinary Clinic 10 Respondents 11 I have read and fully discussed with Respondent Hong Rak Park the terms and conditions 12 and other matters contained in this Stipulated Surrender of License and Order. I approve its form 13 and content. 14 DATED: 15 BONNIE LUTZ, ESQ. Attorney for Respondent 16 17 18 ENDORSEMENT The foregoing Stipulated Surrender of License and Order is hereby respectfully submitted 19 for consideration by the Veterinary Medical Board of the Department of Consumer Affairs. 20 21 Dated: 5/31/19 Respectfully submitted, 22 XAVIER BECERRA Attorney General of California 23 GREGORY J. SALUTE Supervising Deputy Attorney General 24 25 DIONNE MOCHON 26 **Deputy Attorney General** Attorneys for Complainant 27 28 SD2019800616/82199554.docx 5 Stipulated Surrender of License (Case No. 4602019001023)

EXHIBIT 3 - 006

Exhibit A

Decision and Order: In the Matter of the Accusation Against Hong Rak Park, DVM, and Sunnymead Veterinary Clinic, Case No. 1002460829

BEFORE THE VETERINARY MEDICAL BOARD DEPARTMENT OF CONSUMER AFFAIRS STATE OF CALIFORNIA

Case No. 1002460829

In the Matter of the Accusation Against:

HONG RAK PARK, DVM 24588 Sunnymead Blvd. Moreno Valley, CA 92553-3761

Veterinarian License No. VET 6707

and

SUNNYMEAD VETERINARY CLINIC 24588 Sunnymead Blvd. Moreno Valley, CA 92553-3761

Premises Permit No. HSP 3440

Respondent.

DECISION AND ORDER

The attached Stipulated Settlement and Disciplinary Order is hereby adopted by the

Veterinary Medical Board, Department of Consumer Affairs, as its Decision in this matter.

This Decision shall become effective on MAY 2 4 2018

It is so ORDERED APR 2 4 2018

FOR THE VETERINARY MEDICAL BOARD DEPARTMENT OF CONSUMER AFFAIRS

		-
1	XAVIER BECERRA Attorney General of California	
2	Supervising Deputy Attorney General MARICHELLE S. TAHIMIC	
1	Deputy Attorney General State Bar No. 147202	
5	600 West Broadway, Suite 1800 San Diego, CA 92101	
6	P.O. Box 85266 San Diego, CA 92186-5266	
7	Telephone: (619) 738-9435 Facsimile: (619) 645-2061	
8	Attorneys for Complainant	
9	BEFORI VETERINARY MI	E THE EDICAL BOARD
10	DEPARTMENT OF CO STATE OF CA	DNSUMER AFFAIRS ALIFORNIA
11	In the Matter of the Accusation Against:	
12	HONG RAK PARK, DVM	Case No. 1002460829
13	24588 Sunnymead Blvd. Moreno Valley, CA 92553-3761	STIPULATED SETTLEMENT AND
14	Veterinarian License No. VET 6707	DISCIPLINARY ORDER
15	and	
16	SUNNYMEAD VETERINARY CLINIC	
17	Moreno Valley, CA 92553-3761	
18	Premises Permit No. HSP 3440	
19	Respondents.	
20·		· · ·
-21	IT IS HEREBY STIPULATED AND AGRI	EED by and between the parties to the above-
22	entitled proceedings that the following matters are true:	
23	PARTIES	
24	1. Annemarie Del Mugnaio (Complainant) is the Executive Officer of the Veterinary	
25	Medical Board (Board). She brought this action solely in her official capacity and is represented	
26	in this matter by Xavier Becerra, Attorney General of the State of California, by Marichelle S.	
27	Tahimic, Deputy Attorney General.	
28	///	
	·1	
		STIPULATED SETTLEMENT (1002460829)

Respondents Hong Rak Park and Sunnymead Veterinary Clinic (Respondents) are
 represented in this proceeding by attorney Bonnie Lutz, Klinedinst, PC, whose address is: 5
 Hutton Centre Drive, Ste. 1000, Santa Ana, CA 92707.

3. On or about July 24, 1978, the Board issued Veterinarian License No. VET 6707 to
Hong Rak Park (Respondent Park). The Veterinarian License was in full force and effect at all
times relevant to the charges brought in Accusation No. 1002460829, and will expire on May 31,
2018, unless renewed.

4. On or about September 30, 1981, the Board issued Premises Permit No. HSP 3440 to
Sunnymead Veterinary Clinic (Respondent Clinic). Respondent Park is, and has been, the
managing licensee of Sunnymead Veterinary Clinic since September 30, 1981. The Premises
Permit was in full force and effect at all times relevant to the charges brought in Accusation No.
1002460829, and will expire on May 31, 2018, unless renewed.

JURISDICTION

Accusation No. 1002460829 was filed before the Board, and is currently pending
against Respondent. The Accusation and all other statutorily required documents were properly
served on Respondent on August 10, 2017. Respondents timely filed their Notice of Defense
contesting the Accusation.

18 6. A copy of Accusation No. 1002460829 is attached as exhibit A and incorporated
19 herein by reference.

20

13

ADVISEMENT AND WAIVERS

7. Respondents have carefully read, fully discussed with counsel, and understands the
charges and allegations in Accusation No. 1002460829. Respondents have also carefully read,
fully discussed with counsel, and understands the effects of this Stipulated Settlement and
Disciplinary Order.

8. Respondents are fully aware of their legal rights in this matter, including the right to a
hearing on the charges and allegations in the Accusation; the right to confront and cross-examine
the witnesses against him; the right to present evidence and to testify on their own behalf; the
right to the issuance of subpoenas to compel the attendance of witnesses and the production of

documents; the right to reconsideration and court review of an adverse decision; and all other rights accorded by the California Administrative Procedure Act and other applicable laws.

1

2

3

4

5

6

7

8

9

10

11

9. Respondents voluntarily, knowingly, and intelligently waives and gives up each and every right set forth above.

CULPABILITY

10. Respondents admit the truth of each and every charge and allegation in Accusation No. 1002460829.

11. Respondents agree that their Veterinarian License and Premises Permit are subject to discipline and they agree to be bound by the Board's probationary terms as set forth in the Disciplinary Order below.

<u>CONTINGENCY</u>

This stipulation shall be subject to approval by the Veterinary Medical Board. 12. 12 Respondents understand and agree that counsel for Complainant and the staff of the Veterinary 13 Medical Board may communicate directly with the Board regarding this stipulation and 14 settlement, without notice to or participation by Respondents or their counsel. By signing the 15 stipulation, Respondents understand and agree that they may not withdraw their agreement or 16 seek to rescind the stipulation prior to the time the Board considers and acts upon it. If the Board 17 fails to adopt this stipulation as its Decision and Order, the Stipulated Settlement and Disciplinary 18 Order shall be of no force or effect, except for this paragraph, it shall be inadmissible in any legal 19 action between the parties, and the Board shall not be disqualified from further action by having 20 considered this matter. 21

13. The parties understand and agree that Portable Document Format (PDF) and facsimile
copies of this Stipulated Settlement and Disciplinary Order, including PDF and facsimile
signatures thereto, shall have the same force and effect as the originals.

14. This Stipulated Settlement and Disciplinary Order is intended by the parties to be an
integrated writing representing the complete, final, and exclusive embodiment of their agreement.
It supersedes any and all prior or contemporaneous agreements, understandings, discussions,
negotiations, and commitments (written or oral). This Stipulated Settlement and Disciplinary

Order may not be altered, amended, modified, supplemented, or otherwise changed except by a 1 writing executed by an authorized representative of each of the parties. 2

15. In consideration of the foregoing admissions and stipulations, the parties agree that 3 the Board may, without further notice or formal proceeding, issue and enter the following 4 Disciplinary Order: 5

DISCIPLINARY ORDER

IT IS HEREBY ORDERED that Veterinarian License No. VET 6707 issued to Respondent 7 Hong Rak Park and Premises Permit No. HSP 3440 issued to Respondent Sunnymead Veterinary 8 Clinic are revoked. However, the revocations are stayed and Respondents are each placed on 9 probation for four (4) years on the following terms and conditions. 10

11

6

Obey All Laws, 1.

Respondents shall obey all federal and state laws and regulations substantially related to the 12 practice of veterinary medicine. Further, within thirty (30) days of any arrest or conviction. 13 Respondents shall report to the Board and provide proof of compliance with the terms and 14 conditions of the court order including, but not limited to, probation and restitution requirements. 15

16

2. Quarterly Reports and Interviews

Respondents shall report quarterly to the Board or its designee, under penalty of perjury, on · 17 forms provided by the Board, stating whether there has been compliance with all terms and 18 conditions of probation. In addition, the Board at its discretion may request additional in-person 19 reports of the probationary terms and conditions. If the final written quarterly report is not made 20 as directed, the period of probation shall be extended until such time as the final report is received 21 by the Board. Respondents shall make available all patient records, hospital records, books, logs, 22 and other documents to the Board, upon request. 23

24

28

3. Cooperation with Probation Surveillance

Respondents shall comply with the Board's probation surveillance program. All costs for 25 probation monitoring shall be borne by Respondents. Probation monitoring costs are set at a rate 26 of \$100 per month for the duration of the probation. Respondents shall notify the Board of any 27 change of name or address or address of record within thirty (30) days of the change,

Respondents shall notify the Board immediately in writing if Respondents leave California to reside or practice in another state. Respondents shall notify the Board immediately upon return to California.

4. No Preceptorships or Supervision of Interns

Respondent Park shall not supervise a registered intern and shall not perform any of the duties of a preceptor.

5. Notice to Employers

Respondents shall notify all present and prospective employers of the decision in this case
and the terms, conditions, and restrictions imposed on Respondents by the decision in this case.
Within thirty (30) days of the effective date of this decision and within fifteen (15) days of
Respondents undertaking new employment, Respondents shall cause his or her employer to report
to the Board in writing, acknowledging the employer has read the Accusation and decision in this
case and understands Respondents' terms and conditions of probation. Relief veterinarians shall
notify employers immediately.

15

1

2

3

4

5

6

7

6. Notice to Employees

Respondents shall, upon or before the effective date of this decision, post or circulate a notice which actually recites the offenses for which Respondents have been disciplined and the terms and conditions of probation, to all registered veterinary employees, and to any preceptor, intern or extern involved in his or her veterinary practice. Within fifteen (15) days of the effective date of this decision, Respondents shall cause his/its employees to report to the Board in writing, acknowledging the employees have read the Accusation and decision in the case and understand Respondents' terms and conditions of probation.

23 24 25

26

27

28

7. Owners and Officers (Corporations or Partnerships): Knowledge of the Law Respondents shall provide, within thirty (30) days after the effective date of the decision, signed and dated statements from the owners, officers, or any owner or holder of ten percent (10%) or more of the interest in Respondent Clinic's stock, stating said individuals have read and are familiar with federal and state laws and regulations governing the practice of veterinary medicine.

8. Tolling of Probation

If Respondent Park resides out of state upon or after effective date of the decision, he must comply with the following conditions only: obey all laws, quarterly reports and interviews, tolling of probation, continuing education and cost recovery. If Respondent Park returns to California, Respondents must comply or be subject to all probationary conditions for the period of probation.

Respondents, during probation, shall engage in the practice of veterinary medicine in
California for a minimum of 24 hours per week or as determined by the Board. Should
Respondents fail to engage in the practice of veterinary medicine in California as set forth above,
the time outside of the practice shall not apply to reduction of the probationary terms.

10

1

2

3

4

5

9. Violation of Probation

If Respondents violate probation in any respect, the Board, after giving Respondents notice and the opportunity to be heard, may revoke probation and carry out the disciplinary order that was stayed. If an accusation or petition to revoke probation is filed against Respondents during probation, or if the Attorney General's office has been requested to prepare any disciplinary action against Respondents' license and/or permit, the Board shall have continuing jurisdiction until the matter is final, and the period of probation shall be extended until the matter is final.

17

10. Completion of Probation

All costs for probation monitoring and/or mandatory premises inspections shall be borne by
Respondents. Failure to pay all costs due shall result in an extension of probation until the matter
is resolved and costs paid. Upon successful completion of probation and all payment of all fees
due, Respondents' license and premises permit will be fully restored.

22

23

24

25

26

11. Cost Recovery and Payment of Fines

Pursuant to Section 125.3 of the California Business and Professions Code, within thirty (30) days of the effective date of this decision, Respondents shall pay to the Board its enforcement costs including investigation and prosecution in the amount of \$3,337.50, plus fines in the amount of \$2,500 (pursuant to Condition 20 below).

- 27 || ///
- 28 ///

12. Suspension – Individual License

As part of probation, Respondent Park (VET 6707) is suspended from the practice of veterinary medicine for seven (7) days beginning the effective date of this decision. During said suspension, Respondent Park shall not enter any veterinary hospital which is registered by the Board. Additionally, Respondent Park shall not manage, administer, or be a consultant to any veterinary hospital or veterinarian during the period of actual suspension and shall not engage in any veterinary-related service or activity.

13. Suspension – Premises

As part of probation, Premises License Number HSP 3440, issued to Respondent
Sunnymead Veterinary Clinic is suspended for seven (3) days, beginning the effective date of this
decision. During said period of suspension, said premises may not be used by any party for any
act constituting the practice of veterinary medicine, surgery, dentistry, and/or the various
branches thereof.

14

8

1

14. Posted Notice of Suspension

Respondents shall post a notice of the Board's Order of Suspension, in a place clearly
visible to the public. The notice, provided by the Board, shall remain posted during the entire
period of actual suspension.

18

19

15. Limitation on Practice/Inspections

During probation, Respondent Park is prohibited from the following:

1. Practicing veterinary medicine from a location or mobile veterinary practice which does
not have a current premises permit issued by the Board; and,

22 2. If Respondent is the owner or managing licensee of a veterinary practice the location or 23 mobile veterinary practice must not only have a current premises permit issued by the Board, but 24 must also be subject to inspections by a Board representative to determine whether the location or 25 veterinary practice meets minimum standards for a veterinary practice. The inspections will be 26 conducted on an announced or unannounced basis and shall be held_during normal business 27 hours. The Board reserves the right to conduct these inspections on at least a quarterly basis 28 during probation. Respondent shall pay the Board for the cost of each inspection, which is \$500.

16. Supervised Practice

Respondent Park shall practice only under the supervision of a veterinarian approved by the
Board. The supervision directed may be continuous supervision, substantial supervision, partial
supervision, or supervision by daily review, as deemed necessary by the Board. All costs involved
with practice supervision shall be borne by Respondent.

Each supervisor shall have been licensed in California for at least five (5) years and not 6 have ever been subject to any disciplinary action by the Board. The supervisor shall be 7 independent, with no prior business or personal relationship with Respondent and the supervisor 8 shall not be in a familial relationship with or be an employee, partner, or associate of Respondent. 9 Within thirty (30) days of the effective date of the decision, Respondent shall have his 10 supervisor submit a report to the Board in writing stating the supervisor has read the decision in 11 Case No. 1002460829. Should Respondent change employment, Respondent shall have his new 12 supervisor, within fifteen (15) days after employment commences, submit a report to the Board in 13 writing stating the supervisor has read the decision in Case No. 1002460829. 14

Respondent's supervisor shall, on a basis to be determined by the Board, review and
evaluate all or a designated portion of patient records of those patients for whom Respondent
provides treatment or consultation during the period of supervised practice. The supervisor shall
review these records to assess:



22

1

1) the medical necessity and appropriateness of Respondent's treatment;

20 2) Respondent's compliance with community standards of practice in the diagnosis and
21 treatment of animal patients;

3) Respondent's maintenance of necessary and appropriate treatment;

4) Respondent's maintenance of necessary and appropriate records and chart entries; and
5) Respondent's compliance with existing statutes and regulations governing the practice of
veterinary medicine.

Respondent's supervisor shall file monthly reports with the Board. These reports shall be in a form designated by the Board and shall include a narrative section where the supervisor
 provides his or her conclusions and opinions concerning the issues described above and the basis

for his or her conclusions and opinions. Additionally, the supervisor shall maintain and submit with his or her monthly reports a log designating the patient charts reviewed, the date(s) of service reviewed, and the date upon which the review occurred. If the supervisor terminates or is otherwise no longer available, Respondent shall not practice until a new supervisor has been approved by the Board.

If respondent is an employee rather a veterinary hospital owner, the supervisor shall additionally notify the Board of the dates and locations of all employment of respondent, during each month covered by his/her report.

17. No Ownership

With the exception of Sunnymead Veterinary Clinic (Premises Permit HSP 3440),
Respondent Park shall not have any legal or beneficial interest in any business, firm, partnership,
or corporation currently or hereinafter licensed or registered by the Board and shall not own any
veterinary hospital.

14

1

2

3

4

5

6

7

8

9

18. No Management or Administration

With the exception of Sunnymead Veterinary Clinic (Premises Permit HSP 3440),
Respondent Park shall not manage or be the administrator of any veterinary hospital.

17

19. Continuing Education

Within sixty (60) days of the effective date of this decision, and on an annual basis thereafter, Respondent Park shall submit to the Board for its prior approval, educational programs or courses related to: (1) recordkeeping, and (2) client communication. Each educational program or course shall not be less than sixteen hours per year, for each year of probation. Upon successful completion of the programs or courses, Respondent shall provide proof to the Board. These programs or courses shall be in addition to the Continuing Education required of all licensees. All costs shall be borne by Respondent.

20. Fine

Respondents shall pay to the Board a fine in the amount of \$2,500.00 pursuant to Business and Professions Code sections 4875 and 4883.

9

28

///

25

26

21. Ethics Training

Respondent Park shall submit to the Board for its prior approval, an ethios training course
for a minimum of twenty (20) hours per year for the first two (2) years of the probationary period.
Upon successful completion of the course, Respondent Park shall provide proof to the Board, All:
costs shall be borne by Respondent,

6

17

23

24

25

26

27 28

1

22. License Surrender While ou Probation/Suspension

Following the effective date of this Decision, should Respondent Park cease to practice 7 veterinary medicine due to retirement or health issues, or be otherwise unable to satisfy the terms 8 and conditions of probation, Respondent Park may tender his license to practice veterinary 9 medicine and premises permit to the Board for surrender. The Board or its designee has the 10 discretion to grant the request for surrender or to take any other action it deems appropriate and 11 reasonable. Upon formal acceptance of the license and permit surrender, Respondents will no 12 longer be subject to the terms and conditions of probation. The surrender constitutes a record of 13 discipline and shall become a part of the Respondents' license history with the Board, Respondent 14 must relinquish his veterinary license and premises permit to the Board within ten (10) days of 15 receiving notification from the Board that the surrender has been accepted. 16

ACCEPTANCE

18 I have carefully read the above Stipulated Settlement and Disciplinary Order and have fully 19 discussed it with my attorney, Bonnie Lutz. I understand the stipulation and the effect it will have 20 on my Veterinarian License and Premises Permit. I enter into this Stipulated Settlement and 21 Disciplinary Order voluntarily, knowingly, and intelligently, and agree to be bound by the 22 Decision and Order of the Veterinary Medical Board.

DATED:

HONG RAK PARK Respondent Individually and as the authorized representative of Sunnymead Veterinary Clinic

10

STIFULATED SETTLEMENT (1002460829)

I have read and fully discussed with Respondent Hong Rak Park the terms and conditions and other matters contained in the above Stipulated Settlement and Disciplinary Order. 1 approve its form and content.

DATED:

1

2

3

4

5

б

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

2\$

26

27

28

VIE LUTZ BON

Attorney for Respondent

ENDORSEMENT

11

The foregoing Stipulated Settlement and Disciplinary Order is hereby respectfully submitted for consideration by the Veterinary Medical Board.

Dated: Feb. 15, 2018

Respectfully submitted, .

XAVIER BECERRA Attorney General of California ANTOINETTE B. CINCOTTA Supervising Deputy Attorney General

MARICHELLE S TAMMIC Deputy Attorney General Attorneys for Complainant

SD2017704742/33175353.doc

STIPULATED SETTLEMENT (1002460829)

L.

Exhibit A

Accusation No. 1002460829

EXHIBIT 3 - 020

	· · · · · · · · · · · · · · · · · · ·	· .	
		FILED - STATE OF CALIFORNIA	
':		Sacraménto, CA:onAIG_0 3 2017	
1		By: felen Park	
1	Attorney General of California		
2	ANTOINETTE B. CINCOTTA Supervising Deputy Attorney General		
3	MARICHELLE S. TAHIMIC		
4	Deputy Attorney General State Bar No. 147392		
5	600 West Broadway, Suite 1800		
ر م	P.O. Box 85266		
6	San Diego, CA 92186-5266 Telephone: (619) 738-9435		
7	Facsimile: (619) 645-2061		
8	Allorneys for Complainant		
9	BEFOF VETERINARY M	THE THE FOARD	
10	DEPARTMENT OF C	ONSUMER AFFAIRS	
11	STATE OF C	ALIFORNIA	
1.1	In the Matter of the Accusation Against:	Case No. 1002460829	
12	HONG RAK PARK, DVM		
13	Moreno Valley, CA 92553-3761		
14	Veterinarian License No. VET 6707	ACCUSATION	
15	and		
16	SUNNYMEAD VETERINARY CLINIC		
17	24588 Sunnymead Blvd. Moreno Valley, CA 92553-3761		
18	Premises Permit No. HSP 3440		
19	Respondents.		
20			
21	Complainant alleges.		
~	companiant anogos.		
2.2	PART	IES	
23	1. Annemarie Del Mugnaio (Complainant) brings this Accusation solely in her official		
24 ·	capacity as the Executive Officer of the Veterinary Medical Board (Board), Department of		
25	Consumer Affairs.		
26	2. On or about July 24, 1978, the Board issued Veterinarian License Number VET 6707		
27	to Hong Rak Park, DVM (Respondent). The Vete	o Hong Rak Park, DVM (Respondent). The Veterinarian License was in full force and offerst at	
28	all times relevant to the charges brought herein and	Il times relevant to the charges brought herein and will evalue on May 21, 0010 and effect at	
		- mai expire on may 51, 2016, unless renewed.	
•	1		
11		(HONG RAK PARK) ACCUSATION	

3. On or about September 30, 1981, the Board issued Premises Permit Number HSP
 3440 to Sunnymead Veterinary Clinic. Hong Rak Park, DVM, has been the managing licensee of
 Sunnymead Veterinary Clinic since September 30, 1981. The Premises Permit was in full force
 and effect at all times relevant to the charges brought herein and will expire on May 31, 2018,
 unless renewed.

1. 2. 1

JURISDICTION

7 4. This Accusation is brought before the Board under the authority of the following
8 laws. All section references are to the Business and Professions Code (Code) unless otherwise
9 indicated.

Section 4875 of the Code provides, in pertinent part, that the Board may revoke or
 suspend the license of any person to practice veterinary medicine, or any branch thereof, in this
 state for any causes provided in the Veterinary Medicine Practice Act (Bus. & Prof. Code, '4800,
 et seq.). In addition, the Board has the authority to assess a fine not in excess of \$5,000 against a
 licensee for any of the causes specified in section 4883 of that Code. Such fine may be assessed
 in lieu of, or in addition to, a suspension or revocation.

6. Section 4853.6 of the Code provides, in pertinent part, that the Board shall withhold,
suspend or revoke registration of veterinary premises when the license of the licensee manager to
practice veterinary medicine is revoked or suspended.

Section 118(b) of the Code provides, in pertinent part, that the expiration of a license
 shall not deprive a board of jurisdiction to proceed with a disciplinary action during the period⁻
 within which the license may be renewed, restored, reissued or reinstated. Under Code section
 4843.5, the Board may renew an expired license at any time within five years after the expiration.

STATUTORY AND REGULATORY PROVISIONS

Section 4883 of the Code states:

б

23

24

25

26

27

28

8.

The board may deny, revoke, or suspend a license or assess a fine as provided in Section 4875 for any of the following:

(g) Unprofessional conduct, that includes, but is not limited to, the following:

2

(HONG RAK PARK) ACCUSATION

*** *

1

2

3

4.

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

25

26

27

28

(i) Fraud, deception, negligence, or incompetence in the practice of veterinary medicine.

(o) Violation, or the assisting or abetting violation, of any regulations adopted by the board pursuant to this chapter.

9. Section 4855 of the Code states:

A veterinarian subject to the provisions of this chapter [the Veterinary Medicine Practice Act] shall, as required by regulation of the board, keep a written record of all animals receiving veterinary services, and provide a summary of that record to the owner of animals receiving veterinary services, when requested. The minimum amount of information which shall be included in written records and summaries shall be established by the board. The minimum duration of time for which a licensed premise shall retain the written record or a complete copy of the written record shall be determined by the board.

10. Title 16, California Code of Regulations (CCR), section 2030.5 states:

(a) A Licensee Manager is the California licensed veterinarian named as the Licensee Manager on a facility's premises permit.

(b) The Licensee Manager is responsible for ensuring that the premises for which he/she is manager complies with the requirements in sections 4853, 4854, 4855 and 4856 of the Business and Professions Code, Division 2, Chapter 11, Article 3. The Licensee Manager is responsible for ensuring that the physical and operational components of a premises meet the minimum standards of practice as set forth in sections 2030 through 2032.5 of the California Code of Regulations, Title 16, Division 20, Article 4.

(c) The Licensee Manager is responsible for ensuring that no unlicensed activity is occurring within the premises or in any location where any function of veterinary medicine, veterinary surgery or veterinary dentistry is being conducted off the premises under the auspices of this premises license.

(d) The Licensee Manager shall maintain whatever physical presence is reasonable within the facility to ensure that the requirements in (a) - (c) are met.

(e) Each licensed veterinarian shall be responsible for their individual violations of the Veterinary Medicine Practice Act or any regulation adopted thereunder.

24

11. Title 16, CCR, section 2032 states, "The delivery of veterinary care shall be provided

in a competent and humane manner. All aspects of veterinary medicine shall be performed in a

manner consistent with current veterinary medical practice in this state."

|| ///

(HONG RAK PARK) ACCUSATION

Title 16, CCR, section 2032.05 states, "When treating a patient, a veterinarian shall 12. use appropriate and humane care to minimize pain and distress before, during and after 2 performing any procedure(s)," 3 Title 16, CCR, section 2032.1, states: 4 13. 5 (a) Except where the patient is a wild animal or its owner is unknown, it shall constitute unprofessional conduct for a veterinarian to administer or prescribe a б drug, medicine, appliance, or application or treatment of whatever nature for the prevention, cure, or relief of a wound, fracture or bodily injury or disease of an 7 animal without having first established a veterinarian-client-patient relationship with the animal patient or patients and the client. It shall also constitute unprofessional conduct for a veterinarian to prescribe, dispense, or furnish either a veterinary drug, as defined by Section 1747.1, Title 16, California Code of 8 9 Regulations, or a dangerous drug, as defined by Section 4022 of the code, without having first established a veterinarian-client-patient relationship with the animal 10 patient or patients and the client. (b) A veterinarian-client-patient relationship shall exist when all of the following 11 12 (1) The veterinarian has assumed responsibility for making medical 13 judgments regarding the health of the animal(s) and the need for medical treatment, has discussed with the client a course of treatment and if applicable 14 has instructed the client as to the appropriate directions for administering the drugs or treatments. 15 (2) The veterinarian has sufficient knowledge of the animal(s) to initiate at 16 least a general or preliminary diagnosis of the medical condition of the animal(s). This means that the veterinarian has recently seen and is personally acquainted 17 with the care of the animal(s) by virtue of an examination of the animal or by medically appropriate and timely visits to the premises where the animals are 18 kept, and 19 20 Title 16, CCR section 2032.3 states: 14. 21 (a) Every veterinarian performing any act requiring a license pursuant to the provisions of Chapter 11, Division 2, of the code, upon any animal or group of. 22animals shall prepare a legible, written or computer generated record concerning the animal or animals which shall contain the following information: · 23 (1) Name or initials of the veterinarian responsible for entries. 24 (2) Name, address and phone number of the client. 25 (3) Name or identity of the animal, herd or flock. 26 (4)-Except-for herds or flocks, age, sex, breed, species, and color of the 27 animal 28 (5) Dates (beginning and ending) of custody of the animal, if applicable. (HONG RAK PARK) ACCUSATION

(6) A history or pertinent information as it pertains to each animal, herd, or flock's medical status.

(7) Data, including that obtained by instrumentation, from the physical examination.

(8) Treatment and intended treatment plan, including medications, dosages and frequency of use.

(9) Records for surgical procedures shall include a description of the procedure, the name of the surgeon, the type of sedative/anesthetic agents used, their route of administration, and their strength if available in more than one strength.

(10) Diagnosis or tentative diagnosis at the beginning of custody of animal.

(11) If relevant, a prognosis of the animal's condition.

(12) All medications and treatments prescribed and dispensed, including strength, dosage, quantity, and frequency.

(13) Daily progress, if relevant, and disposition of the case.

COST RECOVERY

14 15. Section 125.3 of the Code provides, in pertinent part, that the Board may request the 15 administrative law judge to direct a licentiate found to have committed a violation or violations of 16 the licensing act to pay a sum not to exceed the reasonable costs of the investigation and 17 enforcement of the case, with failure of the licentiate to comply subjecting the license to not being 18 renewed or reinstated. If a case settles, recovery of investigation and enforcement costs may be 19 included in a stipulated settlement.

FACTS

CASE NO. NV 2016 350 - "JASMINE"

16. On or about Friday, September 25, 2015, A.M. brought her spayed, 19-month old Siamese cat named "Jasmine" to Respondent at Sunnymead Veterinary Clinic (Clinic) to have only her front paws declawed. Jasmine was hospitalized overnight and picked up on September 26, 2015. At discharge on September 26, 2015, a staff person advised A.M. that Jasmine's two front paws had been declawed and gave instructions about the administration of medicine. A.M. was not given any other instructions. A.M. was told that it was not necessary to bring Jasmine

5

28

1

.2

3

4

5

6

7

8

9

10

11

12

13

20

21

22

Ž3

24

25

26

27

(HONG RAK PARK) ACCUSATION

back for a follow up appointment. Jasmine was brought out to A.M. in a pet carrier. Jasmine
 appeared to be in pain and was groggy.

17. Later, on the evening of September 26, 2015, A.M. noticed that Jasmine's stomach 3 had been shaved and there were sutures over the tattoo that indicated Jasmine had already been 4 spayed. On Monday, September 28, 2015, A.M. contacted the veterinary clinic to inquire why 5 Jasmine had stitches when she was brought in only to have her two front paws declawed. After 6 being placed on hold several times and speaking with different staff members, A.M. was advised 7 there had been a mix-up and Jasmine was mistaken for another cat that had been brought in for a 8 spay and a declaw. Respondent performed the procedures. A.M. was refunded the \$85 she paid 9 to declaw Jasmine. A.M. was not advised of the error in attempting to spay Jasmine at the time it 10 was discovered nor upon discharge. AM. was left to discover the attempted spay on her own. 11

12 18. Jasmine's veterinary record indicated she was brought in for declaw surgery. There
13 was no description of the declaw surgery. The anesthesia used was

Ketamine/Acepromazine/Atropine. Ketamine is a dissociative, anesthetic drug that has some
analgesic effects. It provides short term, inadequate levels of analgesia unless used in
conjunction with an opiod in a constant rate infusion. Acepromazine and Atropine provide no
analgesia.

18 19. The "Surgical Notes" described the spay: a midline incision was made, the uterus
19 was not found, the incision was closed and nylon sutures placed. The record did not mention
20 discharge instructions regarding suture removal and bandage removal.

20. The record identified the medications to be given were "amoxillin (50 mg/ml) Give 1
ml bid for 14 days" and "Tor/Val 1 ml bid for 14 days." No route of administration was noted.
Furthermore, the dosage/strength was not noted for Torbugesic/valium. A.M.'s invoice was for
amoxicillin oral 50 mg/30 ml, which is equivalent to 1.6 mg/ml. However, 1 ml amoxicillin
50 mg/ml is not equivalent to amoxicillin 1.6 mg/ml. Torbugesic is mainly used for mild sedation
and provides inadequate pain relief for a declaw or spay.

21. The veterinary records did not document Jasmine's overnight hospitalization. There was no record of a post-surgical examination on September 26, 2017, nor any treatment

27

28

б

(HONG RAK PARK) ACCUSATION
1	performed on September 26, 2015. The invoice given to A.M. stated services were provided on
2	September 26, 2015. There was a notation in the transcribed records dated September 25, 2015,
3	of client communication regarding the accidental spay and refund. This information was absent
4	in the handwritten patient charts.
5	FIRST CAUSE FOR DISCIPLINE
6	(Recordkeeping Violations)
7	22. Respondent is subject to disciplinary action under Code section 4883, subdivision (o),
8	in conjunction with title 16, CCR, section 2032.3, subdivision (a), for violations regarding the
9	veterinary records of Jasmine, as set forth in paragraphs 16-21 above and incorporated by this
10	reference, in that:
11	a. the surgery report was inadequate regarding the declawing surgery and follow up
12	instructions;
13	b. client communications were improperly dated;
14	c. notations regarding Torbugesic/valium and amoxicillin 50 mg/30 ml were inadequate;
15	and,
16	d. the record lacked any information regarding hospitalization.
17	SECOND CAUSE FOR DISCIPLINE
18	(Failure to Exercise Minimum Standard of Practice)
19	23. Respondent is subject to disciplinary action under Code section 4883, subdivision (0),
20	in conjunction with title 16, CCR, section 2032, for failing to perform veterinary services for
21	Jasmine in a manner consistent with current veterinary medical practice, as set forth in paragraphs
22	16-21 above and incorporated by this reference, in that:
23	a. Jasmine's veterinary record was incomplete;
24	b. Respondent failed to adequately communicate instructions regarding re-checking
25	Jasmine and removal of sutures and bandages;
26	c. communication with A.M. was improperly dated;
27	d. surgical discharge instructions were inadequate; and,
28	e. post-surgical hospitalization notes were missing.
	7

١.

į

(HONG RAK PARK) ACCUSATION

EXHIBIT 3 - 027

THIRD CAUSE FOR DISCIPLINE

(Failure to Use Humane Treatment)

24. Respondent is subject to disciplinary action under Code section 4883, subdivision (o),
in conjunction with title 16, CCR, section 2032.05, subdivision (a), for failure to use appropriate
and humane care to minimize pain and distress before, during and after Jasmine's surgery, as set
forth in paragraphs 16-21 above and incorporated by this reference,

FOURTH CAUSE FOR DISCIPLINE

(Unprofessional Conduct)

9 25. Respondent is subject to disciplinary action under Code section 4883, subdivision (g),
10 for unprofessional conduct in providing veterinary services to Jasmine, as set forth in paragraphs
11 16-21 above and incorporated by this reference, in that:

a. Respondent failed to communicate with A.M. about the erroneous surgery performed;
b. Respondent failed to use appropriate and humane care to minimize pain and distress
before, during and after Jasmine's surgery;

c. Respondent failed to maintain a complete veterinary record;

16 d. Respondent failed to adequately communicate instructions regarding re-checking
17 Jasmine and removal of sutures and bandages;

e. communication with A.M. was improperly dated;

f. surgical discharge instructions were inadequate; and,

g. post-surgical hospitalization notes were missing.

CASE NO. SV 2016 355 - "MUNCHKIN"

22 26. On or about November 3, 2015, at approximately 9:30 a.m., B.N. took "Munchkin," a
23 10-year old Schnoodle, to Respondent at the Clinic for the purpose of euthanasia. B.N. stated her
24 dog was ill. After a long wait, B.N. was taken to the back of the Clinic where clinic staff took
25 Munchkin from her. B.N. paid the bill for euthanasia and left.

26 27

28

1

2

7

8

15

18

19

20

21

27. This was Munchkin's first visit to the Clinic, however, no history was obtained, no examination performed and no recommendations were documented as having been made regarding whether euthanasia was in the best interest of Munchkin. There was no evaluation to

-8

(HONG RAK PARK) ACCUSATION

determine whether Munchkin was rabies-free prior to euthanasia. B.N. dropped Munchkin off at the Clinic and no veterinarian-client-patient relationship was established.

The only authorization for euthanasia was the single word "euthanasia" in the patient 28. chart with a signature line and signature of B.N. A Euthanasia Authorization form was not used and information typically included in such forms was missing. At a minimum, and pursuant to standard practice, the authorization form should include: clinic name; date; animal identification;. owner identification; attestation of ownership or authority to give consent; and a declaration that to the best of one's knowledge, the animal had not bitten any person or animal during the last fifteen days and had not been exposed to the rabies virus; and, the authorizing person's signature.

29. Under B.N.'s signature, information was blacked out such that it was illegible. 10 Rather than obscuring the entire text, the text to be modified may be crossed out but leaving it 11 still legible, signed and dated. 12

13 30. On November 4, 2015, B.N. received a call from T.S. at the Clinic who inquired whether T.S. could turn Munchkin over to a rescue organization. When B.N. expressed her 14 surprise that Munchkin had not been euthanized the day before, T.S. stated that they "didn't get 15 around to doing it." B.N. denied the request and reminded T.S. that she had paid for the service 16 and insisted that it be performed. Munchkin was euthanized on November 4, 2015.

FIFTH CAUSE FOR DISCIPLINE

(Record keeping Violations)

Respondent is subject to disciplinary action under Code section 4883, subdivision (o), 31. in conjunction with title 16, CCR, section 2032.3, subdivision (a), for violations regarding the veterinary records of Munchkin, as set forth in paragraphs 26-30 above and incorporated by this reference, in that:

9

a. Munchkin's records lack a history, examination, information regarding rabies. Respondent's recommendation regarding euthanasia and an adequate authorization for euthanasia; and,

, the records were improperly redacted.

111 28

1

2

3

4

5

6

7

8

9

17

18

19.

20

21

22

23

24

25

26

27

(HONG RAK PARK) ACCUSATION

SIXTH CAUSE FOR DISCIPLINE

1

2

3

4

5

6

7

8

17

18

19

20

21

22

23

24

25

(Failure to Establish Veterinarian-Client-Patient Relationship)

Respondent is subject to disciplinary action under Code section 4883, subdivision (o), 32. in conjunction with title 16, CCR, section 2032.1, for euthanizing Munchkin without establishing a veterinarian-client-patient relationship, as set forth in paragraphs 26-30 above and incorporated by this reference.

SEVENTH CAUSE FOR DISCIPLINE

(Failure to Exercise Minimum Standard of Practice)

Respondent is subject to disciplinary action under Code section 4883, subdivision (o), 9 33. in conjunction with title 16, CCR, section 2032, for failing to perform veterinary services for 10 Munchkin in a manner consistent with current veterinary medical practice, as set forth in 11 paragraphs 26-30 above and incorporated by this reference, in that: 12

Respondent inappropriately redacted, or allowed to be redacted, information in 13 a. Munchkin's records: 14

Respondent performed euthanasia on Munchkin without ascertaining that Munchkin 15 b. was rabies-free; and, 16

> Respondent used an incomplete or inadequate euthanasia authorization form. с.

EIGHTH CAUSE FOR DISCIPLINE

(Negligence)

Respondent is subject to disciplinary action under Code section 4883, subdivision (i), 34. for negligence in that Respondent performed euthanasia on Munchkin without an appropriate veterinarian-client-patient relationship, as set forth in paragraphs 26-30 above and incorporated by this reference.

NINTH CAUSE FOR DISCIPLINE

(Unprofessional Conduct)

Respondent is subject to disciplinary action under Code section 4883, subdivision (g), 35, 26 for unprofessional conduct in providing veterinary services to Munchkin, as set forth in 2728

paragraphs 26-30 above and incorporated by this reference, in that:

10

(HONG RAK PARK) ACCUSATION

Respondent failed to obtain Munchkin's history, perform an examination, obtain a, 1 information regarding rabies, Respondent's recommendation regarding euthanasia and an 2 adequate authorization for euthanasia; 3 Respondent improperly redacted Munchkins' records were improperly redacted; b. 4 Respondent performed euthanasia on Munchkin without an appropriate veterinarian-5 C. client-patient relationship; 6 d. Respondent performed euthanasia on Munchkin without ascertaining that Munchkin 7 was rabies-free; and, 8 Respondent used an incomplete or inadequate euthanasia authorization form. 9 e, DISCIPLINE CONSIDERATIONS 10 To determine the degree of discipline, if any, to be imposed on Respondent, 36. 11 Complainant alleges that on or about November 7, 2012, in a prior action, the Veterinary Medical 12^{-1} Board issued Citation Number 2377-C and ordered Respondent to pay a civil penalty of \$500.00. 13 That Citation is now final and is incorporated by reference as if fully set forth. 14 PRAYER 15 WHEREFORE, Complainant requests that a hearing be held on the matters herein alleged, 16 and that following the hearing, the Veterinary Medical Board issue a decision: 17 Revoking or suspending Veterinarian License Number VET 6707, issued to Hong 1. 18 Rak Park, DVM; 19 Revoking or suspending Premises Permit HSP 3440 issued to Sunnymead Veterinary 2. 20Clinic; 21 Assessing a fine against Hong Rak Park, DVM, not in excess of \$5,000 for any of the 22 З. causes specified in Business and Professions Code section 4883; 23 4. Ordering Hong Rak Park, DVM, to pay the Veterinary Medical Board the reasonable 24 costs of the investigation and enforcement of this case, pursuant to Business and Professions 25 Code section 125,3; and, 26 27 28 11 (HONG RAK PARK) ACCUSATION

EXHIBIT 3 - 031

•

Taking such other and further action as deemed necessary and proper. 4, 2017-DATED; ANNEMARIE DEL MUGNAIO Executive Officer Veterinary Medical Board Department of Consumer Affairs State of California Complainant SD2017704742 12725027.docx 2,7 (HONG RAK PARK) ACCUSATION EXHIBIT 3 - 032

EXHIBIT 3 - 033

3010 FLB S.1 FR 0: 1"

ATTORNEY GENERAL

EXHIBIT 4

CLEAR FORM



BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY - GAVIN NEWBOM, GOVERNOR DEPARTMENT OF CONSUMER AFFAIRS + VETERINARY MEDICAL BOARD 1747 North Market Blvd., Suite 230, Sacramento, CA 95834-2978 P (916) 515-5220 | Toll-Free (866) 229-0170 | www.vmb.ca.gov



PETITION FOR REINSTATEMENT OR MODIFICATION OF PENALTY

INSTRUCTIONS: Please type or print neatly. All blanks must be completed; if not applicable enter N/A. If more space is needed attach additional sheets. Attached to this application should be a "Narrative Statement" and two original verified recommendations from a veterinarian licensed by the Board who has personal knowledge of activities since the disciplinary action was imposed.

Reinstatement of Revoked/Surrendered License or Registration Modification of Probation Termination of Probation NOTE: A Petition for Modification and/or Termination of Probation can be filed together. If you are requesting Modification, you must specify in your "Narrative Statement" the term(s) and condition(s) of your probation that you want reduced or modified and provide an explanation. Please check all boxes above that apply. PERSONAL INFORMATION NAME: First HONG R PARK Other name(s) licensed under, if any: Grade Dr. Fullerton 310 Flintridge Dr. Fullerton City State Zip BOME TELEPHONE NUMBER City State Zip IOME TELEPHONE NUMBER () CA License or Registration Number 6707 Are you licensed by any other state(s) or country(ifés) (please include license number(s), issue date(s), and status of license(s ATTORNEY INFORMATION (if Applicable) // Will you be represented by an attorney? No Yes (If "Yes," please provide the following information)	TYPE OF PETITION [Reference Busine	ss and Professi	ons Code section 4887]		
NOTE: A Petition for Modification and/or Termination of Probation can be filed together. If you are requesting Modification, you must specify in your "Narrative Statement" the term(s) and condition(s) of your probation that you want reduced or modified and provide an explanation. Please check all boxes above that apply. PERSONAL INFORMATION NAME: First HONG R YARK Other name(s) licensed under, if any: HOME ADDRESS: Number & Street State Zip JIO / Flin fridge Dr Fullerton G 92 & 3.5 HOME TELEPHONE NUMBER Can gat gat () () E-mail address: Calciense or Registration Number G 7 0 7 Calciense or Registration Number Are you licensed by any other state(s) or country(ifs) (please include license number(s), issue date(s), and status of license(s ATTORNEY INFORMATION (If Applicable) //// Yes (If "Yes," please provide the following information) NAME: Barnaria Lucco	Reinstatement of Revoked/Surrendered License of	or Registration	Modification of Probatio	on Termin	ation of Probation
PERSONAL INFORMATION NAME: First Middle Last HONG R PARK Other name(s) licensed under, if any: 310/ F/:Nfridge Dr Fullerton 92835 HOME ADDRESS: Number & Street City State Zip 310/ F/:nfridge Dr Fullerton CG 9283.5 HOME TELEPHONE NUMBER WORK TELEPHONE NUMBER CELL NUMBER () () CA License or Registration Number 6707 Are you licensed by any other state(s) or country(ifes) (please include license number(s), issue date(s), and status of license(s) Are you licensed by an attorney? No Yes (If "Yes," please provide the following information) NAME: Bannei 2 UT Z	NOTE: A Petition for Modification and/o Modification, you must specify in your "N that you want reduced or modified and p	or Termination of Varrative Stateme provide an explan	Probation can be filed toge ent" the term(s) and condit ation. Please check all be	ether. If you are ion(s) of your pr oxes above that	requesting obation apply.
NAME: First Middle Last HONG R PARK Other name(s) licensed under, if any: JOI Flintridge Dr Fullerton G 92835 HOME ADDRESS: Number & Street City State Zip JIO Flintridge Dr Fullerton CG 92835 HOME ADDRESS: Number & Street City State Zip JIO Flintridge Dr Fullerton CG 9283.5 HOME TELEPHONE NUMBER WORK TELEPHONE NUMBER CELL NUMBER () () CA License or Registration Number () CA License or Registration Number 6707 Are you licensed by any other state(s) or country(ifs) (please include license number(s), issue date(s), and status of license(s ATTORNEY INFORMATION (If Applicable) Ves (If "Yes," please provide the following information) NAME: Bannual Lines	PERSONAL INFORMATION				- College - Coll
HONG R YARK Other name(s) licensed under, if any: 3101 Fintridge Dr Fullerton 92835 HOME ADDRESS: Number & Street City State Zip 3101 Fintridge Dr Fullerton CG 9283.5 HOME TELEPHONE NUMBER WORK TELEPHONE NUMBER CELL NUMBER () () CA License or Registration Number 6707 Are you licensed by any other state(s) or country(ifs) (please include license number(s), issue date(s), and status of license(s ATTORNEY INFORMATION (If Applicable) Ves (If "Yes," please provide the following information) NAME: Bannui, 2 ur z	NAME: First	Middle	3	Last	
Other name(s) licensed under, if any: 3+0+F(3)+r; dge D_F Fullerton G 92835 HOME ADDRESS: Number & Street City State Zip 310 F): n fridge Dr Fullerton CA 92835 HOME ADDRESS: Number & Street City State Zip 310 F): n fridge Dr Fullerton CA 9283.5 HOME TELEPHONE NUMBER WORK TELEPHONE NUMBER CELL NUMBER () () CA License or Registration Number 6707 Are you licensed by any other state(s) or country(ifs) (please include license number(s), issue date(s), and status of license(s ATTORNEY INFORMATION (If Applicable) Ves (If "Yes," please provide the following information) NAME: Bannué 1 1173	HONG	R		PARK	
HOME ADDRESS: Number & Street City State Zip 3101 F1:nfridge Dr Fullerfon Ca 9283 HOME TELEPHONE NUMBER WORK TELEPHONE NUMBER CELL NUMBER () () CA License or Registration Number 6707 Are you licensed by any other state(s) or country(ies) (please include license number(s), issue date(s), and status of license(s) ATTORNEY INFORMATION (If Applicable) Ves (If "Yes," please provide the following information) NAME: Rannei, 1 ust z	Other name(s) licensed under, if any: -3-1-0-1-Ff;n+r	idge Du	Fullecton	Ca	92835
310 Fl:nfrldge Dr Fullerton CG 9283 HOME TELEPHONE NUMBER WORK TELEPHONE NUMBER CELL NUMBER () () CA License or Registration Number () () CA License or Registration Number 6707 Are you licensed by any other state(s) or country(iés) (please include license number(s), issue date(s), and status of license(s ATTORNEY INFORMATION (If Applicable) Ves (If "Yes," please provide the following information) NAME: Bannuis Just z	HOME ADDRESS: Number & Street		City	State	Zip
HOME TELEPHONE NUMBER WORK TELEPHONE NUMBER CELL NUMBER () () () E-mail address: CA License or Registration Number 6707 Are you licensed by any other state(s) or country(iés) (please include license number(s), issue date(s), and status of license(s ATTORNEY INFORMATION (If Applicable) / Will you be represented by an attorney? No NAME: Rannui, Just	310/ Flintria	dge Dr	Fullerton	CG	92835
() () E-mail address: CA License or Registration Number 6707 Are you licensed by any other state(s) or country(iés) (please include license number(s), issue date(s), and status of license(s ATTORNEY INFORMATION (If Applicable) Will you be represented by an attorney? No Yes (If "Yes," please provide the following information) NAME:	HOME TELEPHONE NUMBER	WORK TELE	PHONE NUMBER	CELL NUMB	ER
E-mail address: Are you licensed by any other state(s) or country(iés) (please include license number(s), issue date(s), and status of license(s ATTORNEY INFORMATION (If Applicable) Will you be represented by an attorney? No NAME: Rannui, 2007 No No No No No No No No No No	()	()			
Are you licensed by any other state(s) or country(iés) (please include license number(s), issue date(s), and status of license(s ATTORNEY INFORMATION (If Applicable) Will you be represented by an attorney? No Yes (If "Yes," please provide the following information)	E-mail address:		CA License or Registra	tion Number	
Are you licensed by any other state(s) or country(iés) (please include license number(s), issue date(s), and status of license(s ATTORNEY INFORMATION (If Applicable) Will you be represented by an attorney? No NAME: Reprint 2 uses			6707		
ATTORNEY INFORMATION (If Applicable) Will you be represented by an attorney? No Yes (If "Yes," please provide the following information) NAME: Rannui, Luizz	Are you licensed by any other state(s) or country	/(iês) (please inclu	ide license number(s), issue	e date(s), and sta	tus of license(s)):
Will you be represented by an attorney? No Yes (If "Yes," please provide the following information)	ATTORNEY INFORMATION (If Applicable	le)	1	******	
NAME: Rannie 11172	Will you be represented by an attorney?	No 7	Yes (If "Yes," please pro	vide the followin	g information)
	NAME: Bonnie LUTZ				
ADDRESS: 2 Park Plaza Suite 1250 IRVINE CA. 92614	ADDRESS: 2 Park Plaza J	uite 1250	IRVINE CA.	92614	
PHONE: 949-201-0720	PHONE: 949-201-0720				
DISCIPLINARY INFORMATION	DISCIPLINARY INFORMATION	A MALINE ALL COMPLETE			
Provide a brief explanation in your "Narrative Statement" as to the cause for the disciplinary action (e.g., negligence or incompetence, self use of drugs or alcohol, extreme departures from sanitary conditions, conviction of a crime, etc.)	Provide a brief explanation in your "Narrative s incompetence, self use of drugs or alcohol, ex	Statement" as to treme departure	the cause for the disciplina s from sanitary conditions	ary action (e.g., r , conviction of a	regligence or crime, etc.)
Have you ever had your license revoked, suspended, voluntarily surrendered, denied, or placed on X No Yes	Have you ever had your license revoked, suspen probation in any other state or country?	ided, voluntarily su	rrendered, denied, or place	d on X No	Yes
(If Yes, give a brief cause for administrative action or license denial in your "Narrative Statement" section, including date and discipline ordered (e.g., 5 years probation.)	(If Yes, give a brief cause for administrative ad and discipline ordered (e.g., 5 years probation	ction or license de 1.)	enial in your "Narrative Sta	tement" section	, including dates

VETERINARIAN/REGISTERED TECHNICIAN BACKGROUND Total number of years in veterinary practice: CONTINUING EDUCATION (List continuing education completed since the date of the disciplinary action) PLEASE SEE ATTACHED SOCUMENTS CURRENT OCCUPATION OTHER THAN VETERINARIAN OR REGISTERED VET TECHNICIAN (Answer only if currently not practicing as a Veterinarian or Registered Vet Technician) List employer, address, e-mail address, phone number, job title, and duties: NONE EMPLOYMENT HISTORY (list for the past 5 years only) Provide the employer's name, address, phone number, job title and dates of employment: Surveymead Veterinary Clinic until 2019 REHABILITATION Describe any rehabiliative or corrective measures you have taken since your license/registration was disciplined. List dates, nature of programs or courses, and current status. You may include any community service or volunteer work. PIEASE SEE ATTACHED DOCUMENTS.

CURRENT COMPLIANCE			
Since the effective date of your last Veterinary Medical Board disciplinary action have you:			
1. Been placed on criminal probation or parole?	Yes	X	No
2. Been charged in any pending criminal action by any state, local or federal agency or court?	Yes	X	No
 Been convicted of any criminal offense? (A conviction includes a no contest plea; disregard traffic offenses with a \$100 fine or less.) 	Yes	X	No
4. Been charged or disciplined by any other veterinary board?	Yes	X	No
5. Surrendered your license to any other veterinary board?	Yes	X	No
6. Had your licensee manager's premise permit disciplined?	Yes	\Box	No
7. Had any civil malpractice claims filed against you of \$10,000 or more?	Yes	X	No
8. Become addicted to the use of narcotics or controlled substances?	Yes	X	No
9. Become addicted to or received treatment for the use of alcohol?	Yes	X	No
10. Been hospitalized for alcohol or drug problems or for mental illness?	Yes	X	No
NOTE: If your answer is "Yes" to any of the above questions, please explain in the "I	Narrative S	tatem	ent."
COST RECOVERY			
Was cost recovery ordered? O Yes No If yes, what is the remaining balance?			
When is payment anticipated?			
DECLARATION			
Executed on July 27, 20 22, at Irvine (City)	<u>,</u> C) (Stat	te)
I declare under penalty of perjury under the laws of the State of California that th correct and that all statements and documents attached in support of this petition	e foregoin n are true a	g is tru and co	ue and prrect.
HONG R PARK Petitioner (print name)	Philh	, 	
The information in this document is being requested by the Veterinary Medical Board (Board) p Professions Code section 4887. In carrying out its licensing or disciplinary responsibilities, the information to make a determination on your petition for reinstatement or modification of penalty access the Board's records containing your personal information as defined in Civil Code section Custodian of Records is the Executive Officer at the address shown on the first page.	ursuant to B Board requ y. You have n 1798.3. Th	usines ires thi a right he	s and s t to

-

Page 3 of 3

EXHIBIT 5

Veterinary Medical Board Regarding Petition for Reinstatement of Veterinary License

Please consider this my narrative statement in the Petition for Reinstatement of Veterinary License.

Continuing Education Credits

Since I surrendered my California veterinarian license on July 25, 2019, I have completed over 80 hours of continuing education.

Specifically, I attended the Chicago Veterinary Convention in 2019 in person for 30 hours of CE and a ZOOM conference in 2020 for 10 hours of CE.

I read Clinician's Brief and Today's Veterinary Practice regularly one or two hours every day. I also participate in webinars that are RACE approved for one hour of CE almost every week.

I attend the Orange Belt Veterinary Medical Association meetings in Riverside on a monthly basis.

Community Service

I joined the Christian Veterinary Mission in Nicaragua for 10 days in February 2020.

I lead the Bible study group at Sober Living Ministry at Calvary Chapel in Anaheim Hills every Friday evening from 6-7.

For years I assisted with the homeless ministry located at the corner of University Ave. and Brocton Ave. in Riverside every morning. Now that I have moved to Fullerton, I participate in a homeless ministry at the corner of Orangethorpe and Euclid avenues.

Every Sunday afternoon from 2:30 - 3:00 I participate in a homeless ministry in Lincoln Park in Riverside that is associated with Calvary Chapel.

Future Plans

In the future, if the Veterinary Medical Board reinstates my veterinary license, I hope to learn more about veterinary acupuncture and pain management, perform relief or part time veterinary work and continue my work with the Christian Veterinary Mission.

Explanation for Action Regarding Premises Permit

I checked "Yes" for the question regarding whether my licensee manager's premise permit had been disciplined because pursuant to the terms of my Stipulated Surrender of License and Order, my veterinary practice holding premises registration number HSP 3440 was required to be closed or sold.

signature

Ifong Rah park

21096963.2

EXHIBIT 6

Hong Park, DVM

Email:

Veterinarian License Number 6707

08/01/1981 – 05/22/2019 Sunnymead Veterinary Clinic [Owner] 24588 Sunnymead B1. Moreno Valley, CA 92553

03/1976 – 07/30/1981 Arlington Animal Hospital – [previously owned by Dr Marion Hammarlund] 4229 Van Buren Bl. Riverside, CA 92503

Education: College of Veterinary Medicine Graduated:

21188083.2

EXHIBIT 7

How to Attend PacVet Live

Within 10 days of registering, you should receive a confirmation email(s) which include the webinar join link which is unique to you. If you have registered for more than one day of webinars, you will receive separate emails for each day. Each day will have a new join link so look for the date of the webinar on the invitation to ensure you are using the correct log-in. You will also be sent follow-up reminder emails. If you do not receive a confirmation email, please email us at info@pacvet.net or call 800.655.2862.

Example



How to Log On

On the day of the webinar, click the URL **join link 10 minutes prior** to the beginning of the webinar. This will launch the Zoom program. If you are using Zoom for the first time, you will receive a prompt to download the program to your device. Once it has downloaded, follow your system's instructions for installing the software. This should just take a few minutes.

If you will be attending from your phone or tablet, you will need to install the Zoom app.

If you will be attending all sessions offered in a day, simply log in once and remained logged in for all offered sessions.

	0
GERTIFICA	FE OF COMPLETION
The individua	I named below
Hong	Park
has satisfied all requirements fo	or the successful completion of
Communicat	ions Program
2019-05-24	Jason B. Coe
1/Mattalia	Gailos ONDill
POWERED BY THE NAVC	Gens D'Neill, CPA, CIA Chief Esecutive Officer North American Veterinary Community
Course means if a require vesta for the before hours of costs native education 1 jointids for barrier house for mainteen of the one stepping of exists or stepping and the stepping of the st	a millichnessing rap sAVICID MICE appointed. However, participants alsocial Lie scarae trus pome stores on read an involved will alloop a AECE chosens. Successful or a "involved" my consistantian to uncertaint all the properties. Construct 16 with 56 caps work how of combining adjacation, in a conductor with the RACE entropy with an store and analyzed to combine or discussion. In a conductor with the RACE entropy with an store and analyzed to combine or conductor advance million RACE.
P Brother annu	Program #20343

1027-39341

Page 1 of 1

1/28/2021

clinician's brief 📀 ZOMEDICA

CE CERTIFICATE OF ATTENDANCE

AWARDED TO:

State of Licensure:

License Number:

FOR COMPLETING:

Diagnostic & Treatment Challenges in Canine Hypothyroidism

Date of Completion: January 28, 2021

BRIEF MEDIA ≥

Provided by Educational Concepts AAVSB RACEProvider #305

The American Association of Veterinary State Boards RACE committee has reviewed and approved this program iprogram number 309-7652511 as meeting the Standards adopted by the AAVSB for a maximum of 1 ione) hour for Veterinarians and Veterinary Technicians. This program has been approved for interactive Distance delivery in the RACE Category of Medical Program.

This approvals valid in jurisdictions which recognize ANUS RACE, however, participant care responsible for ascertaining each board's CE requirements, RACE does not "accredit" or "endorse" or "certily" any program or person, nor does RACE approval validate the content of the program.

clinician's brief



Diagnostic & Treatment Challenges in Canine Hypothyroidism

TOP 5 TAKEAWAYS

Thank you for joining Zomedica and *Clinician's Brief* for this webinar on canine hypothyroidism and making an accurate diagnosis and appropriate treatment plan. We hope you found the information valuable.

Dr. J. catherine Scott Monrieff

FOLLOWING ARE 5 KEY TAKEAWAYS FROM THE WEBINAR TO BEAR IN MIND AS YOU CONTINUE TO PRACTICE HIGH-QUALITY MEDICINE.



For routine diagnosis of canine hypothyroidism, total T4 ± free T4 and TSH should be used. Total T4 alone is not diagnostic in most cases. Additional testing beyond total T4, free T4, and TSH may be required to confirm diagnosis.



Laboratory data should be evaluated in context. Signalment, including breed, age, and clinical signs, should play a role in deciding whether a dog requires additional testing and/or treatment.



A therapeutic trial of L-thyroxine may be necessary. Laboratory data may not always give a definitive diagnosis. A therapeutic trial should be considered if clinical signs and signalment are highly suggestive of hypothyroidism but laboratory results are inconclusive.



Hypothyroidism is overdiagnosed in dogs. Therapeutic trials of L-thyroxine should not be continued indefinitely without re-evaluating patient status, and not accounting for systemic illness during diagnosis and treatment can often lead to overdiagnosis.



Thyroiditis may complicate diagnosis and treatment of hypothyroldism. The presence of antithyroglobulin, anti-T3, and/or anti-T4 antibodies does not necessarily indicate functional thyroid failure but should increase suspicion for hypothyroidism.

clinician's brief



EXHIBIT 7 - 004

clinician's brief airvet

LE CENTIFICATE OF ATTENDANCE

AWARDED TO:

State of Licensure:

License Number:

FOR COMPLETING:

Creating Confidence in Curbside Care: What We Know a Year Later

Date of Completion: February 23, 2021

BRIEF MEDIA

Provided by Educational Concepts FAVSB RACE Provider #309

The American Association of Veterinary State Boards RACE committee has reviewed and approved this program (program number 309-765747) as meeting the Standards adopted by the AAVSE for a maximum of 1 (one) hour for Veterinarians and Veterinary Technicians. This program has been approved for Interactive Distance delivery in the RACE Category of Non-Medical Program.

This approval is valid in jurisdictions which recognize AAVSB RACE; however, participants are responsible for ascentaining each board's CE requirements. RACE does not "accredit" or "endorse" or "certify" any program or person, nor does RACE approval validate the content of the program.

CERTIFICATE OF COMPLETION

The individual named below

Hong Park

has satisfied all requirements for the successful completion of

The Coughing Dog: Is it Cardiac or Respiratory?



VetFolio POWERED BY THE NAVC Alan Spier, Mike Dolinka

GENS ENGIL

Gene O'Neill, CPA, CIA Chief Executive Officer North American Veterinary Community

Course meets the requirements for the below hours of continuing education in jurisdictions which recognize AAVSB RACE approval, however, participants should be aware that some boards have fimilations of the number of hours accepted in certain categories and/or restrictions on certain methods of delivery. RACE does not "accredit" or "endorse" or "certify" any program or person, nor does RACE approval validate the content of the program.

This program, a section of the program. (The Coughing Dog: What you may not know about diagnosis, technique and radiographic interpretation, 20-811870) issues ______ interactive CE Credits of the 1.00 approved hour of continuing education. In accordance with the RACE Standards Section 2.05, d. an Established Provider may use portions of their program as stand alone presentations for continuing education credit.

Provider #50-27933 Program #20-811870



CE CERTIFICATE OF ATTENDANCE

AWARDED TO:

State of Licensure:

License Number:

FOR COMPLETING:

Secrets to Successfully Manage Feline Urethral Obstruction

Date of Completion: March 9, 2021

BRIEF MEDIA"

Provided by Educational Concepts #AVSB RACE Provider #309

The American Association of Veterinary State Boards RACE committee has reviewed and approved this program (program number 309-769915) as meeting the Standards adopted by the AAVSB for a maximum of 1 (one) heur for Veterinarians and Veterinary Technicians. This program has been approved for Interactive Distance delivery in the RACE Category of Medical Program. This approval is valid in jurisdictions which recognize AAVSE RACE; however, participants are responsible for ascertaining each board's CE requirements. RACE does not "accredit" or "endorse" or "certify" any program or person. nor does RACE approval validate the content of the program.

3/19/2021

clinician's brief

CE CERTIFICATE OF ATTENDANCE

AWARDED TO:

Hong Park

State of Licensure: California, California

License Number: 6707, 67

FOR COMPLETING:

DECISION-MAKING IN GONADECTOMY

Date of Completion: March 19, 2021

BRIEF MEDIA

Provided by Educational Concepts PO Box 3385 Tube OK 74156-3389 AAVS8 RACE Provider#500

This program 20-815212 is approved by the AAVSB RACE to offer a total of 1.00 CE Credits (1.00 max) being available to any one veterinariant and/or 1.00 Veterinary Technician CECendles (1.00 max). This RACE approved is for the subject matter categories of: Medical Program using the delivery method of Non-Interactive Distance.

This approvals valid in jurisdictions which recognize AAVSB PACE however, participants are reportable for accertaining such based % CE requirements: RACE does not "accredit" or "endorse" or "certify" any program or believ, nor does RACE approval validate the content of the program.

SHOW

CE Certificate of Attendance

This is to certify that: Hong Park

License #

State:

3/31/2027

Has completed the following continuing education live webinar Veterinary Point-of-Care Pleural Space and Lung Ultrasound (PLUS) for Everyday Practice!

Date: March 31, 2021

CE hours: 1:00

Signature:

Authorized Signature:

Daniel Read Senior Vice President CloserStill Vet US





4/29/2021

clinician's brief ZOETIS PETCARE

CE CERTIFICATE OF ATTENDANCE

AWARDED TO:

State of Licensure:

License Number:

FOR COMPLETING:

Turn Back Time: Helping Cats with Chronic OA Pain Live Better

Date of Completion: April 29, 2021

BRIEF MEDIA

Provided by Educational Concepts AAVSB RACE Provider #309

The American Association of Veterinary State Boards RACE committee has reviewed and approved this program (program number 309-795707) as meeting the Standards adopted by the AAVSE for a maxim um of 1 (one) hour for Veterinarians and Veterinary Technicians. This program has been approved for Interactive Distance delivery in the RACE Category of Medical Program. This approval is valid in jurisdictions which recognize AAVSB RACE; however, participants are responsible forassentaining each board's CE requirements; RACE does not "accredit" or "endorse" or "certify" any program or person, nor does RACE approval validate the content of the program.

CERTIFICATE OF COMPLETION

The individual named below

Hong Park

has satisfied all requirements for the successful completion of

Euthanasia Reimagined: Best Practices in the Modern Age



5/5/202

VetFolio POWERED BY THE NAVC Kathleen Cooney

PRESENTER

HENS ENSILL

Gene O'Neill, CPA, CIA Chief Executive Officer North American Veterinary Community

Course meets the requirements for the below hours of continuing education in jurisdictions which recognize AAVSB RACE approval; however, participants should be aware that some boards have limitations of the number of hours accepted in certain categories and/or restrictions on certain methods of delivery. RACE does not "accredit" or "endorse" or "certify" any program or person, nor does RACE approval validate the content of the program.

This program Euthanasia Reimagined: Best Practices in the Modern Age LIVE has been approved for 1.00 hour of interactive continuing education credit in jurisdictions that recognize RACE approval.

Provider #50-27933 Program 20-797977

5/20/2024



Use of Serum Thyroid Hormones for Feline Thyroid Disease

Date of Completion: May 20, 2023.

BRIEF MEDIA

Added by SA History Contrast Added Taxis Tracing +100

The Propose Association of fourthesy data loss is the Proposition for residual only approach the proposition of protemps 225, Weight a model of the Development by the Data for a methyway of 2 fore) have no Weight and a and interview Proposition. This program for item approach in interview Distance data my in the Refer Company of Antibula may as



6/19 20 27 28/2020C By Day (E 21 hrs

Sessions By Day

FRIDAY, JUNE 19		SATU	RDAY, JUNE 20	SATU	JRDAY, JUNE 27	SUNDAY, JUNE 28	
TRACK TOPIC SPEAKER	SMALL ANIMAL Gastroenterology Jacqueline Whittemore, DVM, Ph.D., DACVIM (SAIM)	TRACK TOPIC SPEAKER	SMALL ANIMAL/WELLNESS Neurology Carrie Jurney, DVM, DACVIM (Neurology), CCFP	TRACK TOPIC SPEAKER	AVIAN / EXOTIC Small Mammals / Backyard Poultry Susan Orosz, Ph.D., DVM, DABVP (Avian), DECZM (Avian)	TRACK TOPIC SPEAKER	SMALL ANIMAL Ophthalmology Sara Thomasy, DVM, Ph.D., DACVO
1:00 PM - 1:50 PM	Chronic Enteropathy in the Cat Sponsored by ILITRAMARY SCIENCES, INC.	9:00 AM - 9:50 AM	SMALL ANIMAL Spinal Radiographs Sponsored by CSAOTE North america	9:00 AM - 9:50 AM	The Respiratory System in Small Mammals: Common Diseases	9:00 AM - 9:50 AM	Practical Corneal Ulcer Management I: Superficial Corneal Ulcers Sponsored by B C P B C P
2:00 PM - 2:50 PM	Fat Cat Gone Wrong – Send Hepatic Lipidosis Packing Sponsored by ILLTRAINARY SCIENCES, INC.	- 10:00 AM - 10:50 AM	SMALL ANIMAL Don't Let Vestibular Disease Spin You Around Sonsored by CSAOTE north america	10:00 AM - 10:50 AM	Managing Old Hens and Roosters	10:00 AM - 10:50 AM	Practical Corneal Ulcer Management II: Deep Corneal Ulcers Sponsored by B C P B C P
3:00 PM - 3:50 PM	PLE – Abandon Hope or Business as Usual? Sponsored by UTRAINARY VETERINARY SCIENCES, NC.	11:00 AM - 11:50 AM	WELLNESS Diagnosing Well-being Sponsored by Gilling Boehringer Ingelheim	TRACK TOPIC SPEAKER	AVIAN/EXOTIC Avian Scott Echols, DVM, DABVP (Avian Practice)	11:00 AM - 11:50 AM	Eyelid Surgeries to Incorporate into Your Clinic Sponsored by
4:00 PM- 4:50 PM	Gastrointestinal Applications of Probiotics – An Evidenced-Based Review Sponsored by	12:00 PM - 12:50 PM	WELLNESS When Veterinary Medicine Kicks You in the Teeth: A Survival Guide Sponsored by Boehringer Ingelheim	11:00 AM - 11:50 AM	Common Surgical Procedures in Poultry (Part 1)	12:00 PM - 12:50 PM	FHV-1 Management: What's New That I Can Do? Sponsored by
2	20 minute break			12:00 PM - 12:50 PM	Common Surgical Procedures in Poultry (Part 2)	20 minute break	
TOPIC SPEAKER	Use of Antibiotics in Animals Adam Smith, DVM					TRACK TOPIC SPEAKER	TECHNICIAN Emergency Critical Care Megan Brashear, BS, CVT, VTS, ECC
5:10 PM - 6:00 PM	Use of Antibiotics in Animals ‡					1:10 PM - 2:00 PM	Shock Təlk
<i>‡</i> This course satisfies requirement on the j	s the one hour of California CE udicious use of medically important		1:1	۲		2:10 PM - 3:00 PM	The Art of Nursing
antimicrobiai aruĝs.			TV:	sha (onsuns		3:10 PM - 4:00 PM	Basic ECG Interpretation
1		-	1-	301 715	A592	4:10 PM - 5:00 PM	Critically Important Critical Thinking Skills

CVMA .

Web 10 873 4331 2355

EXHIBIT 7 - 013

How to Attend PacVet Live

Within 10 days of registering, you should receive a confirmation email(s) which include the webinar join link which is unique to you. If you have registered for more than one day of webinars, you will receive separate emails for each day. Each day will have a new join link so look for the date of the webinar on the invitation to ensure you are using the correct log-in. You will also be sent follow-up reminder emails. If you do not receive a confirmation email, please email us at info@pacvet.net or call 800.655.2862.

Example



How to Log On

On the day of the webinar, click the URL **join link 10 minutes prior** to the beginning of the webinar. This will launch the Zoom program. If you are using Zoom for the first time, you will receive a prompt to download the program to your device. Once it has downloaded, follow your system's instructions for installing the software. This should just take a few minutes.

If you will be attending from your phone or tablet, you will need to install the Zoom app.

If you will be attending all sessions offered in a day, simply log in once and remained logged in for all offered sessions.

If you are not able to attend all sessions offered in one day, log on 10 minutes before the session(s) you wish to attend. You can log off and log back on using the same log-in link.

Try Out Zoom Ahead of Time

If you are new to using Zoom and would like to try it out in advance of the conference, we are offering test run sessions each Friday leading up to the conference from 12:30 PM to 1:00 PM. Although it is scheduled for 30 minutes, it should only take a few minutes. To take advantage of this offer, email info@cvma.net or call 800.655.2862 and we will send you log-in instructions.

Please note the PacVet Live sessions are intended to be offered as live interactive presentations only and will not be offered as a recording.

System Requirements

You can view PacVet Live from your computer, tablet or mobile device. Click here for more information.

You can be signed in to Zoom on one computer, one tablet, and one phone at a time. If you sign into an additional device while logged into another device of the same type, you will be logged out automatically on the first device.

Special Assistance

To request a reasonable accommodation (e.g., alternate formats) to participate in this conference, please contact Della Yee by June 1, 2020, by email at dyee@cvma.net or by calling 800.655.2862, TTY 711 with your specific accommodation needs.

Lecture Notes

The lecture notes can be viewed on the conference app or on the PacVet website powered by VIN. Lecture notes are downloadable from both the conference app and the PacVet website. Please note the conference app will only be available for download through the Play Store or the Apple store through August 31.

Conference App

The PacVet Live app provides complete information about the conference, including the schedule, sessions, speaker information, sponsors and exhibitors, conference evaluations, raffles, and push notifications. Download the conference app at the Google Play or Apple store.

CE Credits

PacVet Live offers 21 hours of California-approved continuing education.

One hour of continuing education (CE) is defined as 50 minutes of presentation and a 10-minute break. Question and answer time is included as presentation time.

CE Certificate Distribution

You will receive a CE certificate by July 2 via email. Check off which dates and sessions you attended and retain for your records. Please note that attendance is recorded through Zoom each time you log into a session.

CE Requirements

The California Veterinary Medical Association is a statutorily approved CE provider. Additional information on mandatory CE can be found at cvma.net.

California Veterinarians are required to complete 36 hours of acceptable CE during the two-year license period immediately preceding the license expiration date.

All 36 hours may be earned by attending scientific programs, such as medical and surgical courses. Up to 24 hours of business/practice management related courses will be accepted for each renewal period. A maximum of six (6) hours can be earned by self-study methods, such as non-interactive Internet courses, reading journals, listening to audiotapes, or viewing video for each renewal period.

As of January 1, 2018, a veterinary licensee must complete a minimum of one credit hour on the judicious use of medically important antimicrobial drugs every four years for license renewal. For example, if your license expired on March 31, 2018, you will need to complete a judicious use course between April 1, 2018 and March 31, 2022. After the initial course has been completed, you will need to complete a judicious use course at least every other renewal period.

PacVet Live offers a one-hour course that satisfies the California requirement on the judicious use of medically important antimicrobial drugs.

California Registered Veterinary Technicians are required to complete 20 hours of acceptable CE during the two-year license period immediately preceding the license expiration date.

All 20 hours may be earned by attending scientific programs, such as medical and surgical courses. Up to 15 hours of business/practice management related courses will be accepted for each renewal period. A maximum of four (4) hours can be earned by self-study methods, such as correspondence courses, independent study and home study programs, reading journals, video, or audio presentations related to veterinary technology or related fields.

PacVet Live offers 4 hours of technician-specific CE. These hours will be applicable toward alternate route certification in California.

CVMA Certified Veterinary Assistants must complete a minimum of 10 hours of acceptable continuing education every two years to maintain their certification.

Veterinarians from other states

Most states will accept CVMA-sponsored CE. Contact your state veterinary medical board or licensing agency to determine which Pacific Veterinary Conference CE courses qualify in your state.

Distribution of Materials

PacVet Live prohibits the unauthorized distribution of any materials (printed or electronic) at its conference. It is prohibited to video or record any of the CE sessions. Attendees who violate this prohibition may be expelled from the conference without a refund.

Contact Information

Contact PacVet Live staff prior to the virtual conference with any questions or special requirements at 800.655.2862 or via email at info@PacVet.net.

WWW. CVMB. net Laura phillips Trisha Consunji Pass word 735506 916-649-0599



Nown lood

https://mail.yahoo.com/d/folders/1/messages/115750/ACx2y51yhlwtYO3xXQj44EDDcMY:2.2?.src=fp&fullscreen=1

Page 1 of 2

SHOW

CE Certificate of Attendance

This is to certify that: Hong Park License #: State:

Was in attendance at Vet Show @ Home

Date: **June 21-23, 2021** CE hours earned: **7** Signature:

Authorized Signature:

Daniel Read Senior Vice President CloserStill Vet US





This program, 20-843225. has been approved for 62.00 hours of continuing education credit to any veterinarian and/or veterinary technician in junsdictions that recognize RACE approval. A participant can receive a maximum of 24.00 hours of continuing education credit for this program.

RACE Category: Medical Program, Non-Medical Program. Course Type: Live Course Method of Delivery: Interactive Distance

14	VetFolio	
CERTIFICA	TE OF COMPLETION	
The	individual named below	
н	ONG R PARK	
has satisfied all requir	ements for the successful completion of	
Canine Dental Rac	liography: What Lies Beneath	
<u>1</u> <u>2021-06-</u>	23 GENSE ENSIL	
CE HOURS DATE	Gene O'Neill , CPA, CIA Chief Executive Officer	
6/21 - 6/23/2021 Vet show G home 1) / MHA _ John Thomason 8 hrs CE 8 CE lerkog fisis throubsertopours 50-70. spiro oyte phisphorous V 2) / mounosoppressive Thorapy Hemotocrif 1 PCV. V Gludicut: coia spheroupt.) prednisolome 2mg/kg daily prednisome Img Big Babesra Barfonly Anaplasmo Atopica (cyclosporine) Ehrlichir Neonichety sig Azathioprine Rodryman & spot the * Mycophenolate in Dogs Lyme. Hea Jurm 3) Vetorinary Acopuncture Rage 1/2 Savage wolf traitor unezz ungezz Condone = exarse, forgive Zepan

6/22/2021 Or christine Egger Vetshow@home 7:00/Am by The most common Anesthetic complication and emerging How to Address them

Atelectasis Hypercapnia Hypercopnia Pa CO2 60-85 mg H9 Sa Vage दो गुरु इन्हे Naloxone He Hyperkalemen - Ca solucionate 0,5-1.5 MDR/109 Atropine - 5.02 - 0.05 mg/kg Apr DIDIM /KP Elbow dysplasia pr. Kerin Benjamino 2) 12:45 a common Juvenile discase process (aronoid process of ulna Sclevos's of ulna Baequan Synovetin

3) The Efficient, Effective (and often Elusive) Diagnosis of Feline Gartavintestinal Disease Dr Craig Wabb

10:30 Am

6/23/2021 Vetshow @ home) Maximizing Regional Amesthesia to Keep your oral surge patient (ntraoral Regional Amesthesia (ntraoral Regional Amesthesia

Bupmen-rphe 15 pg 0.05ml + 0.95ml Bupivacaine 7 0000 0,25ml inject each site 20007 2) Overcoming Surgical Exptraction complications and ways to prevent them in the First place Du Christopher Snyder 25 Accasilying glass

clinician's brief



CE CERTIFICATE OF ATTENDANCE

AWARDED TO:

HONG & Park DVM

State of Licensure: 6707 CA,

License Number:

FOR COMPLETING:

Update on the Management of Stress-Associated Illnesses in Cats

Date of Completion: July 14, 2021

BRIEF MEDIA"

Provided by Educational Concepts AAVSB RACE Provider #309

The American Association of Veterinary State Boards RACE committee has reviewed and approved this program (program number 309-798923) as meeting the Standards adopted by the AAVSB for a maximum of 1 (one) hour for Veterinarians and Veterinary Technicians. This program has been approved for Interactive Distance delivery in the RACE Category of Medical Program.

This approval is valid in jurisdictions which recognize AAVSB RACE: however, participants are responsible for ascertaining each board's CE requirements. RACE does not "accredit" or "endorse" or "certify" any program or person, nor does RACE approval validate the content of the program.

CE Certificate of Completion | Feline Dental Radiography

From: SignalPET (marketing@signalpet.com)

To:

Date: Tuesday, July 27, 2021, 01:09 PM PDT

I SignalPET[®]

Certificate of Completion

This certifies that

Hong Park

has attended "Feline Dental Radiography", and is therefore awarded ONE HOUR CE CREDIT.

> Date: July 21, 2021 Presenter: Dr. Donnell Hansen, DAVDC

> > Program Number: 20-868310 Provider Number: 50-28777

This program has been approved for one hour of continuing education credit in jurisdictions that recognize RACE approval.



Neil Shaw, DVM, DACVIM (SAIM)

https://mail.yahoo.com/d/folders/1/messages/117192?.src=fp

Page 1 of 2

8/5/2021



CE Certificate of Attendance

This is to certify that: HONG R PARK License #: State:

Has completed the following continuing education live webinar Practical Small Animal Ultrasound: AFAST Scanning Techniques

Date: August 5, 2021

GE hours: 1.00 Signature: HR Park pim

Dhe

Authorized Signature:

Daniel Read Senior Vice President CloserStill Vet US



This program, 20-873594, has been approved for 1.00 hour of continuing education credit to any veterinarian and/or veterinary technician in jurisdictions that recognize RACE approval.

Provider: 50-28147 RACE Category: Medical Program

Method of Delivery: Interactive-Distance

Page 1 of 1

8/18/2021

clinician's brief Pro PLAN VETERINARY DIETS

CE CERTIFICATE OF ATTENDANCE

AWARDED TO:

State of Licensure:

License Number:

FOR COMPLETING:

My Dog Is Itchy! But I Already Changed the Diet: Food Allergies, Diagnosis, & Client Management

Date of Completion: August 18, 2021

BRIEF MEDIA

Provided by Educational Concepts AAVSB RACE Provider #309

The American Association of Veterinary State Boards RACE committee has reviewed and approved this program (program number 309-867840) as meeting the Standards adopted by the AAVSB for a maximum of 1 (one) hour for Veterinarians and Veterinary Technicians. This program has been approved for Interactive Distance delivery in the RACE Category of Medical Program. This approval is valid in jurisdictions which recognize AAVSB RACE; however, participants are responsible for ascertaining each board's CE requirements. RACE does not "accredit" or "endorse" or "certify" any program or person, nor does RACE approval validate the content of the program.

8/19/2021



The American Association of Veterinary State Boards RACE committee has reviewed and approved this program (program number 309-846187) as meeting the Standards adopted by the AAVSB for a maximum of 1 (one) hour for Veterinarians and Veterinary Technicians. This program has been approved for Interactive Distance delivery in the RACE Category of Medical Program. This approval is valid in jurisdictions which recognize AAVSB RACE; however, participants are responsible for ascertaining each board's CE requirements, RACE does not "accredit" or "endorse" or "certify" any program or person, nor does RACE approval validate the content of the program.

8/24/2021



CE CERTIFICATE OF ATTENDANCE

AWARDED TO:

HONG R PARK

State of Licensure:

License Number:

FOR COMPLETING:

When Life Gives You Lyme(s): Common Misconceptions & Protecting Patients from *Borrelia burgdorferi*

Date of Completion: August 24, 2021

BRIEF MEDIA

Provided by Educational Concepts AAVSB RACE Provider #309

The American Association of Veterinary State Boards RACE committee has reviewed and approved this program (program number 309-866435) as meeting the Standards adopted by the AAVSB for a maximum of 1 (one) hour for Veterinarians and Veterinary Technicians. This program has been approved for Interactive Distance delivery in the RACE Category of Medical Program. This approvals valid in jurtsdictions which recognize. ANVS 3 RACE; however, participants are responsible for ascertaining geach board is CE requirements. RACEdoes not "accredit" or "endonse" or "certify" any program or person. Non does RACE approval validate the content of the program.

9/22/2021

clinician's brief

PROPLAN VETERINARY DIETS

CE CERTIFICATE OF ATTENDANCE

AWARDED TO:

State of Licensure:

License Number:

FOR COMPLETING:

Why Isn't the Weight Coming Off? Strategies for Successful Weight Loss

Date of Completion: September 22, 2021

BRIEF MEDIA"

AVSB RACE Provider \$500

he American Association of Veterinary State Soards RACE committee has reviewed and approved this program (program under 309-841885) as meeting the Standards adopted by the AAVSB for a maximum of 3 (one) hour for Veterinarians nd Veterinary Technicians. This program has been approved for Interactive Distance delivery in the RACE Category of Indical Program.

The approval scalar in present on some for designing AASSB RACE bowever, participants are responsible for ascertaining auch board's C1 requirements. RACE does not "accerdin" or "entionse" or "certify" any program or person non does TACE approval validate the content of on program.

9/28/2021





Treating Canine Lymphoma in Primary Care: How to Use the Latest Diagnostics & Treatment Options to Optimize Patient Outcomes

Data of Completion: September 26, 203

BRIEF MEDIA

ANNEL BACK Franklin COL

The same the Autophysical Version of the Same Sold generative strategies and the Appendix Same Sold generation where SAME The Autophysical Version of a property of the Autophysical Same Sold generative Same Sold and the Sa Same Sold Version of Same Sold generative Same Sold generative Same Sold generative Same Sold generative Same Sold Same Sold generative Sa Same Sold generative Sa Same Sold generative Same So Same Sold The second secon

10/6/2021

clinician's brief

PRO PLAN VETERINARY DIETS

CE CERTIFICATE OF ATTENDANCE

AWARDED TO:

State of Licensure:

License Number:

FOR COMPLETING:

Growing Old Gracefully: Nutritional Management of the Senior Pet

Date of Completion: October 6, 2021

BRIEF MEDIA

AVS5 RACE Provider #201

The American Asposition of Veterinary State Boards RACE committee has reviewed and approved this program (program number 200-650923) as meeting the Standards adopted by the AAVSB for a maximum of 1 (one) hear for Weterinarians and Veterinary Technicians. This program has been approved for interactive Distance delivery in the RACE Category of addical Program.

This approval is valid in joined planes which recognize An/SB RACE horsever, participants at reciponsible for assessming which bears a CT requirements. RACE does not incorrectly or "wall one" of 7 certify" any program of parks which does RACE approval validate the context of the program.



ORANGE BELT VETERINARY MEDICAL ASSOCIATION

Continuing Education Certificate

This is to certify that on October 19, 2021, HONG R PARK DVM

attended a continuing education meeting for 1.0 hour credit. The topic and speaker for this meeting was:

"Understanding Pet Food – Basic & Clinical Nutrition"

Dr. Amber Cohn Blue Buffalo Natural Veterinary Diet

Carol L. Milam

Carol L. Milam Executive Secretary Orange Belt VMA



Certificate of Veterinary Continuing Education

This certificate is presented to

HONG R PARK

(participant)

for successful completion of RACE[®]-approved course,

Can You See It Now: Al Integration Into Radiology for the General Practice

on October 23, 2021

Presented by adam Chustman, Drm, MBA

MBA- Votorinany Office

Chief Veterinary Officer | dvm360®

This program has been approved for 1 hour of Continuing Education in jurisdictions which recognize AAVSB RACE®-approval.

RACE® Program No: 20-847137 Delivery Method: Non-interactive Distance License State: Program Category: <u>Medical</u> AAVSB Provider No: <u>209</u> License # (if applicable) <u>67 67</u>

The Registry of Approved Continuing Education (RACE[®]) is a program of the American Association of Veterinary State Boards (AAVSB). RACE[®]-approved continuing education is recognized by most of the AAVSB Member Boards; however, participants should verify recognition with their boards and councils and should be aware that some have limitations on the number of hours accepted in certain categories and/or restrictions of certain methods of delivery of continuing education. Participants should contact their veterinary boards to determine if a program meets their criteria for continuing education. Learn more at: www.aavsb.com or contact race@aavsb.com or call 877.698.882. dvm360® is a franchise of MJH Life Sciences. Inc. and not affiliated with AAVSB.

10/27/2021

clinician's brief



CE CERTIFICATE OF ATTENDANCE

AWARDED TO:

State of Licensure:

License Number:

FOR COMPLETING:

Wound Healing: Reckoning with the Past, Understanding the Present, & Creating a More Inclusive Veterinary Profession for the Future

ate of Completion: October 27, 2021

BRIEF MEDIA

Provided by Educational Concepts AAVSB RACE Provider#300

The American Association of Veterinory State Boards RACE committee has reviewed and approved this program (program umber 20-051369) as meeting the Standards adopted by the AAVSB for a maximum of 2 (one) hour for Veterinarians and Veterinary Technicians. This program has been approved for Interactive Distance delivery in the RACE Category of Nondecidal Program. This approval is valid in jurnal channel which recognize AAVSE BACE, However, juricipante ver aspans bit for exectphining and his and 3 C1 requirements. BACE does not "accredit" or "endorse" or "certify" any origitam or parts in soil does BACE approval validate the contest of the program.



CERTIFICATE OF ATTENDANCE

HONG R PARK DUM

has attended a continuing education symposium

Participant Signature & Date: Participant State(s) of Licensure: Participant License #(s): # of CE Hours:

8/2021

(1 Hour)

PROGRAM TITLE:

Cytopoint: Essential Facts and New Information You Need to Know! (AAVSB RACE Approval #20-876192)

DATE: SPEAKER(S): LOCATION: PRESENTED BY:

Online Zoetis, Parsippany, NJ AAVSB RACE Provider #192

Dana Liska, DVM, DACVD

SUBJECT CATEGORY: METHOD OF DELIVERY: Medical Live

November 8, 2021

Authorized By:

Zoetis Representative

This program has been approved for 1 hour of continuing education credit in jurisdictions that recognize RACE approval



CERTIFICATE OF ATTENDANCE

HONG R PARK DVm has attended a continuing education symposium

Participant Signature & Date:

11/8/2021 HNP

Participant State(s) of Licensure:

Participant License #(s):

of CE Hours:

(1 Hour)

PROGRAM TITLE:

SPEAKER(S):

DATE:

Apoquel: Essential Facts and New Information You Need to Know! (AAVSB RACE Approval #20-876188)

November 8, 2021 Dana Liska, DVM, DACVD

Online

LOCATION: PRESENTED BY:

Zoetis, Parsippany, NJ AAVSB RACE Provider #192

SUBJECT CATEGORY: METHOD OF DELIVERY:

Medical Live

Authorized By:

Zoetis Representative

This program has been approved for 1 hour of continuing education credit in jurisdictions that recognize RACE approval

11/17/2021



Hong r park prm

Diagnosing & Managing Chronic Enteropathy & Inflammatory Bowel Disease

BRIEF MEDIA

11/11/2021



HONG R PARK own

Wound Closure Academy: Focus on Surgical Knot-Tying

BRIEF MEDIA



CE CERTIFICATE OF ATTENDANCE

AWARDED TO:

CA

6707

HONG R PARK

State of Licensure:

License Number:

FOR COMPLETING:

Secrets to Successfully Manage Feline Urethral Obstruction

Date of Completion: 12/28/202/

BRIEF MEDIA

Provided by Educational Concepts AVVSB RACE Provider #309

The American Association of Veterinary State Boards RACE committee has reviewed and approved this program (program number 309-814530) as meeting the Standards adapted by the AAUS 8 for a maximum of 1 ione) heur for Veterinarians and Veterinary Technicians. This program has been approved for Non-Interactive Distance delivery in the RACE Category of Medical Program.

This appreval is valid in jurisdictions which recognize AAVS 8 RACE (however, participants are responsible for ascertaining each to ard SC requirements. RACE does not "accredit" or "endorse" or "certify" any program or person, nor does RACE approval validate the content of the program. - Yahoo Mail

Back 02-17-22 CE Certificate Sparage.pdf

Prize 1 of 1



Back certificat	te-vetce-race.pdf Popel tool t	2/19/222
ι		
1	HONG R PARK, DVM	
Inbox	has attended	
Unread	VETCE VIRTUAL: FRESH SKILLS IN VETERINARY DENTISTRY	
Starred		
Drafts	Completed on February 19, 2022	
Sent	This program 898895 is approved by the AAVSB RACE to offer a total of 3.00 CE Credita (3.00 max) being available to any one veterinariani and/ or 3.00 Veterinary Technician CE Credita (3.00 max).	
Archive	The NECL ACCEPTERT of the facility of international of the factor score (in terms of the access) and the factor is the score of th	
Spam	~	
Trash	S Vec/redTeam	
~ Less	www.VethedTeam.com CEGVVetMedTeam.com	
Views		
Folders		
F New I		
15990		
at n t.		
Breez		
CMS		
confe		
CPA		
CURE		
CURE CVMA		
CURE CVMA DNA		
CURE CVM/ DNA Globa		
CURE CVM/ DNA Globa gmail		
CURE CVM/ DNA Globa gmail home		
CURE CVM/ DNA Globa gmail home labelc		
CURE CVM/ DNA Globa gmail home labelc Medli		
CURE CVMA DNA Globa gmail home labelc Medlii missik		
CURE CVMA DNA Globa gmail home labelc Medlii missik		
CURE CVM/ DNA Globa gmail home labelc Medlii missik Notes		
CURE CVM/ DNA Globa gmail home labelc Medlii missik Notes Palm Prope		
CURE CVM/ DNA Globa gmail home labelc Medli(missik Notes Palm Prope SORF		
CURE CVM/ DNA Globa gmail home Iabelc Medli(missik Notes Palm Prope SORF Synce		
CURE CVM/ DNA Globa gmail home labelc Medlii missic Notes Palm Prope SORF Synce traffic		
CURE CVM/ DNA Globa gmail home labelc Medlii missik Notes Palm Prope SORF Synce traffic		

(3,710 unread) -

- Yahoo Mail

07/03/2022, 11:09 PM

2/28/2022

clinician's brief covetrus 📚

AWARDED TO:

State of Licensure: California, California

License Number: 6707, 6707

FOR COMPLETING:

Date of Completion: February 27, 2022

BRIEF MEDIA

Provided by Educational Concepts PO Box 2389 Tuisa OK 74104 - 2389 AAVSB RACE Provider \$309

The American Association of Veterinary State Boards RACE committee has reviewed and approved this program (program number 20-886527) as meeting the Standards adopted by the AAVS6 for a maximum of 1 [one] hour for Veterinarians and Veterinary Technicians. This program has been approved for Non-Interactive Distance delivery in the RACE Category of Non-Medical Program. This approval is valid in jurisdictions which recognize AAVSB RACE; however, participants are responsible for a scentaining each board's CE requirements, RACE does not "accredit" or "endorse" or "centify" any program or person, nor does RACE approval validate the content of the program.

The Contract Care



CONTINUING EDUCATION CERTIFICATE

For:

HONG PARK DUM #6707

Attendee Name and License

MedVet Virtual CE Thursday, March 31, 2022 Total CE Credit Hours: 1.0

Essentials of Blunt Trauma

by Rebecca McQuitty, DVM, Diplomate, ACVECC MedVet Silicon Valley RACE program approval # 904315 Live Interactive Distance

This program is approved for 1.0 hour of continuing education credit in jurisdictions that recognize RACE approval. As RACE program providers, MedVet will upload the attendance roster to RACEtrack following each event for attendance to be centrally recorded and tracked with license information pertaining to attendees of each credit hour. To learn more about RACEtrack, visit: https://aavsb.org/racetrack

3/31/2020

4/24/2022



4/26/2022

Certificate of Qualification

THIS ACKNOWLEDGES THAT

Hong Park

has been trained

Diagnosis and Treatment of Elbow Arthritis



RACE Medical Program #20-902456

This program has been approved for 1 hour of continuing education credit in jurisdictions that recognize RACE approval.

E UBRION THERAPEUTICS

April 26, 2022

4/26/2022

and support of the second second second

Property and the second

Vet Team Providing Educational Pullivarys to Great Carpers

HONG R PARK, DVM

has attended

INTEGRATING CANINE LIQUID BIOPSY TESTING INTO YOUR PRACTICE

Completed on April 26, 2022

This program 909271 is approved by the AAVS8 RACE to offer a total of 1.00 CE Credits (1.00 max) being available to any one veterinarian: and/ or 1.00 Veterinary Technician CE Credits (1.00 max).

This RACE approval is for the subject matter categories of: Medical using the delivery method of Stminar/Lecture 6. Interactive Distance. This approval is valid in Jurisdictions which recognize AAVSB RACE; however, participants are responsible for ascertaining each board's CE requirements. RACE does not "accredit" or "endorse" or "certify" any program or person, nor does RACE approval validate the content of the program.

> VetMedTeam www.VetMedTeam.com CE@VetMedTeam.com

RACE Provider #26277

https://mail.yahoo.com/d/folders/1/messages/146786/ABRHGf0q9GJBYmq2bwAyylGmvAQ:2?.src=fp&fullscreen=1

Page 1 of 2

5/16/2022

CERTIFICATE OF COMPLETION

The individual named below

HONG R Park

has satisfied all requirements for the successful completion of

Respiratory Emergencies: Don't Let Them Take Your Breath Away

2022-05-16



Bradley Harris

GENS ENGILL

Gene O'Neill, CPA, CIA Chief Executive Officer North American Veterinary Community

Course meets the requirements for the below hours of continuing education in jurisdictions which recognize AAVSB RACE approval; however, participants should be aware that some boards have limitations of the number of hours accepted in certain categories and/or restrictions on certain methods of delivery. RACE does not "accredit" or "endorse" or "certify" any program or person, nor does RACE approval validate the content of the program. This program, Respiratory Emergencies: Don't Let Them Take Your Breath Away, issues 1 interactive CE Credit hour of continuing education. In accordance with the RACE

Standards Section 2.05, d. an Established Provider may use portions of their program as stand alone presentations for continuing education credit.

Provider #50-27933 Program #20-903456



CERTIFICATE OF ATTENDANCE

has	s attended a continuing education symposium	
Participant Signature & Date:	Ang n park nom	5/19/2022
Participant State(s) of Licensur	e: California	
Participant License #(s):	6707	
# of CE Hours:	(1 Hour)	

PROGRAM TITLE: Cytology: Lets Get Digital, Virtual Lab Expertise in Your Practice! (AAVSB RACE Tracking #20-860841)

DATE:	May 19, 2022
LOCATION:	Online
SPEAKER(S):	Cory Penn, DVM Sarah Barrett, DVM, PhD, DACVP
PRESENTED BY:	Zoetis, Parsippany, NJ AAVSB RACE Provider #77
SUBJECT CATEGORY:	Non-Medical
METHOD OF DELIVERY:	Live

Authorized By:

Zoetis Representative

This program has been approved for 1 hour of continuing education credit in jurisdictions that recognize RACE approval.

CERTIFICATE

HSM2020-019

Natural Thermal Therapy Institute

Los Angeles, California

This is to certify that

Hong Rak, Park



Having successfully completed the required coursework and training In Infrared Thermal Therapy Is awarded as

Thermal Therapist

<u>August 15th, 2020</u> Date awarded





Dean of Studies Sungyeon Lee

CE DOCUMENTATION

#/ 3/1/2021

clinician's brief

Top 5 Suggestions of Canine Hyperadrenocorticism

Todd Archer, DVM, MS, DACVIM, Mississippi State University

ENDOCRINOLOGY & METABOLIC DISEASES | OCTOBER 2013 | PEER REVIEWED



Canine hyperadrenocorticism is a clinical disorder characterized by several common clinical signs, including polyuria, polydipsia, polyphagia, alopecia, thin skin, a potbellied appearance, and panting.¹ Hyperadrenocorticism 5 suggestions of K-9 Hyperadrenocorticism

Oct. /2018 Clinician Brief Pr. Todd Archer

1) Stress Leukogram & thrombocytosis V lymphopenia A Leukocytosis V eosinopenia A Neutrophilia

A thrombo aytos:s

2) Flevated Liver enzymes Ast sGOT Alanine aminotransferase (ALP) ALT SGPT

3 Hyperalycemia 30-40-10 4 Hypercholesterolemia - 90% Irom Liplysis in Adipose tissue 5 Dilute Urine From polyuria and poly dipsid 90 % Urine SG 1.007-1.015 to Some dogs PUPP Symptom

Some dogs PUPD sympton CBC chemistry not much change - still thonk about (ushings Run hormon test

> And the second states on the States (and states), where the second states is shown and they "be a get for the second states 1.1.5 block with open these on controls, such the Down and States 1.1.5 block with states 1.1.5 block with open these on controls, such the Down and States 1.1 block with states and the second states (and states the second states for the "state") of the second states of the second states (block and states the second states for the "states").

results from excess cortisol production secondary to either an adrenal tumor or a pituitary tumor, causing excessive production of adrenocorticotropic hormone (and, subsequently, an excess production of cortisol).¹

After a patient has been assessed through a detailed history and physical examination, preliminary testing should be performed prior to specific endocrine testing and should include CBC, serum chemistry profile, and urinalysis. Findings consistent with canine hyperadrenocorticism suggest that further endocrine testing is needed to arrive at a specific diagnosis of canine hyperadrenocorticism.

Following are the author's 5 most common findings seen on CBC, serum chemistry profile, and urinalysis results in patients with confirmed canine hyperadrenocorticism.

Stress Leukogram & Thrombocytosis A stress leukogram is a common but nonspecific finding in dogs with hyperadrenocorticism. It often consists of lymphopenia, eosinopenia, leukocytosis characterized by mature neutrophilia, and, occasionally, monocytosis.² Multiple factors contribute to the development of mature neutrophilia, including an increased release of mature neutrophils from the bone marrow, a shift of marginated neutrophils from the periphery into circulation, and/or a decreased amount of neutrophils leaving the circulation into tissue.² Lymphopenia occurs as a result of a redistribution of lymphocytes within the circulation, as well as possible lympholysis.² Eosinopenia occurs through steroidinduced sequestration of eosinophils in bone marrow and in other tissues.² If monocytosis is present, it is thought to result from a shift of marginated monocytes from the periphery into circulation.²

A high-normal-to-increased platelet count may also be found on CBC. As many as 75% to 80% of dogs may have thrombocytosis at the time of diagnosis.¹

Feedback

Elevated Liver Enzymes

Serum alkaline phosphatase (ALP) and alanine aminotransferase (ALT) are often elevated in dogs with hyperadrenocorticism. ALP tissue activity can be found in the intestine, kidney, liver, and bone.³ The liver is thought to contribute the majority of ALP measured on serum chemistry profile, with bone being a minor contributor.¹ Little to no intestinal or renal ALP isoenzyme activity has been found in the serum of dogs because of the extremely short half-life.¹ In the liver, the primary location of ALP is the bile canalicular membrane of hepatocytes.³ In dogs, steroids (exogenous or endogenous) cause an increase in ALP of hepatic origin (ie, the corticosteroid-induced isoenzyme of ALP). This steroid-induced increase in ALP is the most common abnormality found on serum chemistry profile in dogs with hyperadrenocorticism, with incidence at diagnosis often as high as 85% to 95%.⁴

ALT is a cellular leakage enzyme, and elevations are primarily thought to come from hepatocyte injury/damage. ALT also originates from skeletal muscle, and elevated ALT could come from muscle trauma or a myopathy. Measurement of creatinine kinase can help distinguish the source of increased ALT between liver and muscle. In dogs with hyperadrenocorticism, the increase in ALT is thought to occur secondary to hepatocyte damage from swollen hepatocytes, hepatocellular necrosis, accumulation of glycogen, and/or disturbances in hepatic blood flow.⁴

Whereas increases in ALT are typically mild, increases in ALP can range from mild to severe, with severe increases being as high as 10 times the upper limit of the normal reference interval. Liver enzyme elevations vary widely among affected individual dogs.⁴

Hyperglycemia
Dogs with hyperadrenocorticism often have mild hyperglycemia
(30%-40% of affected patients).⁵ The ability of cortisol to increase hepatic
gluconeogenesis—as well as its antagonistic effects on insulin in peripheral tissue,
which decrease peripheral utilization of glucose—can cause blood glucose to
increase.⁴ Hypercortisolism-induced hyperinsulinemia may subsequently develop as the pancreas continues to secrete insulin in an attempt to maintain normoglycemia; however, many dogs will have only mild hyperglycemia at diagnosis. A small subset of dogs will have overt diabetes (glucose, >250 mg/dL [>13.875 mmol/L] with glucosuria and consistent clinical signs) in addition to hyperadrenocorticism.⁴ Thus, the elevation in glucose must be critically evaluated to determine if diabetes is present.

Hypercholesterolemia

Elevated cholesterol is often noted on serum chemistry profile results in dogs with hyperadrenocorticism. Glucocorticoids can increase lipolysis in adipose tissue, generating both free fatty acids and glycerol, which serve as substrates for gluconeogenesis. This lipolysis in adipose tissue leads to an increase in blood cholesterol. Approximately 90% of dogs with hyperadrenocorticism will have hypercholesterolemia at diagnosis.¹

Dilute Urine

Two of the most common clinical signs associated with canine hyperadrenocorticism are polyuria and polydipsia, which are observed in approximately 90% of patients with hyperadrenocorticism.⁴ Although the causes of polyuria and polydipsia can include several factors, polyuria has generally been thought to develop before polydipsia. The influence of cortisol at the level of the kidney causes an impaired tubule response to antidiuretic hormone,⁶ which prevents appropriate water reabsorption and causes urine to be less concentrated. Polydipsia subsequently develops to maintain hydration. This is considered a form of secondary nephrogenic diabetes insipidus in which there is a lack of kidney response to antidiuretic hormone. In most dogs, urine specific gravity is less than 1.030⁴; these dogs are also often found to be isosthenuric (ie, having a urine specific gravity of 1.007-1.015).⁷

Conclusion

A minority of patients with hyperadrenocorticism may be presented with polyuria,

polydipsia, and dilute urine but have no other clinical abnormalities on CBC, serum chemistry profile, or urinalysis. Lack of a stress leukogram, liver enzyme elevation, hyperglycemia, or hypercholesterolemia should not prevent clinicians from performing specific endocrine testing for canine hyperadrenocorticism. Although most dogs with hyperadrenocorticism will have one or more abnormalities on CBC and serum chemistry profile, the condition should still be included on the differential list in any dog with polyuria and polydipsia, dilute urine, and normal CBC and serum chemistry profile results.

ALP = alkaline phosphatase, ALT = alanine aminotransferase

REFERENCES

- Behrend EN. Canine hyperadrenocorticism. In: Feldman EC, Nelson RW, Reusch C, Scott-Moncrieff JC, eds. *Canine and Feline Endocrinology*. 4th ed. St. Louis, MO: Elsevier; 2015:377-451.
- Schultze AE. Interpretation of canine leukocyte responses. In: Weiss DJ, Wardrop KJ, eds. *Schalm's Veterinary Hematology*. 6th ed. Ames, IA: Wiley-Blackwell; 2010:321-334.
- Kramer JW, Hoffmann WE. Clinical enzymology. In: Kaneko JJ, Harvey JW, Bruss ML, eds. *Clinical Biochemistry of Domestic Animals*. 5th ed. San Diego, CA: Academic Press; 1997:303-325.
- Pérez-Alenza MD, Melián C. Hyperadrenocorticism in dogs. In: Ettinger SJ, Feldman EC, eds. *Textbook of Veterinary Internal Medicine*. 8th ed. St. Louis, MO: Elsevier; 2017:1795-1811.
- Melián C, Pérez-Alenza MD, Peterson ME. Hyperadrenocorticism in dogs. In: Ettinger SJ, Feldman EC, eds. *Textbook of Veterinary Internal Medicine*. 7th ed. St. Louis, MO: Elsevier; 2010:1816-1840.
- 6. Lunn KF. Managing the patient with polyuria and polydipsia. In:

Bonagura JD, Twedt DC, eds. *Kirk's Current Veterinary Therapy XIV*. St. Louis, MO: Elsevier; 2009:32-62.

 Chew DJ, DiBartola SP, Schenck PA. Clinical evaluation of the urinary tract. In: Chew DJ, DiBartola SP, Schenck P, eds. *Canine and Feline Nephrology and Urology*. 2nd ed. St. Louis, MO: Elsevier; 2011:32-62.

AUTHOR

Todd Archer

DVM, MS, DACVIM Mississippi State University

Todd Archer, DVM, MS, DACVIM (SAIM), is an associate professor of small animal internal medicine at Mississippi State University, where he also earned his DVM and master's degree and completed an internship and residency in small animal internal medicine. Dr. Archer's clinical interests include endocrinology, hematology, and immunology.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found here.

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. For questions or inquiries please contact

us.

WikipediA

Anabolism

Anabolism $(/\underline{\partial}' \underline{n}\underline{a}\underline{b}\underline{\partial}\underline{l}\underline{s}\underline{m}/)$ is the set of metabolic pathways that construct molecules from smaller units.^[1] These reactions require energy, known also as an endergonic process.^[2] Anabolism is the building-up aspect of metabolism, whereas <u>catabolism</u> is the breaking-down aspect. Anabolism is usually synonymous with biosynthesis.

Pa	thway
	Energy source
	Cofactors
	Substrates
Fu	Inctions
	Anabolic hormones
	Photosynthetic carbohydrate synthesis
	Amino acid biosynthesis
15,	Glycogen storage
	Gluconeogenesis
Re	gulation
Ety	ymology
Re	ferences

Pathway

Polymerization, an anabolic pathway used to build macromolecules such as nucleic acids, proteins, and polysaccharides, uses condensation reactions to join monomers.^[3] Macromolecules are created from smaller molecules using enzymes and cofactors.

Energy source

Anabolism is powered by catabolism, where large molecules are broken down into smaller parts and then used up in cellular respiration. Many anabolic processes are powered by the cleavage of adenosine triphosphate (ATP).^[4] Anabolism usually involves reduction and decreases entropy,

king it unfavorable without energy input.^[5] The starting materials, called the precursor molecules,

are joined together using the chemical energy made available from hydrolyzing ATP, reducing the cofactors NAD⁺, NADP⁺, and FAD, or performing other favorable side reactions.^[6] Occasionally it can also be driven by entropy without energy input, in cases like the formation of the phospholipid ' 'ayer of a cell, where hydrophobic interactions aggregate the molecules.^[7]

Cofactors

The reducing agents NADH. NADPH, and FADH₂,^[8] as well as metal ions,^[3] act as cofactors at various steps in anabolic pathways. NADH. NADPH, and FADH₂ act as electron carriers, while charged metal ions within enzymes stabilize charged functional groups on substrates.





Substrates

Lostrates for anabolism are mostly intermediates taken from catabolic pathways during periods of high energy charge in the cell.^[9]

Functions

Anabolic processes build organs and tissues. These processes produce growth and differentiation of cells and increase in body size, a process that involves synthesis of complex molecules. Examples of anabolic processes include the growth and mineralization of bone and increases in muscle mass.

Anabolic hormones

Endocrinologists have traditionally classified hormones as anabolic or catabolic, depending on which part of metabolism they stimulate. The classic anabolic hormones are the anabolic steroids, which stimulate protein synthesis and muscle growth, and insulin.

Photosynthetic carbohydrate synthesis

Photosynthetic carbohydrate synthesis in plants and certain bacteria is an anabolic process that produces glucose, cellulose, starch, lipids, and proteins from CO_2 .^[5] It uses the energy produced from the light-driven reactions of photosynthesis, and creates the precursors to these large molecules via

bon assimilation in the photosynthetic carbon reduction cycle, a.k.a. the Calvin cycle.^[9]

Amino acid biosynthesis

All amino acids are formed from intermediates in the catabolic processes of glycolysis, the citric acid cycle, or the pentose phosphate pathway. From glycolysis, glucose 6-phosphate is a precursor for histidine; 3-phosphoglycerate is a precursor for glycine and cysteine; phosphoenol pyruvate, combined with the 3-phosphoglycerate-derivative 4-phosphate, ervthrose forms tryptophan, phenylalanine, and tyrosine; and pyruvate is a precursor for alanine, valine, leucine, and isoleucine. From the citric acid cycle, αketoglutarate is converted into glutamate and subsequently glutamine, proline, and arginine; and oxaloacetate is converted into aspartate and subsequently asparagine, methionine, threonine, ~~d lysine.[9]

Glycogen storage

During periods of high blood sugar, glucose 6phosphate from glycolysis is diverted to the glycogen-storing pathway. It is changed to



Amino acid biosynthesis from intermediates of glycolysis and the citric acid cycle.

glucose-1-phosphate by phosphoglucomutase and then to UDP-glucose by UTP--glucose-1-phosphate uridylyltransferase. Glycogen synthase adds this UDP-glucose to a glycogen chain.^[9]

Gluconeogenesis

Glucagon is traditionally a catabolic hormone, but also stimulates the anabolic process of gluconeogenesis by the liver, and to a lesser extent the kidney cortex and intestines, during starvation to prevent low blood sugar.^[8] It is the process of converting pyruvate into glucose. Pyruvate can come from the breakdown of glucose, lactate, amino acids, or glycerol.^[10] The gluconeogenesis pathway has many reversible enzymatic processes in common with glycolysis, but it is not the process of glycolysis in reverse. It uses different irreversible enzymes to ensure the overall pathway runs in one direction only.^[10]

Regulation

Anabolism operates with separate enzymes from catalysis, which undergo irreversible steps at some

int in their pathways. This allows the cell to regulate the rate of production and prevent an infinite loop, also known as a futile cycle, from forming with catabolism.^[9]

The balance between anabolism and catabolism is sensitive to ADP and ATP, otherwise known as the energy charge of the cell. High amounts of ATP cause cells to favor the anabolic pathway and slow catabolic activity, while excess ADP slows anabolism and favors catabolism.^[9] These pathways are also regulated by <u>circadian rhythms</u>, with processes such as <u>glycolysis</u> fluctuating to match an animal's normal periods of activity throughout the day.^[11]

Etymology

The word *anabolism* is from New Latin, which got the roots from <u>Greek</u>: ἀνἀ, "upward" and βἀλλειν, "to throw".

References

- de Bolster MW (1997). "Glossary of Terms Used in Bioinorganic Chemistry: Anabolism" (https://we b.archive.org/web/20071030105041/http://www.chem.qmul.ac.uk/iupac/bioinorg/AB.html). International Union of Pure and Applied Chemistry. Archived from the original (http://www.chem.q mul.ac.uk/iupac/bioinorg/AB.html#20) on 30 October 2007. Retrieved 2007-10-30.
- Z. Rye C, Wise R, Jurukovski V, Choi J, Avissar Y (2013). *Biology* (https://cnx.org/contents/GFy_h8c u@11.6:rZudN6XP@2/Introduction). Rice University, Houston Texas: OpenStax. ISBN 978-1-938168-09-3.
- Alberts B, Johnson A, Julian L, Raff M, Roberts K, Walter P (2002). *Molecular Biology of the Cell* (https://web.archive.org/web/20170927035510/https://www.ncbi.nlm.nih.gov/books/NBK21054/) (5th ed.). CRC Press. ISBN 978-0-8153-3218-3. Archived from the original (https://www.ncbi.nlm. nih.gov/books/NBK21054/) on 27 September 2017. Retrieved 2018-11-01. Alt URL (https://archive .org/details/MolecularBiologyOfTheCell5th)
- 4. Nicholls DG, Ferguson SJ (2002). *Bioenergetics* (3rd ed.). Academic Press. ISBN 978-0-12-518121-1.
- 5. Ahern K, Rajagopal I (2013). *Biochemistry Free and Easy* (https://biochem.science.oregonstate.e du/files/biochem/ahern/BiochemistryFreeandEasy3.pdf) (PDF) (2nd ed.). Oregon State University.
- 6. Voet D, Voet JG, Pratt CW (2013). Fundamentals of biochemistry : life at the molecular level (Fourth ed.). Hoboken, NJ: Wiley. ISBN 978-0-470-54784-7. OCLC 738349533 (https://www.world cat.org/oclc/738349533).
- Hanin I, Pepeu G (2013-11-11). Phospholipids: biochemical, pharmaceutical, and analytical considerations. New York. ISBN 978-1-4757-1364-0. OCLC 885405600 (https://www.worldcat.org/ oclc/885405600).
- 8. Jakubowski H (2002). "An Overview of Metabolic Pathways Anabolism" (https://bio.libretexts.org/ TextMaps/Biochemistry/Book%3A_Biochemistry_Online_(Jakubowski)/10%3A_Metabolic_Pathwa

ys/B._MP2%3A_An_Overview_of_Metabolic_Pathways_-_Anabolism). *Biochemistry Online*. College of St. Benedict, St. John's University: LibreTexts.

- 9. Nelson DL, Lehninger AL, Cox MM (2013). *Principles of Biochemistry*. New York: W.H. Freeman. ISBN 978-1-4292-3414-6.
- Berg JM, Tymoczko JL, Stryer L (2002). *Biochemistry* (https://archive.org/details/biochemistrychap 00jere) (5th ed.). New York: W.H. Freeman. ISBN 978-0-7167-3051-4. OCLC 48055706 (https://w ww.worldcat.org/oclc/48055706).
- Ramsey KM, Marcheva B, Kohsaka A, Bass J (2007). "The clockwork of metabolism". Annual Review of Nutrition. 27: 219–40. doi:10.1146/annurev.nutr.27.061406.093546 (https://doi.org/10.1 146%2Fannurev.nutr.27.061406.093546). PMID 17430084 (https://pubmed.ncbi.nlm.nih.gov/1743 0084).

Retrieved from "https://en.wikipedia.org/w/index.php?title=Anabolism&oldid=991878957"

This maps was use wellow as a December 2020, at 07:50 (0102).

hind is avaluativ updat the Grandov Converse Attabilities when Attability is togethered transment of the Warmatip Foundation, but , a participant to the Tanza of the and Theory Policy. Weighedistically tagethered tradicities of the Warmatip Foundation, but , a construction representation

WikipediA

Catabolism

Catabolism (/kə'tæbəlɪsm/) is the set of metabolic pathways that breaks down molecules into smaller units that are either oxidized to release energy or used in other anabolic reactions.^[1] Catabolism breaks down large molecules (such as polysaccharides, lipids, nucleic acids, and proteins) into smaller units (such as monosaccharides, fatty acids, nucleotides, and amino acids, respectively). Catabolism is the breaking-down aspect of metabolism, whereas anabolism is the building-up aspect.

Cells use the monomers released from breaking down polymers to either construct new polymer molecules or degrade the monomers further to simple waste products, releasing energy. Cellular wastes include lactic acid, acetic acid, carbon dioxide, ammonia, and urea. The creation of these wastes is usually an oxidation process involving a



Schematical diagram

release of chemical free energy, some of which is lost as heat, but the rest of which is used to drive the synthesis of adenosine triphosphate (ATP). This molecule acts as a way for the cell to transfer the energy released by catabolism to the energy-requiring reactions that make up anabolism. (Catabolism

Leen as destructive metabolism and anabolism as constructive metabolism). Catabolism, therefore, provides the chemical energy necessary for the maintenance and growth of cells. Examples of catabolic processes include glycolysis, the citric acid cycle, the breakdown of muscle protein in order to use amino acids as substrates for gluconeogenesis, the breakdown of fat in adipose tissue to fatty acids, and oxidative deamination of neurotransmitters by monoamine oxidase.

Contents

Catabolic hormones Etymology See also References External links

Catabolic hormones

There are many signals that control catabolism. Most of the known signals are hormones and the molecules involved in metabolism itself. Endocrinologists have traditionally classified many of the hormones as anabolic or catabolic, depending on which part of metabolism they stimulate. The soreled classic catabolic hormones known since the early 20th century are cortisol, glucagon, and arrenaline (and other catecholamines). In recent decades, many more hormones with at least some catabolic effects have been discovered, including cytokines, orexin (also known as hypocretin), and melatonin.

Etymology

The word *catabolism* is from <u>New Latin</u>, which got the roots from <u>Greek</u>: κάτω *kato*, "downward" and βάλλειν *ballein*, "to throw".

See also

- Autophagy
- Dehydration synthesis
- Hydrolysis
- Nocturnal post absorptive catabolism
- Psilacetin § Pharmacology
- Sarcopenia

references

de Bolster, M.W.G. (1997). "Glossary of Terms Used in Bioinorganic Chemistry: Catabolism" (https://web.archive.org/web/20170121172848/http://www.chem.qmul.ac.uk/iupac/bioinorg/CD.html#8#8). International Union of Pure and Applied Chemistry. Archived from the original (http://www.chem.qmul.ac.uk/iupac/bioinorg/CD.html#8) on 2017-01-21. Retrieved 2007-10-30.

External links

Media related to Catabolism at Wikimedia Commons

Retrieved from "https://en.wikipedia.org/w/index.php?title=Catabolism&oldid=1009266081"

This page says had added on 27 Polynomy 2021, of 17 (10 (UTC).

That is available under the Creative Columnois Attribution-SheseAtha Lownser additional works may apply. By using the star, you agree to the Terms of the and Prescy Policy. Wildpedable's a registered tribument of the Volutriada Foundation, for , 4 now-profit arganization



clinician's brief

Part 1: Feline Anesthesia: A Comprehensive Protocol Starts at Home

ANESTHESIOLOGY & PAIN MANAGEMENT SPONSORED



Sponsored by Jurox

 $https://www.cliniciansbrief.com/article/part-1-feline-anesthesia-comprehensive-protocol-starts-home?oly_enc_ld=0674l2232356E8U$

A Good Feline Anesthesia Experience Is Important

Visiting a veterinary hospital can be stressful for many cats, and owners may be hesitant or resistant to bring their cat to the hospital for annual examinations or even treatment of medical conditions. One survey showed that 33% of surveyed cat owners were stressed just thinking about taking their cat to the hospital, and 58% of owners reported feeling that their cat hates going.¹ Hospitals should work to alleviate such concerns by providing the least stressful experience possible to ensure every patient receives the medical care it needs and deserves.

Anesthesia may be required for diagnostic procedures or treatment, which can add an additional level of stress to the patient and owner. In addition, any adverse effects or perceived negative experience related to anesthesia or the procedure could cause the owner to lose confidence in the hospital and prevent future veterinary care. Therefore, patients, owners, and veterinary hospitals and their teams can all benefit significantly from improving the feline anesthetic experience. Such improvements could even potentially increase an owner's willingness to pursue additional procedures that could be beneficial to their cat's future health.

Anesthesia Starts & Ends at Home

Anesthesia should not be restricted to what happens in the hospital. The ultimate goal of patient preparation for anesthesia is to smartly manipulate brain chemistry through behavior modification, changes in environment, and pharmacological intervention so that, at the time of premedication, the cat is tranquil and fear-free. The process of anesthesia should start and end at home. Cats that are presented for a planned procedure may be at the hospital for an entire day, and due to the potential impact of stress on cardiovascular health, flexible preanesthetic protocols should be implemented to prepare patients for their visit. Explore this 2-part article to see how Peaches benefited from implementation of a feline-friendly, low-stress anesthesia strategy that started and ended in his home. This multi-step strategy is outlined in *Figure 1*.



FIGURE 1 The feline anesthesia hospital visit cycle

THE CASE

Peaches, a 10-year-old, neutered male domestic shorthair cat, was scheduled for a comprehensive oral health assessment and dental treatment, if required. Because of his history of anxiety during veterinary visits, the veterinary team provided a previsit protocol that emphasized the importance of an anesthesia-begins-at-home approach to reduce stress.

Step 1: Peaches at Home

Starting 1 to 2 weeks before the scheduled visit, Peaches' owner was advised by the veterinary team to place his carrier in a location in the home where he likes to spend his time. Placing the carrier in a location in which the cat is familiar and comfortable can help the patient become accustomed to the carrier, thus helping to eliminate any anxiety associated with the carrier when used for the journey to

the clinic. Treats can be periodically placed in the carrier to entice the cat to create a positive experience and association. To simulate the day of travel, the carrier door can be closed while the cat is inside, then reopened after the cat has been praised or given a treat.

It is important that cats be transported in a fit-for-purpose carrier. Ideally, carriers should be made of hard plastic, with openings on the top and side, and constructed so the top can be easily removed (*Figure 2*). Soft-sided mesh carriers are also acceptable. Bedding that the cat is familiar with or that has a familiar scent can also be placed in the carrier to ease anxiety (e.g. a blanket the cat lays on that has not been washed, a favorite toy, an item of clothing belonging to the owner). Bedding can also be sprayed with pheromones and the carrier treated with pheromone wipes. Fifteen minutes should be allowed between spraying or wiping the carrier and exposing the cat to the pheromone to allow for the alcohol base of the pheromone formulation to evaporate.



▲ FIGURE 2 A fit-for-purpose cat carrier

It was also emphasized to Peaches' owner to maintain their normal routine at home before the appointment for as long as possible to avoid anxiety escalating before arrival. Peaches was provided his normal meal the night before his visit. Any remaining food was removed in the morning. Water was available at all times prior to travel per the American Association of Feline Practitioners Anesthesia Guidelines.²

Gabapentin (20 mg/kg PO) was administered ≈1 hour prior to travel for anxiety relief.³ Gabapentin, an analog of the neurotransmitter γ -aminobutyric acid, has good oral bioavailability (mean, 89%-95%) and is almost exclusively cleared by the kidney.^{4,5} It appears to work as a ligand of voltage-dependent calcium channels in the CNS, producing anxiolysis and sedation. Gabapentin can be administered with a small amount of wet food (ie, ≤1 tablespoon) or treat. Decreased signs of stress during transportation and examination have been reported in cats after administration of gabapentin.⁶ A reduced gabapentin dose (6-10 mg/kg PO) should be used for patients with chronic kidney disease to avoid oversedation.⁷ Very fearful patients may benefit from an additional loading dose the evening before the appointment. For cats that experience motion sickness, administering maropitant (1-2 mg/kg PO) the night before the appointment is recommended.

Peaches was placed in his carrier and the door secured and left undisturbed for 10 to 15 minutes before departure to prevent him associating closure of the crate with travel. Because Peaches' owner followed the veterinary team's recommendations of previsit conditioning to help Peaches develop positive associations with the carrier, he learned that his carrier can be a safe place.

Step 2: Travel to the Clinic

Peaches' carrier was covered with a pheromone-treated towel, and the carrier was placed in the middle of the back seat of the vehicle and secured with a seat belt. The handle of the carrier should not be grasped during transportation, as this produces a swinging motion, which can scare the cat. Instead, the carrier should be held with both arms underneath it to provide stability (*Figure 3*). If the temperature outside is much different from room temperature, the vehicle should be heated or cooled to bring it to a comfortable temperature before the cat is loaded into the car.



 FIGURE 3 Hands and arms should be used on either side of the carrier to provide stability.

Step 3: Arrival at the Clinic

Ideally, cats should wait in the car with their owners until an examination room is ready to avoid spending time in the lobby/waiting room area. The veterinary team and owner should communicate via phone/text regarding scheduling and performing this relocation in the quickest and least stressful way possible.

Step 4: Examination

Peaches was brought into a feline-friendly examination room (*Figure 4*), which should have:

- 1. A towel that has been pretreated with a feline pheromone spray.
- 2. All equipment required for a physical examination. This equipment should already be in the examination room before the patient's arrival to expedite the process and keep the veterinary team from leaving and reentering the room. Supplies include a rectal thermometer and lubricant, comb, nail clippers, and otoscope. One to two drops of essential oils can also be placed on a towel to try and sooth the patient (see *Suggested Reading*).
- 3. Plastic containers and lids to avoid sudden noises that can occur with metal containers.

- 4. A weigh scale. A scale in a common area outside the examination room increases the number of times the cat is handled, increasing the likelihood of exposing the cat to a stressor and the risk for escape.
- 5. Pheromone spray. The veterinary team should spray towels to be used in the examination room when opening the hospital and at lunchtime. For this particular patient, Feliway^{*} was used, which has been shown to last 4 hours. If new towels need to be sprayed, 15 minutes should be allowed for the alcohol component of the spray to evaporate prior to using the towel or exposing the patient to the treated surface (see *Suggested Reading*).
- Cat-specific music to help soothe patients. Based on published research, David Teie's *Music for Cats* is recommended and can be played in the examination room^{8,9} (also see *Suggested Reading*).
- 7. A raised bench to place a cat carrier on and for an owner to sit on. There should be no spaces in the examination room under which cats can hide. The carrier can be left open as a safe place for them to retreat.



FIGURE 4 An example of a feline-friendly examination room: 1) warm towel to cover cold surfaces; 2) all equipment needed for the visit prior to patient's arrival; 3) plastic containers to avoid loud noises from metal; 4) a scale in the room rather than attempting to weigh patients in a treatment or waiting area; 5) pheromone spray to treat towels and other surfaces; 6) cat-specific music to soothe feline patients; 7) raised bench with a closed bottom where owners can sit and place carriers.

The veterinary team clarified with the owner whether the at-home protocols were followed. If an owner was unsuccessful at administering the previsit medication to the cat, a team member can administer it at the hospital. In such situations, the patient should be left undisturbed while the drug is absorbed and allowed to take effect. A physical examination can be performed once the cat has become sedated.

The dental procedure to be performed and anesthesia were then discussed with Peaches' owner. Any questions an owner has can be answered at this time (e.g. number of extractions, will it hurt).

Conclusion

A comprehensive, low stress anesthetic protocol that begins at home is critical to ensure a smooth veterinary visit for everyone. A good overall experience for Peaches and his owner will encourage future clinic visits and improved lifelong healthcare. Satisfied clients may also recommend your hospital to other cat owners and leave a positive review on social media.

Because the owner followed the recommended protocol, Peaches was calm upon arrival, allowing for a complete physical examination and preoperative blood work. The examination and blood work confirmed Peaches was fit to proceed with his dental examination. An anesthetic and analgesic protocol was created, which will be discussed in part 2 of this article, in which Peaches will resume his hospital visit at the premedication step (*Step 5*) of the feline anesthesia hospital visit cycle (*Figure 1*).

DISCOVER HOW PEACHES' CASE CONCLUDED IN PART 2



Sheilah Robertson, BVMS (Hons), PhD, DACVAA, DECVAA, DACAW, DECAWBM (WSEL), CVA, MRCVS Courtesy Professor, University of Florida Senior Medical Director, Lap of Love Veterinary Hospice Jenny Salpeter, DVM Brick City Cat Hospital 702 Magnolia Ave Ocala, FL 34471 Kirby Pasloske, BSc (Hons), DVM, DVSc, DACVCP, MANZCVSc Jurox (Canada) Inc.

This article was created equally by **Sheilah Robertson**, BVMS (Hons), PhD, DACVAA, DECVAA, DACAW, DECAWBM (WSEL), CVA, MRCVS; **Jenny Salpeter**, DVM; and **Kirby Pasloske**, BSc (Hons), DVM, DVSc, DACVCP, MANZCVSc.

SPECIAL THANKS

We would like to give a special thanks to Peaches and his owner, Kathleen Burda (DVM), for allowing the authors to share Peaches' real life experience. We hope Peaches' experience will help improve the veterinary experience for all our feline friends and their owners.

REFERENCES

- Volk JO, Felsted KE, Thomas JG, Siren CW. Executive summary of the Bayer veterinary care usage study. *J Am Vet Med Assoc.* 2011;238(10):1275-1282.
- Robertson SA, Gogolski SM, Pascoe P, Shafford HL, Sager J, Griffenhagen GM. AAFP feline anesthesia guidelines. *J Feline Med* Surg. 2018;20:602-634.
- van Haaften KA, Forsythe LRE, Stelow EA, Bain MJ. Effects of a single preappointment dose of gabapentin on signs of stress in cats during transportation and veterinary examination. *J Am Vet Med Assoc*. 2017;251(10):1175-1181.
- 4. Siao KT, Pypendop BH, Ilkiw JE. Pharmacokinetics of gabapentin in cats. *Am J Vet Res.* 2010;71(7):817-821.
- Adrian D, Papich MG, Baynes R, Stafford E, Lascelles BDX. The pharmacokinetics of gabapentin in cats. *J Vet Intern Med*. 2018;32(6):1996-2002.
- 6. Pankratz KE, Ferris KK, Griffith EH, Sherman BL. Use of single-dose oral gabapentin to attenuate fear responses in cage-trap confined

community cats: a double-blind, placebo-controlled field trial. *J Feline Med Surg.* 2018;20(6):535-543.

- 7. Trepanier LA. Applying pharmacokinetics to veterinary clinical practice. *Vet Clin North Am Small Anim Pract.* 2013;43(5):1013-26.
- 8. Snowdon CT, Teie D, Savage M. Cats prefer species-appropriate music. *J Appl Anim Behav Sci.* 2015;166:106-11.
- Hampton A, Ford A, Cox RE 3rd, Liu CC, Koh R. Effects of music on behavior and physiological stress response of domestic cats in a veterinary clinic. *J Feline Med Surg.* 2020;22(2):122-128.

SUGGESTED READING

Aura Cacia Tranquility Essential Oil Blend. https://www.auracacia.com/essential-oils/aura-cacia-tranquilityessential-oil-blend0-5-fl-oz. Feliway Blog. How long does FELIWAY take to work? https://blog.feliway.com/us/how-long-does-feliway-take-to-work. Teie D. Music for Cats. Music for Cats website. https://www.musicforcats.com.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found here.

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. For questions or inquiries please contact

us.

Page 11 of 11

#3 detrimental 2123 harmful Gnectofal 見か(ないのなどな みそのいち みちなみをからしを) Vehement bough zofzj indignant Grystory Willow HTEMP statute 7201 coaptation 722. (weat Amarice Financed Re: ns tate 3/412/22. 3/2013/22 (-223/2/2) genetic (ve lated to Gene) Gr abliterate 2/2/14/214 (4230/4) 19/2014) Remove destroy. hide completely Erythema ear (middle aur - concl inner eur Vasculitis Cerumen= ear Way pars flaced to pars tenso malleus Partensa (transmit sound vibration) Verbular Dicesse Semi cevcular canal > control Vesti bular Nerve > control Batance through the bons of middle earto coch leg × mallens - small home carry sound from ear drum to inner ear. most Reptured ear drug heal without Surgery 3- 5weeks my ringotomi - 2 man 21 mon pus of flood dram of fis media of fis interna Ceruminous gland Myperplass it ossiche K-9 Foley urinary catheber (K-9) Cochles ABRY. BAR Passover, Feast of unleavened Bred T, membrane 12222 Hazz Feast of Weeks, Tympanor bulle 4283 2942 Frast of Ingothering Frash of Tabernacle Festival Francest. **EXHIBIT 7 - 078**

Cart Anecthesia

pheromone spray for Carrier Gabapentin 20mg/129 po + small amoun t of gord (stablespoor) Kidney patient 6-10mg/169 po 1. hour prior to travel for Amxiety Kelset Marop: tant (1-2mg/kg po) might before (Cereniq) Spironoladore - Congerties Heirt forfure Mino cyc/ine bopy gdin L to which one not adequately respond to Mitazophe appetite Furssemide and Ale inhibitor St mulant Contrandication Hyperkalemiq, Addison's disare hallmark - 223-3-2 A cute rend failm 3242 Fosinophilic Bronchopneumopath, (FBP) Aldosterme Brouch in Farspiteal pattern Acembibitor Donut mashape circles on Branchi. Successful manige-Love Journ dation) Turst (central pillar) openhonest conversation (mortar-hold is up) abate Subside 22217)21- UNRAZU. Peribronchia/cuffing (Donutshape) AKin Water , gette similer ーシートに、十 号母を、生間記、告記記と のののgency 上をみの 名叫地 Glowing 20242. EVE incrimental 2222 302 30/012 (Z220) dodge - 518/02 (12/8523) equivocal 24 22 25 2 Avora CUR ONEL AZ Sugestion Fickle - 19/10/3/2 Fickle emilion of: spet - zor vicin banish, climinohe dismis Componsation 4 23 (curdent) Rapport-な生え見た のかいをつる (44) Arworking Hard mortan -刻やろ(はえきなきっかかをなきる)) Convictim 初到 , 究到3272 Credo - 신호, 사포선정 (01 50/1000 JEXA1181 7-079

#4

Clinicians Briefs Ta "Ivis Freckles, Nevi, & Melanosis Pr. G:l Ben-shlomo explicit = clear, direct Nevus (2世) - - Spot or Macule (世社) 전 전 선전경 유전적 (회사회원에 원왕이나 카코성 식가 변화 중이나 학을는 없지, 홍반 과반 Fully Kevealed

Freckles 3777

Chricken Brief under Changes in Iris pigmentation TOP 5 Tips on Radiographic Diagnosis of obstructive Foreign Bodies Dr. Nathalie Rademacher. Nays ileus 25201023 / Functional Mechanical Xray 925 Jilled interform 2.5 (1 (25) L5 (Jumber) Histor / Flowa Jilled 2.0 (25) L5 (Jumber) Histor / Flowa Jilled 2.0 (2 (25) L5 (Jumber) Histor / Flowa Jilled 2.0 (2 (25) L5 (Jumber) Histor / However if obstruction is orad, refus sinds stomach can occur and kinsted intestinal disfension major apparant if obstruction is orad, refus into stomach Orad = toward mouth More distal (Aborad) or more complete obstruction lead to greet at later Pacifica (prestorie) 2222

Pacifier (Presofuit) 年4年間 裂裂 Coaptation Device 習号 +asintan-G間加社 contaminated Pollute opaque 岩島間 not transporm striated (straieitid) 3月51 USUrp (221, 豊田之) 第1 4月2

EXHIBIT 7 - 080





Diagnostic & Treatment Challenges in Canine Hypothyroidism

TOP 5 TAKEAWAYS

Thank you for joining Zomedica and *Clinician's Brief* for this webinar on canine hypothyroidism and making an accurate diagnosis and appropriate treatment plan. We hope you found the information valuable. *Pr. J. Catherine Scoff Moncrieff*

FOLLOWING ARE 5 KEY TAKEAWAYS FROM THE WEBINAR TO BEAR IN MIND AS YOU CONTINUE TO PRACTICE HIGH-QUALITY MEDICINE.



For routine diagnosis of canine hypothyroidism, total T4 ± free T4 and TSH should be used. Total T4 alone is not diagnostic in most cases. Additional testing beyond total T4, free T4, and TSH may be required to confirm diagnosis.

•)	
1		4		
	1		1	

Laboratory data should be evaluated in context. Signalment, including breed, age, and clinical signs, should play a role in deciding whether a dog requires additional testing and/or treatment.



A therapeutic trial of L-thyroxine may be necessary. Laboratory data may not always give a definitive diagnosis. A therapeutic trial should be considered if clinical signs and signalment are highly suggestive of hypothyroidism but laboratory results are inconclusive.



Hypothyroidism is overdiagnosed in dogs. Therapeutic trials of L-thyroxine should not be continued indefinitely without re-evaluating patient status, and not accounting for systemic illness during diagnosis and treatment can often lead to overdiagnosis.



Thyroiditis may complicate diagnosis and treatment of hypothyroidism. The presence of antithyroglobulin, anti-T3, and/or anti-T4 antibodies does not necessarily indicate functional thyroid failure but should increase suspicion for hypothyroidism.

clinician's brief



J. Catharine Scott. Mon correla Shyvo:d Fure Ty more sensitive Mapsthynid TSH High I enshywood of Some Hypothyroid 7 TSH Normal We don't know Why

Hypophyand Fr 4 (1.3-4 TSH A 心到等 2002 10-6 人上台 stress 712 TPR 別ろをとい throxine T4 33 ウデス2 ビスE=(9004) Phirsfis ふくそしらき 当好起午到雪 774 中是、日外石 Free Ty TSH m/2 760-780-2828 5- fweek Recheck Sulfonamide) Care Myposhypod phenubashhu) Care olympic Autoritis - u-situp Jun TT4 - chapest. Fest



clinician's brief

Image Gallery: Feline Fundus Diseases

DJ Haeussler, Jr, DVM, MS, DACVO, The Animal Eye Institute, Cincinnati, Ohio

OPHTHALMOLOGY WAY2017 PEER REVIEWED WEB-EXCLUSIVE

Print/View PDF

Fundic examination should be part of all physical examinations (ie, performed on every patient presented for routine checkup). Abnormalities that can affect the fundus of a cat include inherited disease, acquired disease, infectious disease, manifestations of systemic disease, and congenital abnormalities. When examining the feline fundus, clinicians may also appreciate variations of normal anatomy. The more often a practitioner examines the fundus of feline patients, the more comfortable he or she will become identifying normal variants versus abnormalities.



FIGURE 1 Normal feline fundus

Typical appearance of the holangiotic pattern of the feline fundus in an 8-year-old castrated domestic short-haired cat. The retinal vasculature has three pairs of cilioretinal arteries (**red arrows**). The nontapetum is also present at the inferior aspect of the fundus (**white arrow**) and is usually very dark brown. The optic nerve (**black arrow**) is typically located in the tapetum, is nonmyelinated, and is gray to dark gray.¹ Flash artifacts are present in both the superior and inferior aspects of the image (**blue arrows**).

EXHIBIT 7 - 084



FIGURE 2 Nonpigmented nontapetal fundus

Appearance of a normal color dilute, nonpigmented, nontapetal fundus in a 4-year-old spayed domestic short-haired cat. The nontapetal fundus is diffusely nonpigmented, allowing visualization of choroidal vasculature; this appearance is often misdiagnosed as hemorrhage but is normal and unrelated to vision loss.¹ This type of fundus can be seen in breeds such as the Siamese, ragdoll, Birman, Himalayan, and many others. Practitioners should always examine both eyes for comparison. Flash artifacts are present in both the superior and inferior aspects of the image (**blue arrows**).



Page 4 of 15

FIGURE 3 Retinal degeneration; progressive retinal atrophy

A 3-year-old spayed Siamese cat has diffuse tapetal hyperreflectivity, severe vascular attenuation noted by lack of visible vessels on the tapetum (red arrows), and optic nerve pallor (white arrow) consistent with rod-cone degeneration. The condition was initially described in Abyssinian and Somali cats², but the gene mutation causing rod-cone degeneration has since been found in 14 of 41 breeds sampled,² including the Siamese cat. Persian cats can be affected as early as 2 to 3 weeks of age; the condition is usually advanced by 16 weeks of age.² Abyssinian cats are typically affected by 4 weeks of age and show advanced progression by 1 year of age.² Patients typically have dilated pupils and rapidly become completely blind after initial onset. A flash artifact is present just inferior to the optic nerve (blue arrow).



FIGURE 4A Retinal detachment

A 10-year-old spayed Siamese cat was presented for acute-onset blindness and mydriasis associated with systemic hypertension (mean arterial pressure = 215 mm Hg) secondary to uncontrolled azotemia.³ The retinal vessels were apparent without the use of a lens. Note the fluctuant, serous detachment with retinal tissue visualized immediately posterior to the lens from 6 o'clock to 11 o'clock and from 11 o'clock to 3 o'clock (**red lines**). In addition, pinpoint, focal retinal hemorrhage (**black arrow**) is apparent. Despite treatment of underlying systemic disease, the cat did not recover vision. A flash artifact (**blue arrow**) is present centrally at the inferior aspect of the image.



FIGURE 4B Retinal detachment

Appearance of fundus in the Siamese cat in **Figure 4A**, 3 weeks later. A complete serous retinal detachment with subretinal fluid (**red arrows**) and preretinal hemorrhage (**black arrow**) is evident, along with intraretinal hemorrhaging (**white arrows**). An artifact is present at the inferior aspect of the image (**blue arrow**).



FIGURE 5 Hypertensive retinopathy

A 14-year-old castrated domestic short-haired cat with multifocal, diffuse, hypertensive retinopathy. The patient was referred for chronic epiphora associated with herpesvirus, but on complete ophthalmic examination, multifocal retinal detachments, which appear as patchy-lime green areas on the fundus, with subretinal edema were found. Further diagnostic workup revealed hypertension and mild azotemia. After initiating appropriate antihypertensive therapy, the cat became normotensive. After 2 months, retinal edema had resolved. The cat never lost vision. Note the flash artifact (**blue arrow**) at the inferior aspect of the image.



FIGURE 6 Subretinal hemorrhage; hypertensive retinopathy

A 13-year-old castrated domestic short-haired cat with large, diffuse, subretinal hemorrhaging (**white arrow**) secondary to retinal detachment and tearing. The patient had negative direct and consensual pupillary light reflexes, menace response, and dazzle reflex. In addition, both severe systemic hypertension and chronic renal failure were confirmed. Unfortunately, this cat never regained vision. Flash artifacts (**blue arrows**) are noted at the center of the image.


FIGURE 7 Chorioretinal scar

A 14-year-old domestic medium-haired cat with a large chorioretinal scar (white arrow) and retinal degeneration. Definitive cause of the scar cannot be determined based on this image. In patients with retinal detachment secondary to systemic hypertension, this appearance of the retina (ie, reattachment) is common after the patient undergoes proper blood pressure management. A line of demarcation, sometimes described as a high watermark, is evident (**black arrow**) where the edge of the retinal detachment was located. What appears to be a flash artifact in the superior aspect of the images is actually tapetal thinning (red arrow) associated with the chorioretinal scar. Typically with chorioretinal scars, the retina is thin and therefore the tapetum will become hyperreflective with any light that is applied. This patient maintains vision in this eye.



Page 12 of 15

FIGURE 8 Complete retinal detachment with subretinal infiltrate

A 3-year-old spayed domestic short-haired cat with complete retinal detachment and subretinal cellular infiltrate (**white arrows**) secondary to feline immunodeficiency virus (FIV). Other rule-outs for this condition include fungal disease (eg, cryptococcosis, histoplasmosis, blastomycosis), neoplasia, protozoal disease (eg, toxoplasmosis), and viral disease (eg, FeLV). Initially, the patient presented with pars planitis (ie, inflammation associated with the ciliary body), which then progressed to subretinal infiltrate (with adjacent subretinal fluid) and complete retinal detachment. The patient also has subretinal petechiae (**red arrow**). Unfortunately, the cat never regained vision. A flash artifact is present in the inferior aspect of the image (**blue arrow**).

REFERENCES

- Stiles J. Feline ophthalmology. In: Gelatt KN, Gilger BC, Kern TJ, eds. *Veterinary Ophthalmology*, vol II. 5th ed. Ames, IA: Wiley-Blackwell; 2013:1520-1521
- Stiles J. Feline ophthalmology. In: Gelatt KN, Gilger BC, Kern TJ, eds. Veterinary Ophthalmology, vol II. 5th ed. Ames, IA: Wiley-Blackwell; 2013:1525-1527.
- Cullen CL, Web AA. Ocular manifestations of systemic disease. Part 2: the cat. In: Gelatt KN, Gilger BC, Kern TJ, eds. *Veterinary Ophthalmology*, vol II. 5th ed. Ames, IA: Wiley-Blackwell; 2013:1984-

1985.

SUGGESTED READING

Gelatt KN. *Color Atlas of Veterinary Ophthalmology*. Baltimore, MD: Lippincott Williams & Wilkins; 2001:197-254.

Martin CL. *Ophthalmic Disease in Veterinary Medicine*. Alfred Place, London: Manson Publishing; 2005:401-460.

AUTHOR

DJ Haeussler, Jr

DVM, MS, DACVO The Animal Eye Institute, Cincinnati, Ohio

DJ Haeussler Jr, DVM, MS, DACVO, is the founder and owner of The Animal Eye Institute, which has locations in Cincinnati and Dayton, Ohio, and Florence, Kentucky. Dr. Haeussler earned his DVM and MS from The Ohio State University, where he also completed a residency in comparative ophthalmology. He completed 2 internships at Garden State Veterinary Specialists in Tinton Falls, New Jersey. Dr. Haeussler has been published in many peer-reviewed publications and is the author and publisher of *Recognition of Canine Ocular Diseases*. Dr. Haeussler enjoys resident development and lecturing on ophthalmologic disease.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found here.

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice. Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. **For questions or inquiries please contact us.**

EXHIBIT 7 - 096

#7

Clinician's brief * Clevor (vopin: role ophthalmic Solution) New FDA approxed emedic for Dogs

Kendon Kuo, DVM, MS, DACVECC, Auburn University Katherine Gerken, DVM, MS, DACVECC, Auburn University

TOXICOLOGY | JANUARY/FEBRUARY 2021 | PEER REVIEWED

Print/View PDF

Editor's note: The initially published version of this article contained an incorrectly placed arrow. This has been corrected as of January 19, 2021.



https://www.cliniciansbrief.com/article/emesis-induction?utm_mediu...f+Newsletter&utm_campaign=Online+210218&oly_enc_id=067412232356E8U

Feedbac

Page 1 of 4



https://www.cliniciansbrief.com/article/emesis-induction?utm_mediu...+Newsletter&utm_campaign=Online+210218&oly_enc_id=067412232356E8U Page 2 of 4

EXHIBIT 7 - 098



For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units **can be found here.**

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. For questions or inquiries please contact us.

clinician's brief

Differential Diagnosis: Lymphocytosis

Julie Allen, BVMS, MS, MRCVS, DACVIM (SAIM), DACVP (Clinical), Durham, North Carolina

INTERNAL MEDICINE | SEPTEMBER 2020 | PEER REVIEWED



Following are differential diagnoses for patients presented with lymphocytosis.

Age-related cause (eg, dogs and cats <6 months of age often have mild

lymphocytosis due to vaccination or exposure to novel antigens)

- Antigenic stimulation
 - Immune-mediated disease (rare; eg, immune-mediated hemolytic anemia in cats)
 - Infection (most commonly, Ehrlichia canis; rarely, protozoal [eg, Leishmania infantum], Spirocerca lupi, FIV)
- Endocrine disease
 - Hyperthyroidism (cats; usually mild; can be seen prior to diagnosis [possibly epinephrine-related] or secondary to methimazole treatment)
 - Hypoadrenocorticism (primarily dogs; lack of a stress leukogram in a sick patient can indicate disease)
- Lymphoid neoplasia
 - Acute lymphoblastic leukemia
 - Chronic lymphocytic leukemia (± small cell lymphoma)
- Nonlymphoid neoplasia (eg, thymoma)
- Physiologic (eg, epinephrine-induced) response (primarily cats)

REFERENCES

- Avery AC, Avery PR. Determining the significance of persistent lymphocytosis. Vet Clin North Am Small Anim Pract. 2007;37(2):267-282.
- Burton AG, Borjesson DL, Vernau W. Thymoma-associated lymphocytosis in a dog. Vet Clin Pathol. 2014;43(4):584-588.
- Campbell MW, Hess PR, Williams LE. Chronic lymphocytic leukaemia in the cat: 18 cases (2000-2010). *Vet Comp Oncol.* 2013;11(4):256-264.

- Seelig DM, Avery P, Webb T, et al. Canine T-zone lymphoma: unique immunophenotypic features, outcome, and population characteristics. *J Vet Intern Med.* 2014;28(3):878-886.
- Sprague WS, TerWee JA, VandeWoude S. Temporal association of large granular lymphocytosis, neutropenia, proviral load, and FasL mRNA in cats with acute feline immunodeficiency virus infection. *Vet Immunol Immunopathol.* 2010;134(1-2):115-121.
- Wakayama JA, Furrow E, Merkel LK, Armstrong PJ. A retrospective study of dogs with atypical hypoadrenocorticism: a diagnostic cut-off or continuum? J Small Anim Pract. 2017;58(7):365-371.

AUTHOR

Julie Allen

BVMS, MS, MRCVS, DACVIM (SAIM), DACVP (Clinical) Durham, North Carolina

Julie Allen, BVMS, MS, MRCVS, DACVIM (SAIM), DACVP (Clinical), is a former clinical assistant professor of clinical pathology at Cornell University. She earned her veterinary degree from University of Glasgow and her MS from Iowa State University, where she completed a rotating internship in small animal medicine and surgery and a residency in small animal internal medicine. She also completed a residency in clinical pathology at North Carolina State University. Dr. Allen focuses on cachexia/anorexia, endocrinology, and hepatobiliary and pancreatic disease and has committed her career to improving the diagnosis of disease.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found here.

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice. Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part

Top 5 Reproduction Concerns in Dogs

Stefano Romagnoli, DVM, MS, PhD, DECAR University of Padua Padua, Italy



Ovulation Timing

Identifying the day of ovulation in the bitch is becoming increasingly important in small animal practice, not only for maximizing fertility but also for proper management of canine parturition, high-risk pregnancy management, and cycle manipulation with hormone therapy (*Table 1*). The most practical way to identify canine ovulation is to perform vaginal cytology

every 2 to 3 days starting from the onset of proestrus and then running progesterone assays once vaginal epithelial cells reach ≥50% superficial cells (Figure1). Serum progesterone is typically <1.0 ng/mL in early proestrus, around 2.0 (±0.5) ng/mL on the day of luteinizing hormone (LH) surge, and 4-10 ng/mL at the time of ovulation. Canine ovulation may take up to 2 to 3 days; oocytes then require an additional maturation period of 48 to 72 hours before fertilization is possible.1 Canine oocytes are viable for up to 170+ hours postovulation, but because of the time required for canine oocytes to mature, the optimal breeding time is 2 to 4 days postonset of ovulation. Conception can occur, albeit with likely a small litter size, if the bitch is bred as early as 7 days before or as late as 5 days after ovulation.

▲ FIGURE 1 Vaginal smear of a bitch in estrus. The epithelial cells can be defined as keratinized (or cornified) because of their angular borders and because most of their nuclei are pyknotic, faint, or absent. The percentage of keratinized epithelial cells is >80%, which is typical of full heat. 100× objective

TOP 5 REPRODUCTION CONCERNS IN DOGS

- 1. Ovulation Timing
- 2. Pyometra
- 3. Urinary Incontinence
- 4. Benign Prostatic Hypertrophy
- 5. Ovarian Remnant Syndrome

Pyometra

Pyometra is a diestrual disease typical of adult intact bitches. Its occurrence is strongly influenced by sequential progestational stimulation (normal diestrus or treatment with progestins) of the uterus. Females giving birth regularly throughout their reproductive lives are less likely to develop pyometra than those that do so rarely or never (author experience). During the luteal phase of the estrous cycle, the canine endometrium proliferates and secretes endometrial fluid (ie, uterine milk) while the cervix remains closed and myometrial contractility is inhibited (Table 2). Fluid accumulates in the endometrial glands, which then dilate and can become fairly large (diameter, 0.3-2.0 cm; author experience). The endometrial pathology that develops is referred to as cystic endometrial hyperplasia (CEH), which is a precursor to some pyometras, as uterine milk itself constitutes an inflammatory stimulus and is an excellent culture medium for bacteria. CEH is a physiologic phenomenon; its regression starts during the second half of diestrus. CEH may not entirely disappear from some sections of the endometrium with time and repeated open (nonpregnant) cycles; this increases the chance of persistent endometrial inflammation. Gestation is widely thought to be protective and to prevent CEH lesions from developing in areas of the endometrium where placental attachment occurs. However, pyometra can occur in a single uterine horn or part of a horn, with pregnancy in the opposite horn or another portion of the same horn.

Pyometra should always be treated with specific antibiotics (based on culture and susceptibility testing) and fluid therapy. Bitches not intended for breeding should undergo ovariohysterectomy (*Figure 2*, next page). Medical management includes myocontractant drugs such as prostaglandin F2 α (PGF2 α) or prostaglandin E (*Table 3*, next page). Treatment is continued until

TABLE 1

REASONS TO TIME OVULATION IN THE BITCH

Goal	Method Breed on days 2 and 4 postovulation with fresh or fresh-chilled semen or on day 3 and/ or 4 postovulation with frozen semen	
Maximize conception rates and litter size		
Predict date of parturition	Due date is 63 days (+/- 1 day) from ovulation; ovulation must be properly timed using vaginal cytology and serum progesterone assay	
Evaluate proper breeding management in the diagnostic investigation of fertility cases	Bitches bred outside their optimal fertile window will have questionable fertility	
Choose the right time for hormonal administration	Progestogen treatment or estrus-inducing drug administration should be avoided during the 2-month diestrus window to avoid overdosing or lack of efficacy, respectively	

TABLE 2

EFFECTS OF ESTROGEN & PROGESTERONE ON REPRODUCTIVE TISSUES*

Structure	Estrogen	Progesterone	
Endometrium Growth, vascularity, edema of the endometrium		Proliferation and secretory activity of endometrial glands	
Cervix	Relaxation and dilatation	Closure	
Myometrium	Stimulation of contractility	Inhibition of contractility	
Uterine Stimulation of migration lumen of polymorphonuclear cells into the lumen		Inhibition of migration of polymorphonuclear cells into the lumen	

*These effects are observed during endogenous secretion as well as after exogenous administration.

CEH = cystic endometrial hyperplasm LH = luteinizing hormone PGF2 α = prostaglandin F2 α



▲ FIGURE 2 Dilated uterus of a bitch with pyometra

TABLE 3

COMMONLY USED PROSTAGLANDIN COMPOUNDS TO INDUCE LUTEOLYSIS & CAUSE UTERINE CONTRACTILITY IN BITCHES

PGF2 α or E*	Daily Dose	Administrations Per Day/Route
Natural PGF2 α (PGF2 α) Dinoprost (PGF2 α)	50 µcg/kg	2-4/SC (author experience)
Cloprostenol (PGF2 α analog)	1 µcg/kg	1/SC
Alfaprostol (PGF2 α analog)	20 µcg/kg	2/SC
Fenprostalene (PGF2 α analog)	2.5 µcg/kg	1/SC
Misoprostol (PGE)	10 µcg/kg	2/PO

*Prostaglandins should be used with caution to treat a closed-cervix pyometra because of the risk for uterine rupture or for pushing uterine pus retrograde into the oviducts. Most PGF2 α compounds cause some side effects (eg, panting, vomiting, diarrhea) for the first few days of treatment, but adverse events can be avoided by starting with half the normal dose and gradually achieving the full dose within the first 2 to 3 days of therapy. Misoprostol Is a human compound that causes only uterine contractions (no luteolysis) in bitches and queens with only mild GI side effects.

ultrasonographic images show an empty, normal uterus and there is clinicopathologic evidence of absence of leukocytosis. When available, aglepristone (a progesteronereceptor antagonist) can be effective in treating closed-cervix pyometra and can be used safely in breeding bitches. If no progesteronereceptor antagonist is available, surgery is the only option for a closed-cervix pyometra.¹

Urinary Incontinence

Urinary incontinence (UI) is the involuntary loss of urine that occurs when the bladder is still in its filling phase and the animal is typically recumbent and/or standing.

The most common reason for UI in spayed bitches is urethral sphincter mechanism incompetence (USMI)-a reduced urethral closure due to weakening of the urethral sphincter that commonly develops after spaying. USMI is thought to result from lack of estrogenic stimulation.² Ovariectomy or ovariohysterectomy increases the risk for developing UI, as evidenced by its incidence in spayed bitches (up to 20%), and a relative risk for UI ≈8× higher in spayed than intact bitches.^{3,4} Spayed bitches account for ≈75% of canine cases, although the problem is sometimes observed in prepubertal dogs due to congenital conditions.⁴ In prepubertal animals, 1 or both ureters terminating at the apex of the bladder neck, the level of the urethra, or the cranial vagina can cause continuous dribbling of urine. Pathologic development of the urogenital system in intersex conditions can also cause UI.

The treatment of choice for UI caused by USMI involves oral administration of sympathomimetic drugs or estriol (other estrogens should not be used).⁵

Phenylpropanolamine, an α -agonist available for veterinary use in many countries, can be used at 1 mg/kg PO q8-12h. Pseudoephedrine can also be used at 1.5 mg/kg PO q8-12h. Having the bitch maintain a small bladder during periods of recumbency is helpful. In many animals, the efficacy of both sympathomimetic and estriol medications tends to decrease over time despite increasing dosages, perhaps because of estrogen-receptor desensitization. Because of the multifactorial character of this condition, no single treatment is 100% effective, especially long-term. Recently, the gonadotropin-releasing hormone agonist deslorelin has shown some efficacy, providing full continence in \approx 50% of treated bitches and an improved response to other drugs in \approx 20% of bitches.⁶

Benign Prostatic Hyperplasia The prostate of intact male dogs increases in weight until 4 years of age.7 The growth process is characterized by cellular hyperplasia resulting in a smooth, symmetrical, nonpainful enlarged gland. Benign prostatic hyperplasia (BPH) may result in androgen-dependent hypertrophy and the development of cysts of increasing size within the prostatic parenchyma. Small retention cysts may be evident in as many as 16% of dogs by 2 years of age.⁸ Prostatic infectious disease is associated with more cysts and larger gland size; bacteria ascend the urethra and settle in the cystic fluid. Hematogenous spread of bacteria, bacterial seeding from the kidneys and bladder via urine or from the testicles, and epididymis via semen can also occur. BPH incidence increases to >80% with advanced age,7,9 but not all dogs show clinical signs. Prostatic growth and secretion are modulated by 5αdihydrotestosterone (5 α -DHT), the active androgen at the intracellular level. DHT is a metabolite of testosterone produced via the action of 5α reductase.

The most common clinical signs of BPH are bloody penile discharge and hematuria or hematospermia.¹⁰ As the prostate enlarges, dyschezia, dysuria, poor semen quality, or infertility may be observed; this depends on the degree of prostatic fluid alterations. Increased prostatic size and presence of prostatic cysts on abdominal ultrasound are common findings (Figure 3). Urinalysis helps rule out urinary tract disease as a cause of penile discharge. Cystitis, if present, should be treated concurrently. BPH can be distinguished from prostatitis by lack of pain on transrectal prostatic palpation. Acute and chronic prostatitis will both present with leukocytes in the prostatic fluid sediment. Differentiating BPH from prostatic adenocarcinoma (PA) is more challenging, but PA is rare and is less common in intact males. A treatment course for BPH quickly eliminates clinical signs. Fine-needle aspiration or prostatic biopsies are diagnostic for PA.

Castration is curative. Recent studies suggest that incidence of prostatic carcinoma may be higher in castrated dogs than in intact dogs.¹¹ Treatments that do not decrease libido and fertility are finasteride (0.1-0.5 mg/kg [maximum, 5.0 mg] q24h for life) and osaterone acetate (0.25-0.5 mg/kg q24h for





▲ FIGURE 3 Ultrasonographic image of a typical aspect of canine benign prostatic hyperplasia. The prostate is increased in size (measuring 61.2 [diameter 1] × 65.1 mm [diameter 2]) and features 3 cysts, the largest of which (diameter 3) has a diameter of 2.5 cm.

January 2017 cliniciansbrief.com

EXHIBIT 7 - 106

85

7 days). Finasteride works by blocking conversion of testosterone to DHT by interfering with the 5α -reductase enzyme.¹² Osaterone, a progestogen, competitively binds androgen receptors, which prevents testosterone from binding within the prostatic parenchyma. Other treatments include:

- Chlormadinone acetate (0.1-0.3 mg/kg PO q24h for 1 month)¹³
- Deslorelin (one 4.7-mg or 9.4-mg implant works for 6 or 12 months, respectively)
- Delmadinone acetate (1-2 mg/kg IM or SC; repeat in 4-7 days if needed)

Ovarian Remnant Syndrome

Ovarian remnant syndrome (ORS), the occurrence of heat after ovariectomy/ovariohysterectomy, is normally caused by ovarian tissue not completely removed during surgery. It should not be confused with ectopic adrenocortical tissue, which does not produce enough gonadal steroid to produce estrus signs. A less common cause of ORS can be a piece of ovarian tissue accidentally dropped into the abdominal cavity during surgery. Such pieces of tissue can establish vascular connections with the omentum or the serosa of abdominal viscera and become active again, allowing follicular development. Normal cyclicity has been reported in experimental cases of bitches in which a sliced fragment of ovary was purposefully left in the abdomen and later revascularized.14

MEDICATIONS CITED IN THIS ARTICLE NOT COMMERCIALLY AVAILABLE IN THE UNITED STATES FOR TREATING DOGS:

- Aglepristone
 - Deslorelin
 - Osaterone
 - Delmadinone



Bitches with ORS may display signs of proestrus or estrus at regular or irregular intervals. Signs of heat may appear from several months and up to 10+ years.¹³ Estrus signs are often characterized by the normal sequence of physical changes typical of proestrus and estrus (eg, attractiveness to males and acceptance, vulvar swelling and discharge, cornified vaginal cytology), and breeding may be observed. Bitches with ORS may exhibit signs of false pregnancy several weeks to a few months following estrus behavior, and false pregnancy may be the only sign if estrus was silent.

Diagnosing ORS begins with confirmation of estrogen stimulation via a cornified vaginal smear in a spayed dog showing signs of heat and exclusion of exposure to exogenous estrogen. LH or anti-Müllerian hormone (AMH) testing may aid with diagnosis. A negative LH test or a positive AMH test is consistent with retained ovarian tissue. If these are nondiagnostic, further testing involves stimulation testing measuring estradiol and/or progesterone following gonadotropin administration. Lack of response to stimulation testing does not always rule out ORS because some remnants do not seem to respond in a typical fashion; in these cases, exploratory laparotomy may be necessary.

Serum progesterone should be assayed on a serum sample collected 1 to 2 weeks after the end of estrus. A serum progesterone concentration of >2.0 ng/mL indicates presence of active luteal tissue. Laparotomy can be performed looking for a small piece of yellowish tissue at the level of the ovarian stump or the broad ligament. All tissues removed at surgery should be submitted for histopathology.

Conclusion

Practitioners should stay abreast of these challenges to be able to fulfill client expectations and patient needs.

See page 88 for references.



clinician's brief Diabetes Mellitus Part 1: Diagnosis

Rebecka S. Hess, DVM, Diplomate ACVIM, University of Pennsylvania

ENDOCRINOLOGY & METABOLIC DISEASES | OCTOBER 2009 | PEER REVIEWED



Image above. Some diabetic cats develop a peripheral neuropathy characterized by knuckling of the hindlimbs.

Profile

Page 1 of 10

Definition

Diabetes mellitus (DM) is a common endocrinopathy characterized by decreased insulin production or decreased insulin function. In both cases decreased insulin action results in hyperglycemia.¹

Related Article: Diabetes Mellitus Part 2: Treatment

Systems. Insulin is an anabolic hormone which generally moves amino acids, fatty acids, glucose, and electrolytes into cells, and facilitates cell growth by promoting protein, adipose tissue, and glycogen synthesis. Therefore, decreased insulin production affects all cells in the body.

Lack of insulin action results in muscle and adipose tissue catabolism. Hyperglycemia can lead to glomerular disease (in dogs and cats), cataract formation (dogs), or peripheral neuropathy (cats).²⁻⁴

Genetic Implications. The predisposition of some breeds to develop DM indicates that genetic factors exist. Various genes are probably involved in the pathogenesis of canine and feline DM, and the major histocompatibility complex genes may have an important role in the pathogenesis of DM in dogs. Genetic studies have not been reported

in cats.

Incidence/Prevalence.

In dogs, 64 of every 10,000 patients admitted to hospitals have DM.5 In cats, the incidence was determined to be 2.45 cases per 1000 cat-years-of-risk during a 6-year study period.⁶

Signalment

Breed Predilection. Samoyeds, Australian terriers, miniature schnauzers, toy and miniature poodles, and pugs as well as Burmese cats are at increased risk for DM. German shepherds, golden retrievers, and American pit bull terriers are at decreased risk.⁷

Age. The mean age of onset in dogs is 7 to 9 years; in cats the mean age is 10 years. However, any age dog or cat can develop the disease.

Gender. Female dogs and neutered male cats may be at increased risk for DM.

Causes

The etiology of DM is incompletely understood and is likely multifactorial. In dogs, genetic factors and immune-mediated destruction appear to be important etiologic factors. In cats, amyloid deposition may contribute to development of DM.

Risk Factors

Breed predisposition is an important risk factor. Obesity and carbohydrate-rich diets may increase the risk of DM in cats.

Pathophysiology

Lack of insulin action results in hyperglycemia. When hyperglycemia exceeds the renal threshold of 180 mg/dL in dogs and 280 mg/dL in cats, glucose reabsorption in the proximal renal tubules is incomplete and glucosuria develops. Glucose acts as an osmotic agent, drawing fluid into the urine and causing polyuria; polydipsia develops to compensate for loss of water in the urine.

In addition to decreased mobilization of glucose into cells, lessened insulin action also leads to impaired mobilization of amino and fatty acids into cells. Polyphagia develops to compensate for this "starvation" of the cells.



Signs

History. Polyuria and polydipsia, weight loss, and polyphagia are the most common clinical signs observed. Blindness (dogs) and a plantigrade stance (cats) can also develop.

Diabetic cataracts are common in dogs. They are treated surgically; however, it is important to achieve optimal diabetic regulation prior to surgery.

Physical Examination. Animals may appear normal or be severely compromised. Findings may include:

- > Variable body weight: Underweight, normal, or obese
- > Variable hydration status: Normal or dehydrated
- Hepatomegaly
- Cataracts (dogs) (Figure 1)

- Plantigrade stance (cats) (Figure 2)
- Lethargy, weakness, and acetone breath—mainly noted in severely compromised patients with diabetic ketoacidosis

Most diabetic dogs and cats are middle-aged to older patients and may have concurrent disease.^{2,8} History and physical examination findings may be affected by concurrent diseases such as:

Dogs & Cats

- Urinary tract infection
- Acute pancreatitis
- Neoplasia

Mainly Dogs

- Hyperadrenocorticism
- Hypothyroidism

Mainly Cats

- Other infections
- Chronic renal failure
- Hyperthyroidism

Diagnosis

Definitive Diagnosis

All of the following criteria must be satisfied in order to make a definitive diagnosis:

> Appropriate clinical signs and physical examination findings

- Persistent hyperglycemia
- Glucosuria

Differential Diagnosis Dogs & Cats Polyuria/polydipsia:

- Renal or liver disease
- Hypercalcemia
- Hypokalemia
- Drug administration/iatrogenic: Glucocorticoids, diuretics, anticonvulsants, fluid overload

Weight loss & polyphagia:

- Gastrointestinal parasites
- Protein-losing enteropathy or nephropathy

Hyperglycemia:

- > Drug administration: Glucocorticoids, progesterone, megestrol acetate
- Total parenteral nutrition or other dextrose containing IV fluids
- Postprandial hyperglycemia⁹⁻¹¹
- Diestrus
- Acute pancreatitis
- Factitious measurement

Glucosuria:

Primary renal glucosuria

Mainly Dogs

Polyuria/polydipsia:

- Hyperadrenocorticism or hypoadrenocorticism
- Pyometra
- Diabetes insipidus
- Psychogenic disease
- Polycythemia

Weight loss & polyphagia:

Exocrine pancreatic insufficiency

Hyperglycemia:

- Hyperadrenocorticism
- Pheochromocytoma

Mainly Cats

Polyuria/polydipsia:

Hyperthyroidism

Weight loss & polyphagia:

Hyperthyroidism

Hyperglycemia:

Stress

Acromegaly

Laboratory Findings Complete Blood Count^{2,8}

- Usually normal
- ▶ Red blood cells: Hematocrit may be normal, low, or high
- White blood cells: A "stress leukogram" may be present (mature neutrophilia, monocytosis, lymphopenia, and eosinopenia)
- Neutrophilia with a left shift may be present with infection

Serum Biochemical Profile^{2,8}

- Alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase activity may be increased
- Lipemia and/or hypercholesterolemia may be present

Urinalysis^{2,8}

- Specific gravity may be variable
- Proteinuria, bacteruria, or ketonuria may be present in addition to glucosuria

Urine Culture & Sensitivity^{2,8}

Urine culture and sensitivity are always performed in diabetic patients even if white blood cells are not apparent in the urine sediment. Since dogs and cats with DM may be immunocompromised, they may have urinary tract infections with few or no leukocytes present. Additionally, glucosuria increases the risk for urinary tract infections.¹²

Imaging^{2,8}

Imaging is not needed in order to confirm a diagnosis of DM. However, imaging is

frequently performed because it can help assess the presence of other common concurrent disorders such as acute pancreatitis or neoplasia. In a diabetic patient that has no significant concurrent disease, the only finding may be an enlarged liver on abdominal radiographs and a hyperechoic liver on abdominal ultrasound. Other imaging abnormalities depend on the presence of concurrent disease.

Postmortem Findings^{2,8}

Histopathology of the pancreas and liver is nonspecific in diabetic dogs and cats. Amyloid deposition in beta pancreatic cells has been described in about 70% and 35% of diabetic and nondiabetic cats, respectively.

REFERENCES

References

1. **Canine diabetes mellitus.** In Feldman EC, Nelson RM (eds): *Canine and Feline Endocrinology and Reproduction*, 3rd ed—Philadelphia: WB Saunders, 2004.

2. Concurrent disorders in dogs with diabetes mellitus: 221 cases (1993-1998). Hess RS, Saunders H, Van Winkle TJ, et al. *JAVMA* 217:1166-1173, 2000.

 Association between atherosclerosis and glomerulopathy in dogs. Hess RS, Kass PH, Van Winkle TJ. *Intl J Appl Res Vet Med* 4:224-231, 2006.

4. **Systemic hypertension and proteinuria in dogs with diabetes mellitus.** Struble AL, Feldman EC, Nelson RW, Kass PH. *JAVMA* 213:822-825, 1998.

5. Time trends and risk factors for diabetes mellitus in dogs: Analysis of veterinary medical data base records (1970-1999). Guptill L, Glickman L, Glickman N. *Vet J* 165:240-247, 2003.

6. Epizootiologic patterns of diabetes mellitus in cats: 333 cases (1980-1986). Panciera DL, Thomas CB, Eicker SW, et al. *JAVMA* 197:1504-1508, 1990.

7. Breed predisposition of dogs with diabetes mellitus admitted to a tertiary care facility. Hess R, Kass P, Ward C. *JAVMA* 216:1414-1417, 2000.

8. Pretreatment clinical and laboratory evaluation of cats with diabetes mellitus: 104 cases (1992-1994). Crenshaw KL, Peterson ME. *JAVMA* 209:943, 1996.

9. Reduction of renal transport maximum for glucose by inhibition of NA+-glucose cotransporter suppresses blood glucose elevation in dogs. Kiichiro U, Hikaru Y, Akira O, et al. *Biol Pharm Bull* 29:114-118, 2006.

10. Inclusion of low amounts of fructose with an intraduodenal glucose load markedly reduces postprandial hyperglycemia and hyperinsulinemia in the conscious dog. Shiota M, Moore MC, Galassetti P, et al. *Diabetes* 51:469-478, 2002.

11. Effects of six carbohydrate sources on diet digestibility and postprandial glucose and insulin responses in cats. de-Oliveira LD,Carciofi AC, Oliveira MCC, et al. *J Anim Sci* 86:2237-2246, 2008.

12. Neutrophil adherence and movement in poorly and wellcontrolled diabetic dogs. Latimer KS, Mahaffey EA. *Am J Vet Res* 45:1498-1500, 1984.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units **can be found here**.

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. For questions or inquiries please contact us.

Page 10 of 10

clinician's brief

Diabetes Mellitus Part 2: Treatment

Rebecka S. Hess, DVM, Diplomate ACVIM, University of Pennsylvania

ENDOCRINOLOGY & METABOLIC DISEASES | NOVEMBER 2009 | PEEN REVARINES

Medications

Insulin

Intermediate- and long-acting insulins are used for long-term management of diabetes mellitus (DM).

Intermediate-Acting Insulins

- Neutral protamine Hagedorn (NPH) (Humulin N, elanco.com; Novolin N, norvonordisk.com): Validated in dogs and cats, but not approved for use by the FDA^{1,2}
- Purified porcine insulin zinc (Vetsulin & Caninsulin, intervet.com): The only insulin product currently FDA approved for use in dogs and cats^{3,4}
- Protamine zinc insulin (PZIR) (ProZinc, boehringer-ingelheim.com): In final stages of review by the FDA and expected to be approved for cats by end of this year; studies reported in cats⁵

Longer-Acting Insulins

Page 1 of 9

- Glargine insulin (Lantus, sanofi-aventis.us): Studies reported are mainly in cats; not FDA approved for use in dogs or cats⁶
- Detemir insulin (Levemir, norvonordisk.com): Preliminary studies reported in cats; not FDA approved for use in dogs or cats

Administration

All intermediate-acting insulins should be started at a dose of $0.5 \text{ U/kg Q} 12 \text{ H.}^{1,3,6}$ Longer-acting insulins should also be started at 0.5 U/kg.

Dogs almost always require twice-daily insulin. Some cats receiving longer-acting insulins may be treated effectively with once-daily injections, but most cats require twice-daily injections, even when treated with longer-acting insulins.

Veterinary insulin products (porcine insulin zinc, PZIR) are produced in U40 formulations and must be administered with U40 syringes. Human insulin products (NPH, glargine, detemir) are produced in U100 formulations and must be administered with U100 syringes.

Contraindications & Precautions

Insulin can cause hypoglycemia if the dose is too high, a cat or dog has transient DM and no longer requires insulin, the patient did not eat its entire meal but received a full dose of insulin, or the patient exercised excessively without gradual adjustment of diet and insulin.

Mistakenly administering a human insulin product with a U40 syringe results in insulin overdose and may cause potentially fatal hypoglycemia. Administering a veterinary insulin product with a U100 syringe results in insulin underdose and the animal could potentially develop complications such as diabetic ketoacidosis.

Glipizide

Some cats with mild hyperglycemia and no significant concurrent disease may respond well to treatment with an oral hypoglycemic medication. The sulfonylurea glipizide, which stimulates insulin secretion from pancreatic beta cells, is the oral hypoglycemic most studied in diabetic cats. One study7 found that 14% (7/50) of cats with uncomplicated DM responded well to treatment with glipizide alone. Potential side effects of glipizide include vomiting shortly after administration, hypoglycemia, increased serum hepatic enzyme activities, and icterus.

Administration

- > 2.5 mg/cat PO Q 12 H for 2 weeks
- If adverse side effects are not observed by the end of 2 weeks and the cat is still hyperglycemic, the dose is increased to 5 mg/cat PO Q 12 H.
- If blood glucose concentration remains above 300 to 400 mg/dL after 4 weeks, treatment is discontinued and insulin is administered.

Additional Treatment

Activity

Exercise promotes weight loss in obese patients and increases glucose transport and glycogen synthesis. Moderate consistent exercise is recommended at fixed times and patients should be conditioned to exercise gradually. Intense exercise, especially when blood glucose may be low, should be avoided.

Nutrition

Caloric intake should be timed at 12-hour intervals, at a fixed time every day, just prior to insulin injections. The amount of food fed at each meal should also be fixed. If cats do not agree to eat 2 meals a day, they must have food available throughout the day. However, it is useful to offer enticing (appropriate) additional food at 12-hour intervals, just prior to insulin injections.

In dogs, a diet high in insoluble fiber (Prescription Diet w/d,

hillspetnutrition.com; Veterinary Diets DCO, purina.com) promotes weight loss, gradual carbohydrate absorption, decreased postprandial blood glucose fluctuations, and increased insulin sensitivity.⁸ Complex carbohydrates and a fixed protein and restricted fat content also contribute to gradual carbohydrate absorption and decreased postprandial blood glucose fluctuations as well as weight loss.

Diabetic cats are fed a fixed caloric intake of a diet low in carbohydrate content and high in protein (Veterinary Diets DM, purina.com; Prescription Diet m/d, hillspetnutrition.com) with the intent of maintaining optimal body condition.⁹ <u>Client Education</u>

Diabetic animals require life-long, intensive home care as well as constant veterinary monitoring. Owners should:

- Note changes in clinical signs suggestive of hyperglycemia (polyuria/polydipsia, weight loss in spite of good appetite)
- Recognize signs of severe hypoglycemia (ie, seizures, weakness, ataxia). If such signs are observed, the owner can rub corn syrup on the gums until emergency veterinary care can be administered.
- Monitor urine glucose Q 12 H before feeding.
- Note presence or absence of ketones in urine Q 12 H. Ketonuria constitutes an emergency.
- Administer half the dose of insulin and seek veterinary advice if the patient vomits or does not eat its meal.

Cats may infrequently develop transient DM. Intact dogs will rarely develop transient DM that resolves when they are neutered. These cats and dogs may go through a period in which they do not require insulin therapy, and insulin therapy may actually be dangerous, leading to potentially fatal hypoglycemia. Therefore, constant monitoring of clinical signs indicative of insulin overdose (weight gain, lethargy, ataxia, confusion, seizures) and continued monitoring by the veterinarian (glucose curves or fructosamine measurement) are needed.

When presenting care recommendations to owners, it is important to present the gold-standard noted above despite the fact that some owners may not be able (or

EXHIBIT 7 - 121

want) to provide this level of care.

Follow-Up

While 0.5 U/kg is a safe starting dose for insulin, it is usually not the dose that the animal is going to require for long-term treatment. The dose is changed based on clinical signs and glucose curves, which are performed approximately every 2 weeks for 1 to 2 months.

Blood Glucose Curves

- A blood glucose curve is performed by measuring blood glucose concentration every 2 hours for 10 to 12 hours.
- After initial glycemic regulation is achieved (blood glucose should range between 100 and 250 mg/dL for a dog and 100 and 300 mg/dL for a cat), a blood glucose curve is performed every time the owner notices clinical signs consistent with hyperglycemia or hypoglycemia, or when other clinical signs (such as vomiting or signs of lower urinary tract infection) develop.
- If the dog or cat has no clinical problems, a blood glucose curve is performed every 3 to 4 months.

Blood glucose curves and concentrations are always interpreted in view of clinical signs. For example, if a dog is well regulated and has no evidence of polyuria, polydipsia, polyphagia, or weight loss, and blood glucose concentrations range from 180 to 250 mg/dL over a 12-hour period, the dose of insulin does not need to be changed. However, in a dog with the same blood glucose concentrations that has the signs mentioned above, the dose of insulin should be increased.

Serum Fructosamine Concentration

Occasionally cats will not tolerate a glucose curve and blood glucose measurements will not be reliable due to stress hyperglycemia. In this case, serum fructosamine concentration can be used for patient monitoring.

Figure 1: Insulin Dose Too Low

Fructosamine is formed from a nonenzymatic insulin-independent bond of glucose to various serum proteins. Fructosamine level reflects serum blood glucose concentrations over a 1- to 3-week period. Fructosamine can be elevated when the dose of insulin is too low (Figure 1), but it may also be elevated when an insulin dose is too high (Figure 2). Therefore, interpretation of fructosamine concentration, as well as glucose curves, must be performed in consideration of the clinical signs.

Figure 2: Insulin Dose Too High

Somogyi Effect

The Somogyi effect occurs when a high dose of insulin causes potentially fatal hypoglycemia; catecholamines (epinephrine and norepinephrine), glucocorticoids, glucagon, and growth hormone are secreted in response to severe insulin-induced hypoglycemia and cause pronounced hyperglycemia.

Patient Monitoring

In addition to owners monitoring clinical signs, they should also record daily water intake, appetite, insulin dose, glucosuria, and absence of ketonuria. This daily log is brought to the veterinarian at each reexamination. In cats, it may be helpful for the owners to purchase a baby scale and weigh and record the cat's weight once a week.

Complications

Dogs & Cats

- Urinary tract infections
- Peripheral neuropathy
- Glomerulopathy¹⁰

Dogs

- Atherosclerosis¹¹
- Hypertension
- Cataracts
- Uveitis

Course

DM is usually a life-long disease that requires constant adjustment of insulin dose. Cats and dogs may be well regulated for a long time on the same dose of insulin, but will ultimately require adjustments. Concurrent disorders, which develop commonly, complicate the regulation. While the concurrent disorder is untreated, the animal develops insulin resistance and becomes hyperglycemic (Figure 3). Once the concurrent disorder is treated effectively, insulin resistance resolves.

Figure 3: Insulin Resistance Due to Concurrent Disorder

Relative Cost

- Diagnosis: \$
- Evaluation for presence of concurrent disease at time of diagnosis: \$\$\$\$\$
- > Treatment and follow-up care for uncomplicated cases: \$/visit, 3 to 4 visits/year
- Treatment of complicated DM (diabetic ketoacidosis): \$\$\$\$\$

Prognosis

The prognosis for patients with DM is good, as long as the disease is treated and monitored appropriately. This requires significant devotion on the part of the owner and excellent communication between the owner and the veterinarian.

DIABETES MELLITUS-PART 2: TREATMENT • Rebecka S. Hess

References

1. An investigation of the action of NPH human analogue insulin in dogs with naturally-occurring diabetes mellitus. Palm C, Boston R, Refsal K, Hess R. *J Vet Intern Med* 23:50-55, 2009.

2. **Diabetic ketosis and ketoacidosis in cats: 42 cases (1980-1995).** Bruskiewicz KA, Nelson RW, Feldman EC, et al. *JAVMA* 211:188, 1997.

3. Efficacy and safety of a purified porcine insulin zinc suspension for managing diabetes mellitus in dogs. Monroe WE, Laxton D, Fallin EA, et al. *J Vet Intern Med* 19:5, 675-682, 2005.

4. Treatment of 46 cats with porcine lente insulin—A prospective, multicentre study. Michiels L, Reusch CE, Boari A, et al. *J Feline Med Surg* 10:5, 439-451, 2008.
 5. Field safety and efficacy of protamine zinc recombinant human insulin for treatment of diabetes mellitus in cats. Nelson RW, Henley K, Cole C. *J Vet Intern Med* 23:787-793, 2009.

6. Use of glargine and lente insulins in cats with diabetes mellitus. Weaver KE, Rozanski EA, Mahony OM, et al. *J Vet Intern Med* 20:2, 234-238, 2006.

7. Intensive 50-week evaluation of glipizide administration in 50 cats with previously untreated diabetes mellitus. Feldman EC, Nelson RW, Feldman MS. *JAVMA* 210:6, 772-777, 1997.

8. Effects of insoluble and soluble dietary fiber on glycemic control in dogs with naturally occurring insulin-dependent diabetes mellitus. Kimmel S, Michel K, Hess R, et al. *JAVMA* 216:1076-1081, 2000.

9. Use of a high-protein diet in the management of feline diabetes mellitus. Frank G, Anderson W, Pazak H, et al. *Vet Ther* 2:3, 238-246, 2001.

10. Concurrent disorders in dogs with diabetes mellitus: 221 cases (1993-1998). Hess R, Saunders H, Van Winkle T, et al. *JAVMA* 217:1166-1173, 2000.

11. Association between diabetes mellitus, hypothyroidism or
hyperadrenocorticism, and atherosclerosis in dogs. Hess R, Kass P, Van Winkle
T. J Vet Intern Med 17:489-494, 2003.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found here.

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from Clinician's Brief may not be reproduced, distributed, or used in whole or in part

EXHIBIT 7 - 125



clinician's brief

Top 5 Anesthetic Management Differences Between Dogs & Cats

Khursheed Mama, DVM, DACVAA, Colorado State University

ANESTHESIOLOGY & PAIN MANAGEMENT | SEPTEMBER 2020 | PEER REVIEWED



When planning for and managing anesthesia in cats and dogs, there are differences beyond size that should be considered.

Page 1 of 7

Following are 5 of the most common key differences in anesthetic management for cats and dogs according to the author.

Restraint & Instrumentation

Minimal restraint is frequently most effective in achieving efficiency, which is key when working with cats. Previsit oral medications (eg, gabapentin and trazodone) given at home have been shown to minimize anxiety and stress and increase compliance.¹⁻³ Alfaxalone and dexmedetomidine can also help alleviate agitation; these drugs are typically administered IM after the overall health of the cat has been evaluated.

Because of the small size of cats, IV catheterization can be more challenging in cats than in dogs. Although the cephalic vein can be catheterized in both cats and dogs, the medial saphenous vein is more commonly catheterized in cats, and the lateral saphenous vein is more commonly catheterized in dogs. Intubation can also be more challenging in cats because of the size and reactivity of the upper airway. If care is not used, a greater incidence of tracheal tears following intubation is possible^{4,5}; however, use of topical lidocaine on the arytenoids and an appropriate tube without a stiff stylet can greatly minimize these problems. Diligent cuff inflation and disconnection of the tube from the breathing circuit are also important when turning the patient.

Postanesthesia, cortical blindness also has been reported in cats (but not in dogs) and associated with the influence of spring-loaded mouth gags on maxillary artery blood flow^{6,7}; therefore, it is important that use of these devices be minimized or avoided when anesthetizing cats for bronchoscopy, endoscopy, or dentistry.

2

Anesthetic Equipment

A nonrebreathing circuit (eg, Bain) is commonly used to anesthetize cats weighing <11 lb (5 kg). These circuits must be appropriately assembled and used in order to minimize complications, including excessive pressure in the system. A nonrebreathing system also requires higher flow rates on a per-kilogram basis to minimize rebreathing of carbon dioxide, which can dry the respiratory tract and increase patient cooling. Although not routinely used during anesthetic management, there are tools that can help alleviate these concerns by heating and humidifying the breathing system. Pediatric circle systems can be used in cats, but inspiratory and expiratory valves and carbon dioxide absorbent increases the work required for breathing in spontaneously ventilating animals, possibly resulting in fatigue and hypoventilation.

Similar considerations relative to breathing circuits exist for small dogs. Larger dogs can typically be maintained on circle breathing systems with appropriately sized hoses and rebreathing bags.

Medications & Patient Response

Cats differ in their requirements for and responses to numerous medications commonly used in the perianesthetic period. Acepromazine is considered an effective tranquilizer in dogs, particularly when used in combination with other drugs, but equivalent acepromazine-associated tranquilization in cats may not result, despite signs suggesting efficacy (eg, a raised third eyelid). Conversely, dexmedetomidine provides good sedation in both dogs and cats. The anesthetic induction dose needed to facilitate intubation is lower following dexmedetomidine premedication than with acepromazine.⁸

Opioids are reported to cause a higher degree of signs of euphoria or dysphoria in cats than in dogs, especially with IV administration.⁹ The analgesic- and inhalant-sparing effects in cats also differ from those in dogs, and a ceiling effect (ie, increased dose does not result in additional clinical benefits) may occur at a lower dose.¹⁰ Unlike in dogs, large or repeated doses of opioids may result in hyperthermia in cats.¹¹ The cause of hyperthermia is unknown. Elevations in body temperature are not typically reported in dogs, even when panting is observed following administration. Opioid-associated sedation may contribute to lack of hyperthermia in dogs.

Lidocaine given IV with a bolus or constant-rate infusion has been increasingly
used in dogs for its anesthesia-sparing effects and possible analgesic benefits. However, IV lidocaine is not routinely recommended in cats because the associated cardiovascular depression is worse than an equivalent dose of inhalant, and drug-related toxicity is possible.¹² When comparing isoflurane requirements, the minimum alveolar concentration is higher in cats than in dogs.¹³

Monitoring

Cardiovascular and respiratory monitoring can be challenging in cats because of their size and limitations with monitoring equipment not specifically developed for use in cats. For example, many oscillometric noninvasive blood pressure monitors provide only intermittent readings in cats, and obtaining a reliable signal from a Doppler crystal can be difficult. These obstacles can be further complicated by the use of certain drugs (eg, dexmedetomidine) that cause vasoconstriction, bradycardia, and decreased cardiac output. Similar challenges can occur with the use of a pulse oximeter to monitor oxygen saturation. Amplitude of the electrocardiogram may also hinder accurate heart rate measurement and assessment of rhythm changes in cats as compared with dogs. Typically, cats have higher heart rates than dogs, but their blood pressure during anesthesia tends to be more labile or stimulus-responsive. It is therefore important to evaluate physiologic monitors to be used during anesthesia in the clinic to ensure functionality. In addition, using an appropriately sized Doppler crystal or an alternate site (eg, tail vs distal limb) may help improve performance. Similarly, for pulse oximeter probes, placement of a moist gauze sponge over the tongue prior to probe placement can be beneficial.

When a nonrebreathing system is used, side-stream capnography can result in significant underestimation of the end-tidal carbon dioxide tension because of the constant flow of oxygen diluting exhaled gas at the sampling site. A mainstream capnometer can alleviate this issue, but weight on the endotracheal tube can cause kinking or dislodging.

Pain assessment in cats is also more difficult and requires close observation of specific behaviors and interaction with the patient as needed.¹⁴ There are an

increasing number of pain scales and assessment tools available.

Support
Fluid therapy during anesthesia is critical for maintaining blood pressure and vital organ perfusion during anesthesia in cats and dogs. Because older cats are frequently diagnosed with varying stages of renal disease, fluid support is essential in the perianesthetic period.¹⁵ To account for blood volume differences (ie, ≈60-70 mL/kg in cats vs ≈80-90 mL/kg in dogs), the volume of both fluids and blood products should be lowered for cats, especially when administered via bolus. Because universal feline donors do not exist, all cats, including naive cats, should be typed and cross-matched to donors in cases in which use of blood products is anticipated.

Conclusion

Although anesthesia in cats is often thought to be more challenging than in dogs, knowledge of species-specific requirements and responses can help improve patient management during the perianesthetic period.

REFERENCES

- van Haafften KA, Forsythe LRE, Stelow EA, Bain MJ. Effects of a single preappointment dose of gabapentin on signs of stress in cats during transportation and veterinary examination. *J Am Vet Med Assoc*. 2017:251(10):1175-1181.
- Orlando JM, Case BC, Thomson AE, Griffith E, Sherman BL. Use of oral trazodone for sedation in cats: a pilot study. *J Feline Med Surg*. 2016;18(6):476-482.
- 3. Stevens BJ, Frantz EM, Orlando JM, et al. Efficacy of a single dose of trazodone hydrochloride given to cats prior to veterinary visits to reduce signs of transport- and examination-related anxiety. *J Am Vet Med Assoc.* 2016;249(2):202-207.

- Quandt JE. Postintubation tracheal tears in cats. *Clinician's Brief*. 2017;15(6):29-32, 92.
- 5. Mitchell SL, McCarthy R, Rudloff E, Pernell RT. Tracheal rupture associated with intubation in cats: 20 cases (1996-1998). *J Am Vet Med Assoc*. 2000;216(10):1592-1595.
- 6. Stiles J, Weil AB, Packer RA, Lantz GC. Post-anesthetic cortical blindness in cats: twenty cases. *Vet J*. 2012;193(2):367-373.
- Martin-Flores M, Scivani PV, Loew E, Gleed CA, Ludders JW. Maximal and submaximal mouth opening with mouth gags in cats: implications for maxillary artery blood flow. *Vet J.* 2014;200(1):60-64.
- Hunt JR, Grint NJ, Taylor PM, Murrell JC. Sedative and analgesic effects of buprenorphine, combined with either acepromazine or dexmedetomidine, for premedication prior to elective surgery in cats and dogs. *Vet Anaesth Analg.* 2013;40(3):297-307.
- Kamata M, Nagahama S, Kakishima K, Sasaki N, Nishimura R. Comparison of behavioral effects of morphine and fentanyl in dogs and cats. J Vet Med Sci. 2012;74(2):231-234.
- Ferreira TH, Steffey EP, Mama KR, Rezende ML, Aguiar AJA. Determination of the sevoflurane sparing effect of methadone in cats. *Vet Anaesth Analg.* 2011;38(4):310-319.
- Posner LP, Pavuk AA, Roshkar JL, Carter JE, Levine JF. Effects of opioids and anesthetic drugs on body temperature in cats. *Vet Anaesth Analg.* 2010;37(1):35-43.
- Pypendop BH, Ilkiw JE. Assessment of the hemodynamic effects of lidocaine administered IV in isoflurane-anesthetized cats. *Am J Vet Res.* 2005;66(4):661-668.
- 13. Steffey EP, Howland D Jr. Isoflurane potency in the dog and cat. *Am J Vet Res.* 1977;38(11):1833-1836.
- 14. Merola I, Mills DS. Behavioural signs of pain in cats: an expert consensus. *PLoS One*. 2016;11(2):e0150040.

 Grauer GF. Treatment guidelines for chronic kidney disease in dogs & cats: International Renal Interest Society recommendations. *Today's Veterinary Practice*. 2017;7(1):41-53.

AUTHOR

Khursheed Mama

DVM, DACVAA Colorado State University

Khursheed Mama, DVM, DAC Colorado State University. She University and completed an i surgery at University of Guelpl critical patient care at Universi improving anesthetic safety an pain in veterinary patients.

For global readers, a calculator to converto SI units can be found here.

All *Clinician's Brief* content is reviewed fo published content may not reflect recent Material from *Clinician's Brief* may not be without prior permission of Educational

us.

WEBINAR DECISION-MAKING IN GONADECTOMY

RACE-APPROVED (1 CREDIT HOUR)

MARCH 17, 2021

8:00 PM ET (1 HR)

Spay and neuter recommendations are more nuanced than ever before. Make sure you're considering all the factors for your patients and pet owners. Explore the benefits and risks, latest techniques, and age considerations for gonadectomy in dogs and cats in this free CE webinar with Karen M. Tobias, DVM, MS, DACVS.

REGISTER TODAY

ANESTHESIOLOGY & PAIN MANAGEMENT



clinician's brief

Top 5 Tips for Sedation & Anesthesia in Fractious Dogs

Katherine Bennett, DVM, University of Tennessee Christine Egger, DVM, MVSc, CVA, CVH, DACVAA, University of Tennessee

 FIGURE 1 A long extension set directly connected to the catheter, which is placed in the lateral saphenous voin. An injection port is accessible (out of frame).

Aggression represents over 50% of behavior-related problems in dogs,¹ and

fractious animals pose an inherent risk to veterinary staff. Behavior management is the ideal long-term solution for aggressive or fractious animals; however, some surgical or diagnostic procedures require relatively immediate attention and preclude most recommended behavior modifications. Precautions should be taken to ensure both patient and team safety when sedating or anesthetizing these patients.

Following are the authors' tips for safe handling of a sedated or anesthetized fractious dog presented for diagnostic or surgical procedures.

Owner Communication

Communication with the pet owner ahead of the scheduled appointment is critical. Discussion should include current medications, patient behavior at home, and whether the owner is comfortable medicating the patient at home. Owner involvement can help facilitate a team-based approach to safe and effective patient sedation.² In addition, a thorough risk assessment should be explained to the owner, as many sedative medications can have adverse effects on patients with underlying diseases, particularly cardiovascular disease. Patients with underlying systemic disease may require dose alterations and/or alternative drug protocols to account for comorbidities.

Preappointment Preparation

At-home administration of one or more sedatives (eg, trazodone, clonidine, dexmedetomidine, acepromazine, alprazolam; **Table 1**) the day before and the day of the scheduled visit allows for multimodal anxiolysis and can facilitate delivery of additional sedatives in the clinical setting. Caution should be taken when prescribing multiple serotonin-altering medications, as serotonin syndrome is a potentially lethal side effect (see **Serotonin Syndrome**).³ Combining different medications or introducing new serotonin-altering medications to a dog's treatment protocol can have deleterious effects; owners should be informed that, although uncommon, disinhibition of behavioral tendencies⁴ and/or development of aggression⁵ can occur at home. If adverse behavioral effects or signs of serotonin syndrome do not occur, the dose can be gradually increased over 1 to 2 days until the desired dose is reached or the desired effect is achieved.⁶ Alternatively, medications that do not alter serotonin levels (eg, α_2 agonists, benzodiazepines, gabapentin) can be used.

Serotonin Syndrome

Serotonin syndrome, defined as a group of clinical signs associated with administration of serotoninaltering medications (eg, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, antidepressants), although rare in veterinary medicine, can occur when multiple serotonin-altering medications are coadministered.¹⁸ Clinical signs of serotonin syndrome include altered mental status, agitation, nervousness, myoclonus, hyperreflexia, tremors, diarrhea, incoordination, increased heart rate and blood pressure, and hyperthermia.¹⁹ If a patient is already receiving medications for behavior alteration or other reasons, slow introduction of additional medications at lower doses is recommended. Any signs of agitation, restlessness, or myoclonus may suggest serotonin syndrome, and cessation of any additional serotonin-altering medications is recommended.

Common at-home administration protocols include administering oral trazodone, gabapentin, and alprazolam the day before the appointment and on the morning of the scheduled appointment or administering oral acepromazine, gabapentin, and alprazolam, potentially coadministered with maropitant (2 mg/kg PO q24h) to decrease the risk for vomiting after later administration of injectable sedatives

(especially those that contain a pure μ opioid).⁷

TABLE 1

PERIOPERATIVE ANXIOLYTIC & SEDATIVE DOSAGES IN DOGS¹⁵⁻¹⁷

Drug (Drug Category)	Dosage*
Acepromazine (phenothiazine)	0.5-2 mg/kg PO q8h
Alprazolam (benzodiazepine)	0.02-0.04 mg/kg PO q6h
Clonidine (α ₂ agonist)	0.01-0.05 mg/kg PO q12h
Dexmedetomidine gel (a ₂ agonist)	Refer to product insert
Diazepam (benzodiazepine)	1-2 mg/kg PO q8h
Gabapentin (anticonvulsant, neuropathic pain analgesic)	5-10 mg/kg PO q8-12h
Trazodone** (serotonin antagonist and reuptake inhibitor)	2-10 mg/kg PO q8-12h

"Some dosages are anecdotal based on those used in the authors' facility.

**Indicates commonly prescribed medications that, when combined with other serotoninaltering drugs, may place the patient at risk for serotonin syndrome. Careful and controlled introduction of medication combinations can help mitigate risks for serotonin syndrome development.

Sedation Administration

https://www.cliniciansbrief.com/article/top-5-tips-sedation-anesth...f+Newsletter&utm_campaign=Online+211022&oly_enc_ld=0674l2232356E8U Page 4 of 13

EXHIBIT 7 - 136

Top 5 Tips for Sedation & Anesthesia in Fractious Dogs | Clinician's Brief

Many patients may become more stressed in the hospital waiting area, making it

more difficult for sedative medications to reach full efficacy. The owner should be advised to place a muzzle and/or Elizabethan collar on the patient before or just after arrival, if possible. If available, other parts of the hospital (eg, parking lot, grassy relief area, barn) can be used as an environmental distraction for the patient during handling, waiting, and/or sedative administration.⁸ Because dogs use multiple cues (eg, visual, auditory, olfactory) to influence their behavior and/or reactions to their environment,⁹ soft and calm voices and limited personnel involvement are recommended. Pheromone sprays can help reduce anxiety but have not been shown to consistently reduce aggression in dogs.¹⁰

White coat syndrome (ie, the increase in a patient's sympathetic response to stress due to the appearance of medical personnel in white coats or similar clothing) has been well documented in human medicine.¹¹⁻¹³ To reduce the perceived threat of medical personnel, staff members who interact with the patient should avoid wearing white coats or similar hospital clothing while initially handling the patient (ie, from arrival to administration of injectable sedation). Typically, a coat or other outerwear is recommended to be worn over hospital clothing.^{11,12}

Administering sedation via an intramuscular injection (**Table 2**) is preferable and can be done while the patient is walking on a leash, provided the person handling the patient and the person administering the drugs are both experienced enough for a rapid pelvic limb injection and subsequent patient reaction. These drugs are typically used in combination to provide deep sedation and/or general anesthesia. Combining different drug classes (**Table 3**) allows for a dose reduction in all agents, thereby potentially limiting negative adverse effects.

TABLE 2

SEDATIVE DOSAGES IN DOGS¹⁵⁻¹⁷

Drug	Dosage*	Duration of Full Effect**
Acepromazine	0.01-0.03 mg/kg IM	6-8 hours
Alfaxalone	1-3 mg/kg IM	15-20 minutes
Butorphanol	0.1-0.4 mg/kg IM	30-60 minutes
Dexmedetomidine	1-10 μg/kg IM (not to exceed 10 μg/kg)	30-60 minutes
Hydromorphone	0.05-0.1 mg/kg IM	4-6 hours
Ketamine	3-10 mg/kg IM	30-60 minutes
Midazolam	0.1-0.5 mg/kg IM	20-40 minutes
Tiletamine/zolazepam	1-4 mg/kg IM	30-60 minutes

"Some dosages are anecdotal based on those used in the authors' facility.

**Most drugs have a dose-dependent duration of effect (ie, higher doses usually prolong the effect); however, higher doses can also increase the frequency of adverse events.

TABLE 3

SEDATIVE COMBINATIONS & DOSAGE RECOMMENDATIONS IN DOGS¹⁵⁻¹⁷

Drug Combination* Dosage** Effect

Combination 1

Butorphanol	0.4 mg/kg IM	High level of sedation with mild analgesia
Dexmedetomidine	5 μg/kg IM	
Tiletamine/zolazepam	3 mg/kg IM	
Combination 2		
Hydromorphone [†]	0.1 mg/kg IM	Higher degree of analgesia with good
Dexmedetomidine	5 μg/kg IM	sedation
Ketamine	2 mg/kg IM	
Combination 3		
Butorphanol	0.4 mg/kg IM	Dissociative anesthetics or α_2 agonists are not
Alfaxalone	2 mg/kg IM	recommended in patients with questionable
Midazolam	0.5 mg/kg IM	cardiac disease or significant comorbidities

*Opioids can be substituted within their drug class (eg. butorphanol substituted for hydromorphone) if goals for pain management require a different opioid.

**Doses can be adjusted based on recommended dosing ranges (Table 2). Some dosages are anecdotal based on those used in the authors' facility.

[†]Any opioid can be substituted for hydromorphone based on availability.

Other handling techniques involve using a half-wall or chain link fence as a barrier between the patient and the injector/handler. An ideal sedative protocol, as recommended in human medicine, is rapid-acting with minimal side effects, although, without physical examination, adverse effects are difficult to predict in fractious patients.¹³ Of note, most anesthetic drugs are associated with some degree of risk¹⁴; this risk is increased in patients that are unable to be assessed for pre-existing comorbidities (eg, heart disease). Reversible drugs (eg, α_2 agonists, opioids) are preferable, as their adverse effects can be mitigated with reversal agents if necessary.

Some patients may become sedate enough to lose airway protection. Supplies for intubation and appropriate ventilation should always be available for patients that show signs of requiring a protected airway or ventilatory support (eg, cyanosis,

Top 5 Tips for Sedation & Anesthesia in Fractious Dogs | Clinician's Brief

shallow breathing, regurgitation).

Patient Handling While Hospitalized

Fractious patients may require additional precautions for handling and drug administration while hospitalized. Standard monitoring procedures are recommended with the patient sedated or anesthetized. Hospitalization of fractious animals typically requires planning.

Placement of an IV catheter in a pelvic limb can be advantageous, as it provides more room between the patient's head and the injection site. If pelvic limb catheter placement is not feasible, additional placement of long extension sets attached to the IV catheter (**Figure 1**, *top of page*) can facilitate semi-remote drug administration and provides an additional level of safety for the patient and staff.

An Elizabethan collar and/or basket muzzle can be used to provide additional safety for aggressive patients, and allowing patients to wear a harness with an attached leash while in a cage can be helpful when removing them from the confined space (**Figure 2**). Floor-level cages or runs are preferred, as they prevent the need for the handler to lift the patient out of the cage and onto the floor or into a carrier. Muzzles with connections suitable for oxygen delivery are also helpful for providing flow-by oxygen to aggressive patients.



 FIGURE 2 To ensure patient and staff safety, an Elizabethan collar and a harness are used on the patient, with the leash attached to the harness and placed toward the cage door.

Recovery & Discharge

For outpatient procedures (eg, outpatient surgery, diagnostic procedures) requiring sedatives/anesthetic drugs, a basket muzzle can be modified so that the endotracheal tube can be removed through the muzzle, which allows the muzzle to be placed on the patient prior to extubation and be in place at the end of the procedure (**Figure 3**). This facilitates safety in the recovery period while still allowing the patient to be closely monitored.



FIGURE 3 Basket muzzle modified to facilitate extubation (A). Placement of the pilot balloon and endotracheal tube ties through the end of the muzzle is necessary to avoid difficulty extubating the patient (B).

Intravenous catheters can be removed just before discharge. With all tape removed and a bandage left over the catheter, the extension line, which is attached to the catheter hub, can be pulled, thus removing the catheter while keeping the bandage in place for hemostasis (see **Step-by-Step Catheter Removal Video**). Sedatives can be administered intravenously just before catheter removal at the time of discharge and can facilitate a smooth transition from the hospital to the transportation vehicle. The owner should be made aware of the expected nature and duration of the sedation protocol.

Conclusion

Careful planning, communication, and preparation can facilitate a safe and productive appointment for fractious patients that need to be sedated or anesthetized. Multimodal pharmacologic restraint, along with modified approaches to drug administration and patient handling, can mitigate most of the issues encountered with aggressive patients in the hospital setting.

REFERENCES

- Fatjó J, Amat M, Mariotti VM, Luis Ruiz de la Torre J, Manteca X. Analysis of 1040 cases of canine aggression in a referral practice in Spain. J Vet Behav Clin App Res. 2007;2(5):158-165.
- 2. Sueda KL, Malamed R. Canine aggression toward people: a guide for practitioners. *Vet Clin North Am Small Anim Pract.* 2014;44(3):599-628.
- 3. Boyer EW, Shannon M. The serotonin syndrome. *N Engl J Med.* 2005; 352(11):1112-1120.
- 4. Gruen ME, Sherman BL. Use of trazodone as an adjunctive agent in the treatment of canine anxiety disorders: 56 cases (1995-2007). *J Am Vet Med Assoc*. 2008;233(12):1902-1907.
- Gilbert-Gregory SE, Stull JW, Rice MR, Herron ME. Effects of trazodone on behavioral signs of stress in hospitalized dogs. *J Am Vet Med Assoc*. 2016;249(11):1281-1291.
- 6. Thomas DE, Lee JA, Hovda LR. Retrospective evaluation of toxicosis from selective serotonin reuptake inhibitor antidepressants: 313 dogs (2005-2010). *J Vet Emerg Crit Care (San Antonio)*. 2012;22(6):674-681.
- Hay Kraus BL. Efficacy of maropitant in preventing vomiting in dogs pre-medicated with hydromorphone. *Vet Anaesth Analg.* 2013;40(1):28-34.
- 8. Hsu Y, Sun L. Factors associated with aggressive responses in pet dogs. *Appl Anim Behav Sci.* 2010;123(3-4):108-123.
- Luescher AU, Reisner IR. Canine aggression toward familiar people: a new look at an old problem. *Vet Clin North Am Small Anim Pract*. 2008;38(5):1107-1130, vii.
- Mills DS, Ramos D, Estelles MG, Hargrave C. A triple blind placebocontrolled investigation into the assessment of the effect of Dog Appeasing Pheromone (DAP) on anxiety related behaviour of problem

Page 11 of 13

dogs in the veterinary clinic. Appl Anim Behav Sci. 2006;98(1):114-126.

- 11. Pickering TG, James GD, Boddie C, Harshfield GA, Blank S, Laragh JH. How common is white coat hypertension? *JAMA*. 1988;259(2):225-228.
- Wang XX, Shuai W, Peng Q, et al. White coat effect in hypertensive patients: the role of hospital environment or physician presence. *J Am Soc Hypertens*. 2017;11(8):498-502.
- Moore G, Pfaff JA. Assessment and emergency management of the acutely agitated or violent adult. UpToDate. https://www.uptodate.com/contents/assessment-and-emergencymanagement-of-the-acutely-agitated-or-violent-adult. Updated October 2, 2017. Accessed September 12, 2018.
- Brodbelt DC, Flaherty D, Pettifer GR. Anesthetic risk and informed consent. In: Grimm KA, Lamont LA, Tranquilli WJ, Greene SA, Robertson SA, eds. *Veterinary Anesthesia and Analgesia*. 5th ed. Ames, IA: John Wiley & Sons; 2015:11-22.
- 15. Crowell-Davis SL, Seibert LM, Sung W, Parthasarathy V, Curtis TM. Use of clomipramine, alprazolam, and behavior modification for treatment of storm phobia in dogs. *J Am Vet Med Assoc*. 2003;222(6):744-748.
- Grimm KA, Lamont LA, Tranquilli WJ, Greene SA, Robertson SA, eds. *Veterinary Anesthesia and Analgesia: The Fifth Edition of Lumb and Jones.* Ames, IA: John Wiley & Sons; 2015.
- Plumb DC. *Plumb's Veterinary Drug Handbook*. 9th ed. Hoboken, NJ: Wiley-Blackwell; 2018.
- 18. Haberzettl R, Bert B, Fink H, Fox MA. Animal models of the serotonin syndrome: a systematic review. *Behav Brain Res.* 2013;256:328-345.
- Crowell-Davis SL, Poggiagliolmi S. Understanding behavior serotonin syndrome. *Compend Contin Educ Vet.* 2008;30(9):490-493.

AUTHORS

Katherine Bennett

DVM

University of Tennessee

Katherine Bennett, DVM, is an anesthesia resident at University of Tennessee. She earned her DVM from Purdue University. Dr. Bennett's interests include facilitating stress-free and pain-free hospital stays for patients, learning and teaching, and presenting customized CE lectures at conferences and private clinics.

Christine Egger

DVM, MVSc, CVA, CVH, DACVAA University of Tennessee

Christine Egger, DVM, MVSc, CVA, CVH, DACVAA, is a professor at University of Tennessee. She earned her DVM and master's degree from University of Saskatchewan in Saskatoon, Canada. Dr. Egger completed a residency in veterinary anesthesia and is the president of the American College of Veterinary Anesthesia and Analgesia. She is certified in veterinary acupuncture and herbal medicine. Her interests include recognition and treatment of acute and chronic pain.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found here.

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice. Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. For questions or inquiries please contact us.



clinician's brief

Chronic Weight Loss & Diarrhea in a Dog

Micah A. Bishop, DVM, PhD, DACVIM (SAIM), WAVE Veterinary Internal Medicine, Naples, Florida

ENDOCRINOLOGY & METABOLIC DISEASES OCTOBER 2020 PEER REVIEWED

Print/View PDF



Clinical History & Signalment

Trixie, a 2-year-old, 44-lb (20-kg) spayed German shepherd crossbreed, was

Page 1 of 9

presented for an ≈3-month history of chronic, marked weight loss and small bowel diarrhea. Stool was voluminous, pale in color, and soft and unformed in consistency. Her owner reported that Trixie had a good appetite and appeared to be healthy otherwise. Trial treatment with a hypoallergenic and novel protein diet for 3 weeks did not ameliorate the diarrhea or weight loss.

Physical Examination

On physical examination, Trixie was bright, alert, and responsive. Vital signs were within normal limits. Her BCS was 2/9 and she had marked muscle wasting (**Figure**). Abdominal palpation was normal, and soft, yellow feces was detected during rectal examination; flatulence was also noted. The rest of the examination was within normal limits.



 FIGURE Patient showing poor BCS. Image courtesy of Dr. Jörg M. Steiner, Texas A&M University

Diagnosis

Differential diagnoses included intestinal parasitism, chronic enteropathy (eg, food-responsive enteropathy, antibiotic-responsive enteropathy, immunosuppressant-responsive enteropathy), protein-losing enteropathy, juvenile neoplasia, chronic intussusception, chronic foreign body, hypoadrenocorticism (ie, Addison's disease), chronic kidney disease, chronic liver disease, and infection with *Pythium* spp, which is endemic in Florida.¹

CBC, serum chemistry profile, and urinalysis results were within normal limits. Fecal flotation results were negative.

Because of Trixie's dramatic weight loss, abdominal radiography and

ultrasonography were completed on the day of presentation. Radiographs were unremarkable but revealed mild loss of serosal detail, presumably secondary to patient emaciation. Ultrasound images revealed no mural thickening, abdominal mass, lymphadenopathy, or other abnormality. Adrenal glands were slightly decreased in size.

After Trixie was fasted for 12 hours, serum cobalamin (ie, vitamin B_{12}), folate, canine trypsin-like immunoreactivity (cTLI), and baseline cortisol levels were obtained (**Table**). The results demonstrated a decreased cTLI, which was diagnostic for exocrine pancreatic insufficiency. Cobalamin was also decreased, which was consistent with ileal pathology. Baseline cortisol was increased, ruling out hypoadrenocorticism.²

TABLE

GI PANEL RESULTS

Assay	Result	Reference interval
cTLI	1.5 μg/L	5.7-45.2 μg/L
Cobalamin	150 ng/L	251-908 ng/L
Folate	12.8 μg/L	9.7-21.6 μg/L
Cortisol	7 μg/dL	2-6 μg/dL

DIAGNOSIS:

EXOCRINE PANCREATIC INSUFFICIENCY

Treatment & Long-Term Management

Trixie was initially started on pancreatic enzyme replacement powder at 1 tsp/22

lb (10 kg) of body weight mixed with food.³ She was also given 1 cyanocobalamin tablet daily (1 mg PO every 24 hours is recommended for dogs weighing >44 lb [20 kg]).⁴ Her owner was instructed to closely monitor Trixie's stool for improvement in consistency, frequency, and volume and to return to the clinic every 2 weeks for assessment and monitoring for weight gain. Lifelong treatment with enzyme replacement therapy and cyanocobalamin is recommended for exocrine pancreatic insufficiency. Trixie was also empirically dewormed with fenbendazole (50 mg/kg/day for 5 days).⁵

TREATMENT AT A GLANCE

- Pancreatic enzyme replacement therapy is the treatment of choice.⁸ The dose can typically be tapered over time. These enzyme replacement powders typically contain lipase, amylase, and other proteases.³
- Oral cobalamin supplementation can be as effective as parenteral administration, but oral supplementation has not been studied exclusively in EPI patients.⁹ In the author's experience, the supraphysiologic dose of cobalamin has been sufficient for these patients; however, serum cobalamin concentration levels should be rechecked, especially if there is a lack of response to treatment.
- Antibiotic-responsive enteropathy (ie, dysbiosis, small intestinal bacterial overgrowth) is a common complication and may result in partial response to treatment.^{6,7}
- Treatment with enzyme replacement is lifelong and expensive. Enteric-coated tablets may be a less

expensive alternative, as would be fresh, raw pancreas. Uncoated enzymes can cause gingival bleeding, but this usually can be eliminated by decreasing the dose or administering tablets.^{6,10}

- Dietary change is generally not necessary; however, some dogs—especially those with poor response to treatment—may benefit from highly digestible hypoallergenic diets or low-fat diets.⁶
- Eighty percent of dogs respond favorably to therapy, and long-term prognosis is good.^{6,8}

Prognosis & Outcome

Trixie was returned for a recheck examination 2 weeks after presentation. She was rapidly gaining weight, and her stool had improved in quality but was still soft; however, she had also started periodically vomiting daily. Tylosin (25 mg/kg every 12 hours) was given because of her history of low cobalamin in conjunction with the high prevalence of dysbiosis and antibiotic-responsive enteropathy (formerly called small intestinal bacterial overgrowth) associated with exocrine pancreatic insufficiency (EPI).^{6,7} Dysbiosis was most likely associated with changes in motility, lack of bacteriostatic pancreatic juices, and altered immune function.⁶ At the next recheck examination, the owner reported that Trixie was thought to be completely back to normal (ie, prior to the development of clinical signs). There were no GI signs, her BCS was 4/9 and expected to continue to improve, and her weight had increased to 57 lb (26 kg). Over the next few months, her BCS returned to normal (ie, 5/9) and her weight increased to 66 lb (30 kg); pancreatic enzyme replacement therapy was tapered to a lower dose. Tylosin was stopped without recurrence of signs ≈ 6 weeks after diagnosis. Cobalamin supplementation was continued, and Trixie was transitioned to a primary care veterinarian.

TAKE HOME MESSAGES

- Although marked weight loss with chronic smallbowel diarrhea and flatulence is a common clinical sign of EPI, it is beneficial to rule out EPI in any patient with weight loss regardless of GI signs.
- cTLI is a highly sensitive and specific test for EPI that should always be done on a fasted blood sample.¹¹
- Previous administration of pancreatic enzymes does not interfere with cTLI testing.¹²
- Cobalamin and folate derangements are common secondary findings that should be addressed. In a study, low cobalamin was associated with decreased survival.¹² Eighty-two percent of dogs with EPI have decreased serum cobalamin concentrations; however, there is some disagreement as to what the cutoff reference interval should be and whether serum methylmalonic acid concentration should instead be assessed, as this may indicate earlier deficiency.^{13,14}
- Laboratory findings, radiography, and ultrasonography can be used to rule out common differential diagnoses.
- German shepherd dogs and rough-coated collies are predisposed to EPI, likely due to an autosomalrecessive inheritance pattern.¹⁵

REFERENCES

- Westermarck E. Clinical evaluation of patients with chronic diarrhea. In: Steiner JM, ed. Small Animal Gastroenterology. Hannover, Germany: Schlütersche; 2008:127-133.
- Bovens C, Tennat K, Reeve J, Murphy KF. Basal serum cortisol concentration as a screening test for hypoadrenocorticism in dogs. J Vet Intern Med. 2014;28(5):1541-1545.
- 3. Plumb DC. Pancrelipase lipase/protease/amylase. Plumb's Veterinary Drug website.

plumbsveterinarydrugs.com/#!/monograph/yd9au143nd. Updated September 2017. Accessed July 2020.

- Plumb DC. Cyanocobalamin (vitamin B12). Plumb's Veterinary Drug website. plumbsveterinarydrugs.com/#!/monograph/bw326rE9VM. Updated July 2017. Accessed July 2020.
- Plumb DC. Fenbendazole. Plumb's Veterinary Drug website. plumbsveterinarydrugs.com/#!/monograph/luWztPs06N. Updated August 2019. Accessed July 2020.
- Wiberg M. Exocrine pancreatic insufficiency in dogs. In: Bonagura JD, Twedt DC, eds. *Kirk's Current Veterinary Therapy XV*. St Louis, MO: Elsevier; 2014:558-560.
- Isaiah A, Parambeth JC, Steiner JM, Lidbury JA, Suchodolski JS. The fecal microbiome of dogs with exocrine pancreatic insufficiency. *Anaerobe*. 2017;45:50-58.
- 8. Wiberg ME, Lautala H-M, Westermarck E. Response to long-term enzyme replacement treatment in dogs with exocrine pancreatic insufficiency. *J Am Vet Med Assoc*. 1998;213(1):86-90.
- 9. Toresson L, Steiner JM, Razdan P, et al. Comparison of efficacy of oral and parenteral cobalamin supplementation in normalising low cobalamin concentrations in dogs: a randomised controlled study. *Vet*

J. 2018;232:27-32.

- Parambeth JC, Fosgate GT, Suchodolski JS, Lidbury JA, Steiner JM. Randomized placebo controlled clinical trial of an enteric coated micro-pelleted formulation of a pancreatic enzyme supplement in dogs with exocrine pancreatic insufficiency. *J Vet Intern Med.* 2018;32(5):1591-1599.
- Williams DA, Batt RM. Sensitivity and specificity of a radioimmunoassay of serum trypsin-like immunoreactivity for the diagnosis of canine exocrine pancreatic insufficiency. J Am Vet Med Assoc. 1988;192(2):195-201.
- 12. Soetart N, Rochel D, Drut A, et al. Serum cobalamin and folate as prognostic factors in canine exocrine pancreatic insufficiency: An observational cohort study of 299 dogs. *Vet J*. 2019;243:15-20.
- Batchelor DJ, Noble PJ, Taylor RH, Cripps PJ, German AJ. Prognostic factors in canine exocrine pancreatic insufficiency: prolonged survival is likely if clinical remission is achieved. *J Vet Intern Med*. 2007;21(1):54–60.
- Kather S, Grutzner N, Kook PH, Dengler F, Heilmann RM. Review of cobalamin status and disorders of cobalamin metabolism in dogs. *J Vet Intern Med.* 2020;34(1):13-28.
- 15. Clark LA, Wahl JM, Steiner JM, et al. Linkage analysis and gene expression profile of pancreatic acinar atrophy in the German shepherd dog. *Mamm Genome*. 2005;16(12):955-962.

AUTHOR

Micah A. Bishop

DVM, PhD, DACVIM (SAIM) WAVE Veterinary Internal Medicine, Naples, Florida

Micah A. Bishop, DVM, PhD, DACVIM (SAIM), works in a small animal practice in southwest Florida. He earned his DVM from Ross University

and completed an internship at University of Minnesota. He then worked in small animal general practice for several years while earning his PhD from Texas A&M University, where he also completed a small animal internal medicine residency. Dr. Bishop has published multiple manuscripts and abstracts and lectures nationally and internationally.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units **can be found here.**

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice. Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. For questions or inquiries please contact us.

オレト 8/16/201 main 8-9 Demodicos:s Generalized Demodecosis Demodecosis prednisolone X Oclacitinib (Apoquel) - Only apprend to alleray Dermotits or atopic permotits For Demoducesis or Bacteria infection - not approve should use for Dog older than 12 month Lokivetmab (cytopoint) - allergy or atopic permotifs SQ injection effective 4-J Wacks Vermectin _ proceed with coution Sarolaner (Simparica) Safe. Bravecto) Amitraz Dip (mitaban) Use with caufion Enrofloxacin - X Cephaloxin - safe Benzoy peropide shampoo - Safe Clentamicin/Botamethasone - Ponit use of Affected dogs should not be bred

#12 B

4/8/2021

clinician's brief

Isoxazolines for Treatment of Demodicosis

Charlie Pye, DVM, DVSc, DACVD, University of Prince Edward Island, Charlottetown, Prince Edward Island

DERMATOLOGY NOVEMBER/DECEMBER 2020

Print/View PDF

In the literature

Zhou X, Hohman A, Hsu WH. Review of extralabel use of isoxazolines for treatment of demodicosis in dogs and cats. *J Am Vet Med Assoc.* 2020;256(12):1342-1346.

FROM THE PAGE ...

Demodex canis, the most common *Demodex* species leading to canine demodicosis, is a normal part of the skin microbiota but can proliferate secondary to immunocompromise.^{1,2} Demodicosis is characterized by time of onset (juvenile vs adult) and areas affected (localized vs generalized). Localized demodicosis is generally self-limiting, whereas generalized demodicosis can be difficult to treat.

Topical amitraz, the only FDA-approved drug for the treatment of demodicosis in the United

States, has been considered the standard for decades. Treatment requires intense topical therapy and carries risk for severe adverse effects. Topical moxidectin formulations are labeled for demodicosis treatment in other countries but not in the United States. Additional treatments include ivermectin, moxidectin, doramectin, lime sulfur, milbemycin oxime, and isoxazolines.³⁻⁵ Many treatments have a high risk for adverse effects, and some can be cost-prohibitive.

This article reviewed the use of isoxazolines in the treatment of demodicosis in dogs and cats, as well as the safety of orally administered formulations of these drugs.

Isoxazolines are FDA-approved for use against fleas and ticks. Oral canine formulations include afoxolaner, sarolaner, fluralaner, and lotilaner.⁶ Topical fluralaner is available for use in dogs and cats.⁷ Field trials and reports have demonstrated successful treatment of generalized demodicosis using isoxazolines⁸⁻¹⁴:

- Oral fluralaner has been shown to decrease the number of mites identified on scrapings by 100% at day 56.⁸ Topically administered fluralaner had similar efficacy.⁹ Another field study demonstrated parasitological cure in dogs with juvenile and generalized demodicosis within 2 to 4 months.¹⁰
- ▶ Both oral afoxolaner and lotilaner have been shown to reduce mite numbers by ≈99.9% on day 56 and 100% on day 84.^{11,12}
- Sarolaner has been shown to reduce mite numbers by 99.8% within 29 days with no live mites detected thereafter; the control treatment had a lower efficacy with a longer duration of treatment.¹³ A multicenter study found mite counts decreased by 100% by day 150 following monthly administration of sarolaner as compared with the control that resulted in 82.2% reduction at 6 months.¹⁴

No large studies have been performed to investigate efficacy of isoxazoline treatment of feline demodicosis, although reports describe elimination of *D gatoi* and *D cati* after a single dose of oral fluralaner.^{15,16}

Oral fluralaner, afoxolaner, and sarolaner have all been assessed for safety in 8-week-old puppies receiving ≤ 5 times the maximum dose^{17,18}; no major adverse effects or impact on growth have been associated with treatment.^{19,20} In one study, oral sarolaner at ≤ 5 times the maximum dose

was administered to adult beagles, with no adverse effects noted.¹⁹ In another study, oral lotilaner was administered to 112 cats, with no adverse effects documented.²⁰ Oral fluralaner in breeding dogs has not been shown to have significant impact on reproductive performance or semen quality when administered at 3 times the maximum dose from breeding until weaning.⁷

Many historical treatments for demodicosis cannot be used in dogs with the multidrug sensitivity gene (*MDR1* gene, also known as *ABCB1* gene) mutation.²¹ Isoxazolines have the potential to cause neurologic excitation in vertebrates by blocking γ-aminobutyric acid-gated chloride channels. Fluralaner has been evaluated in dogs homozygous for the *MDR1* mutation, and only minor clinical findings not associated with treatment have been observed.²² One report described neurologic signs observed in some dogs when given sarolaner doses higher than recommended.²³ One clinical report noted transient neurologic abnormalities in a young dog after administration of fluralaner at the recommended dose.²³ The FDA has reported adverse neurologic reactions across the isoxazoline class but has stated this class is effective and safe for most animals.²⁴

... TO YOUR PATIENTS

Key pearls to put into practice:

Isoxazolines are not currently labeled for the treatment of demodicosis in the United States, but studies and clinical reports support their clinical use.



Isoxazolines appear to be well-tolerated in most dogs, with minimal adverse effects; however, neurologic adverse effects have been reported.

Findings suggest that fluralaner is well-tolerated in dogs with the MDR1 mutation.

3

REFERENCES

- 1. Ravera I, Altet L, Francino O, et al. Small *Demodex* populations colonize most parts of the skin of healthy dogs. *Vet Dermatol.* 2013;24(1):168-172.
- 2. Singh SK, Dimri U. The immuno-pathological conversions of canine demodicosis. *Vet Parasitol.* 2014;203(1-2):1-5.
- Ghubash R. Parasitic miticidal therapy. Clin Tech Small Anim Pract. 2006;21(3):135-144.
- 4. Medleau L, Willemse T. Efficacy of daily amitraz on generalized demodicosis in dogs. *J Small Anim Pract.* 1995;36(1):3-6.
- 5. Arsenović M, Pezo L, Vasić N, Ćirić R, Stefanović M. The main factors influencing canine demodicosis treatment outcome and determination of optimal therapy. *Parasitol Res.* 2015;114(7):2415-2426.
- FDA. Freedom of Information Summary, original new animal drug application NADA 141–406, Nexgard (afoxolaner chewable tablet, dogs). FDA website. animaldrugsatfda.fda.gov/adafda/app/search/public/document/downloadFoi/3811. Accessed October 25, 2019.
- FDA. Corrected Freedom of Information Summary, original new animal drug application NADA 141–426, Bravecto (fluralaner chewable tablets, dogs). FDA website.

animaldrugsatfda.fda.gov/adafda/app/search/public/document/downloadFoi/1502. Accessed October 25, 2019.

 Fourie JJ, Liebenberg JE, Horak IG, Taenzler J, Heckeroth AR, Frénais R. Efficacy of orally administered fluralaner (Bravecto) or topically applied imidacloprid/moxidectin (Advocate*) against generalized demodicosis in dogs. *Parasit Vectors*. 2015;8:187.

- Fourie JJ, Meyer L, Thomas E. Efficacy of topically administered fluralaner or imidacloprid/moxidectin on dogs with generalised demodicosis. *Parasit Vectors*. 2019;12:59.
- 10. Duangkaew L, Larsuprom L, Anukkul P, Lekcharoensuk C, Chen C. A field trial in Thailand of the efficacy of oral fluralaner for the treatment of dogs with generalized demodicosis. *Vet Dermatol.* 2018;29(3):208-e74.
- 11. Beugnet F, Halos L, Larsen D, de Vos C. Efficacy of oral afoxolaner for the treatment of canine generalised demodicosis. *Parasite*. 2016;23:14.
- Snyder DE, Wiseman S, Liebenberg JE. Efficacy of lotilaner (Credelio), a novel oral isoxazoline against naturally oc¬curring mange mite infestations in dogs caused by *Demodex* spp. *Parasit Vectors*. 2017;10:532.
- 13. Six RH, Becskei C, Mazaleski MM, et al. Efficacy of sarolaner, a novel oral isoxazoline, against two common mite infestations in dogs: Demodex spp. and Otodectes cynotis. *Vet Parasitol.* 2016;222:62-66.
- 14. Becskei C, Cuppens O, Mahabir SP. Efficacy and safety of sarolaner against generalized demodicosis in dogs in European countries: a non-inferiority study. *Vet Dermatol.* 2018;29(3):203-e72.
- 15. Duangkaew L, Hoffman H. Efficacy of oral fluralaner for the treatment of Demodex gatoi in two shelter cats. *Vet Dermatol.* 2018;29(3):262.
- 16. Matricoti I, Maina E. The use of oral fluralaner for the treatment of feline generalised demodicosis: a case report. *J Small Anim Pract*. 2017;58(8):476-479.
- Walther FM, Allan MJ, Roepke RKA, Nuernberger MC. Safety of fluralaner chewable tablets (BravectoTM), a novel systemic antiparasitic drug, in dogs after oral administration. *Parasit Vectors*. 2014;7:87.
- 18. Drag M, Saik J, Harriman J, Larsen D. Safety evaluation of orally administered afoxolaner in 8-week-old dogs. *Vet Parasitol.* 2014;201(3-4):198-203.
- McTier TL, Chubb N, Curtis MP, et al. Discovery of sarolaner: a novel, orally administered, broad-spectrum, isoxazoline ectoparasiticide for dogs. *Vet Parasitol*. 2016;222:3-11.

EXHIBIT 7 - 160

- 20. Cavalleri D, Murphy M, Seewald W, Nanchen S. A randomized, controlled field study to assess the efficacy and safety of lotilaner (CredelioTM) in controlling ticks in client-owned cats in Europe. *Parasit Vectors*. 2018;11(1):411.
- Mealey KL, Bentjen SA, Gay JM, Cantor GH. Ivermectin sensitivity in collies is associated with a deletion mutation of the MDR1 gene. *Pharmacogenetics*. 2001;11(8):727-733.
- Walther FM, Paul AJ, Allan MJ, Roepke RKA, Nuernberger NC. Safety of fluralaner, a novel systemic antiparasitic drug, in MDR1(-/-) collies after oral administration. *Parasit Vectors*. 2014;7:86.
- Gaens D, Rummel C, Schmidt M, Hamann M, Geyer J. Suspected neurological toxicity after oral application of fluralaner (Bravecto) in a Kooikerhondje dog. *BMC Vet Res.* 2019;15(1):283.
- 24. FDA. Animal Drug Safety Communication: FDA alerts pet owners and veterinarians about potential for neurologic adverse events associated with certain flea and tick products. FDA website. www.fda.gov/animal-veterinary/cvm-updates/animal-drugsafety-communication-fda-alerts-pet-owners-and-veterinarians-about-potentialneurologic. Accessed November 25, 2019.

AUTHOR

Charlie Pye

DVM, DVSc, DACVD University of Prince Edward Island, Charlottetown, Prince Edward Island

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found here.

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. For questions or inquiries please contact us.

Page 7 of 7

clinician's brief

Rough Anesthetic Recoveries

Renata S. Costa, DVM, MPhil, MANZCVS, GradDipEd, DACVAA, Midwestern University, Glendale, Arizona

ANESTHESIOLOGY & PAIN MANAGEMENT

Print/View PDF



Anesthetic recovery is a critical part of the anesthesia process.¹⁻ ³ During the recovery period, the effects of anesthetic agents may still be present, and the patient may not have regained full consciousness and can react abruptly and unexpectedly. Therefore, the postanesthetic period requires attentive monitoring. It is also imperative that an appropriate perioperative plan be developed to minimize the risk for a rough recovery and/or to allow for timely intervention before patients accidently cause injury to themselves or those around them.

Patient- and anesthesia-related factors can cause a rough recovery, and understanding common contributing factors can help determine the most likely diagnosis and best treatment plan.* Although it can be difficult to differentiate pain from other behaviors (eg, anxiety, stress, dysphoria)—as many of the physiologic responses are similar⁴⁻⁷—assessment of behavior prior to administering any agents, use of multidimensional pain scales, and knowledge of drug effects and duration of action can help facilitate correct interpretation of behaviors displayed in the postanesthetic period.

The common causes of rough recoveries in dogs and cats discussed in this article are emergence delirium, pain, anxiety, bladder distension, opioid dysphoria, and benzodiazepine disinhibition.^{4-6,8,9} Clinical signs are often similar regardless of the actual cause. Therefore, methodical assessment of the patient, as well as knowledge of when clinical signs started, drugs were administered, and patient pain level can help identify the most likely etiology of the rough recovery (see **Rough Recovery Guidelines**).

ROUGH RECOVERY GUIDELINES

Fast action is crucial if recovery is rough and may cause harm. However, if there is time, the patient should be assessed and the cause of the rough recovery identified prior to administration of any
medication. Following are some treatment options for common causes of rough recovery.

Emergence Delirium

- Small dose of induction agent
- Propofol (0.5-1 mg/kg slow IV; cats and dogs)
 - Stopped when clinical signs subside

Pain

It should be determined how painful the procedure was and whether the patient needs additional analgesia (based on patient response), as well as when the last dose of analgesic was given and the drug's duration of action. Not all patients with rough recovery that vocalize are painful. A pain scale should be used to determine a pain score, as pain assessment can help determine whether analgesia is needed.

Analgesics (ie, opioids, NSAIDs) are needed with a high pain score or when the patient is being assessed and it is not clear whether the patient is in pain.

Anxiety, Fear, & Aggression

Based on assessment of the patient's temperament prior to anesthesia, extra sedation may be needed. If this is the case, one of the following drugs (if there are no contraindications) can be administered and the patient reassessed:

- Low-dose acepromazine (0.01 mg/kg IV; cats and dogs)
- Low-dose dexmedetomidine (0.001 mg/kg IV; cats and dogs)

Bladder Distension

The bladder should be expressed or the patient walked if possible.

Opioid Dysphoria

- Butorphanol (0.1 mg/kg IV or IM; cats and dogs)
- Naloxone (0.005-0.01 mg/kg slow IV; cats and dogs), diluted prior to administration. The usual concentration is 0.4 mg/mL, which should be diluted to obtain a new concentration of 0.04 mg/mL (eg, 1 mL of undiluted naloxone and 9 mL of saline). Recommended rate of administration of the dilution is 0.5-1 mL/40 seconds. Administration should be stopped when clinical signs subside.
 - Naloxone administered too fast or at a dose that is too large can reverse analgesia and cause the patient to become painful. A rescue analgesic protocol should be prepared ahead of time.
 - Careful monitoring is needed, and readministration may be warranted if signs return.

Benzodiazepine (ie, Midazolam/Diazepam)

Disinhibition

- Flumazenil (0.01 mg/kg slow IV; cats and dogs)
 - Stopped when clinical signs subside

Emergence Delirium

Emergence delirium is a state of mental confusion and psychomotor agitation marked by hyperexcitability, restlessness, uncontrolled thrashing, and vocalization. Patients do not interact with humans and are unaware of their environment.^{7,10} Signs are abrupt and usually occur following rapid emergence from anesthesia when the patient has not yet regained complete consciousness. The etiology is unclear, but early anesthesia arousal following use of short-acting inhalation anesthetics may be a contributing factor.^{6,10,11}

Timing of clinical signs can help differentiate emergence delirium from other causes of a rough recovery. Emergence delirium occurs in the immediate recovery period, typically soon after inhalant anesthesia is discontinued. Patients may thrash uncontrollably and require rapid intervention to prevent injury. Administration of a small dose of an induction agent such as propofol (0.5-1 mg/kg slow IV; cats and dogs) is recommended.⁷ Propofol is commonly used due to its fast onset and short duration of action but should be administered slowly until clinical signs subside. Excessive and fast administration should be avoided to reduce the risk for apnea and hypotension due to vasodilation.

Pain

Clinical signs of pain include vocalization, restlessness, hyperventilation or panting, and aggression, especially when painful areas are touched.^{12,13}

Pain can be diagnosed using a pain scale (eg, short-form Glasgow Composite Measure Pain Scale, Colorado State University Acute Pain Scale).^{12,14} Knowledge of the analgesic protocol used, duration of action, and time of administration can also help reach a diagnosis. An analgesic trial with opioids (eg, methadone or hydromorphone [0.1 mg/kg IV], buprenorphine [0.02 mg/kg IV]; cats and dogs) or other analgesic agents (eg, ketamine [0.6 mg/kg/hour CRI; cats and dogs]; NSAIDs) should be instituted and the patient reassessed if there is uncertainty on whether the patient is still painful.

Anxiety, Fear, & Aggression

Anxiety is the uncertainty and fear that result from anticipation of a real or imaginary threat and often impairs physical and psychological functioning. Clinical signs include vocalization, panting, and restlessness.¹⁵

Patients in which adequate pain management has been implemented but persistent vocalization and restlessness continues may be experiencing fear, stress, and/or anxiety. Administration of a tranquilizer or sedative (eg, acepromazine [0.01 mg/kg IV], dexmedetomidine [0.001 mg/kg IV]; cats and dogs) can be considered if there are no contraindications (eg, previous allergic reaction to the agent, patient is hypovolemic)^{4,7}; however, some dogs and cats may only have a temporary response. In these cases, especially if restlessness is due to anxiety, agents such as trazodone (3-10 mg/kg PO) or gabapentin (10-25 mg/kg PO) can be administered. The patient will need to be reassessed after initial treatment, as some patients may require higher doses of these agents. The aim, however, should be to administer the lowest dose possible to minimize the risk for adverse effects while still achieving the desired outcome. Trazodone enhances calmness, reduces anxiety, and produces mild sedation with no apparent relevant adverse effects in dogs.^{16,17}

Patients that are anxious may respond to being held, but this is not always feasible. Nonpharmacologic alternatives include anxiety or pressure wraps (eg, a thunder jacket) that maintain swaddling pressure and acupressure aimed to induce calmness.^{18,19}

Bladder Distension

Bladder-distension-related discomfort may result in vocalization, restlessness, tachycardia, and/or panting.^{4,5,20} The bladder should be palpated and expressed prior to recovery.

During the postanesthetic period, if there are signs of discomfort and restlessness, bladder size and turgidity should be reassessed and the bladder gently expressed if it is distended—this may minimize discomfort.⁵ Ambulatory patients should be walked.

Opioid Dysphoria

Opioids, especially μ agonists (eg, hydromorphone, fentanyl), can result in dysphoric recoveries marked by vocalization, restlessness, hyperthermia, panting, and/or lack of response to human contact.^{4,8} Opioid-related dysphoria is often a diagnosis of exclusion made after pain and bladder distension are ruled out and in patients with no response following administration of sedatives and tranquilizers. In these cases, μ -agonist–opioid administration worsens clinical signs. This highlights the importance of accurate pain assessment prior to administering these agents.

Butorphanol is a \varkappa -agonist, μ -antagonist opioid that can reverse the adverse effects of μ -agonist opioids²¹ and provide mild analgesia. Naloxone is the actual reversal agent and results in rapid resolution of adverse effects^{10,21}; however, this drug has the potential to reverse the analgesic properties of the opioid. To decrease the risk for reversing analgesia, naloxone (0.005-0.01 mg/kg; cats and dogs) should be diluted (see **Rough Recovery Guidelines**) to allow for slow IV administration (0.5-1 mL/40 seconds) and stopped when signs subside. A rescue analgesic protocol should always be prepared ahead of time, and the patient should be pain scored. Clinical signs that stop after reversal confirms the diagnosis of opioid dysphoria.

Benzodiazepine Disinhibition

Benzodiazepine disinhibition is a paradoxical response that follows administration of these sedatives (eg, diazepam, midazolam); this reaction is often observed in healthy dogs and cats. Signs may be seen immediately after administration and/or during the recovery period and include vocalization, hyperexcitability, ataxia, drooling, nystagmus, aggression, and sudden attempts to eat the fluid line and bandages.^{22,23} A higher incidence of disinhibition occurs in healthy patients but the etiology is not completely understood.^{24,25}

Benzodiazepine disinhibition is often a diagnosis of exclusion that is made when the patient fails to respond to analgesics, sedatives, and tranquilizers. Flumazenil (0.01 mg/kg slow IV; cats and dogs) is the reversal agent and results in rapid cessation of clinical signs,^{25,26} confirming the diagnosis of benzodiazepine disinhibition.

Prognosis & Prevention

Reviewing patient history and medical records of previous sedation and anesthetic recoveries before medication is administered can help prevent a rough recovery. It is also important to properly record any rough recovery, treatment provided, and responses to treatment. Knowledge of previously noted complications can help clinicians anticipate potential future issues and implement pre-emptive strategies. Strategies may include modification of the anesthetic protocol and administration of preanesthetic drugs at home²⁷ and/or in the clinic. For example, a cat that previously experienced benzodiazepine-induced disinhibition on recovery should receive a different premedication protocol, or a dog with a known history of opioid-related dysphoria can often be managed with opioid-minimal/opioid-free protocols, emphasizing locoregional analgesia, NSAIDs, and CRIs of nonopioid drugs (eg, lidocaine, dexmedetomidine, ketamine). Consultation with a board-certified specialist in veterinary anesthesia and analgesia can be helpful in these cases.

Using a pain scoring scale prior to starting the procedure and prior to drug administration can help during the recovery period—for example, this can aid in differentiating whether vocalization is due to pain or anxiety. An adequate analgesic protocol is also a key component for optimal perioperative management and return to normal physiologic function. Some agents may need to be readministered depending on the procedure, patient response, type of analgesic used, time of drug administration, and duration of action of each drug. Suboptimal use of analgesics, but also unnecessary administration of drugs (eg, opioids) to nonpainful patients, can result in a rough recovery.

Conclusion

To correctly diagnose a rough anesthetic recovery, it is important to anticipate and reduce pain, anxiety, and fear (using pharmacologic and/or nonpharmacologic methods), as well as to understand the temperament of the patient, procedure, medications, and possible drug interactions. Knowledge of common causes of rough recoveries and appropriate treatment can aid in optimization of the recovery period.

*Drug desages in this article are suggestions. Individual patients should be assessed to establish whether lower or higher doses are required based on adverse effects and patient status. Adequacy of the chosen drug should also be determined.

REFERENCES

- Brodbelt DC, Pfeiffer DU, Young LE, Wood JLN. Risk factors for anaesthetic-related death in cats: results from the confidential enquiry into peri-operative small animal fatalities (CEPSAF). *Br J Anaesth*. 2007;99(5):617-623.
- 2. Brodbelt DC, Pfeiffer DU, Young LE, Wood JLN. Results of the confidential enquiry into perioperative small animal fatalities regarding risk factors for anesthetic-related death in dogs. *J Am Vet Med Assoc.* 2008;233(7):1096-1104.
- 3. Matthews NS, Mohn TJ, Yang M, et al. Factors associated with anesthetic-related death in dogs and cats in primary care veterinary hospitals. *J Am Vet Med Assoc*. 2017;250(6):655-665.
- 4. Hofmeister EH, Herrington JL, Mazzaferro EM. Opioid dysphoria in three dogs. *J Vet Emerg Crit Car.* 2006;16(1):44-49.

- 5. Bednarski R, Grimm K, Harvey R, et al. AAHA anesthesia guidelines for dogs and cats. *J Am Anim Hosp Assoc*. 2011;47(6):377-385.
- Kropf J, Hughes JL. Effect of midazolam on the quality and duration of anaesthetic recovery in healthy dogs undergoing elective ovariohysterectomy or castration. *Vet Anaesth Analg.* 2019;46(5):587-596.
- 7. Grubb T, Sager J, Gaynor J, et al. 2020 AAHA anesthesia and monitoring guidelines for dogs and cats. *J Am Anim Hosp Assoc*. 2020;56(2):59-82.
- Becker WM, Mama KR, Rao S, Palmer RH, Egger EL. Prevalence of dysphoria after fentanyl in dogs undergoing stifle surgery. *Vet Surg.* 2013;42(3):302-307.
- Mathews K, Kronen PW, Lascelles D, et al. Guidelines for recognition, assessment and treatment of pain: WSAVA Global Pain Council members and co-authors of this document. *J Small Anim Pract*. 2014;55(6):E10-E68.
- Moore AD, Anghelescu DL. Emergence delirium in pediatric anesthesia. Paediatr Drugs. 2017;19(1):11-20.
- Kanaya A, Kuratani N, Satoh D, Kurosawa S. Lower incidence of emergence agitation in children after propofol anesthesia compared with sevoflurane: a meta-analysis of randomized controlled trials. J Anesth. 2014;28(1):4-11.
- Reid J, Nolan AM, Hughes JML, Lascelles D, Pawsom P, Scott EM. Development of the short-form Glasgow Composite Measure Pain Scale (CMPS-SF) and derivation of an analgesic intervention score. *Anim Welfare*. 2007;16(S):97-104.
- 13. Calvo G, Holden E, Reid J, et al. Development of a behaviour-based measurement tool with defined intervention level for assessing acute pain in cats. *J Small Anim Pract.* 2014;55(12):622-629.
- 14. Hernandez-Avalos I, Mota-Rojas D, Mora-Medina P, et al. Review of different methods used for clinical recognition and assessment of pain

in dogs and cats. Int J Vet Sci Med. 2019;7(1):43-54.

- 15. Lloyd JKF. Minimising stress for patients in the veterinary hospital: why it is important and what can be done about it. *Vet Sci.* 2017;4(2);22.
- Gruen ME, Sherman BL. Use of trazodone as an adjunctive agent in the treatment of canine anxiety disorders: 56 cases (1995-2007). J Am Vet Med Assoc. 2008;233(12):1902-1907.
- Gruen ME, Roe SC, Griffith E, Hamilton A, Sherman BL. Use of trazodone to facilitate postsurgical confinement in dogs. *J Am Vet Med Assoc.* 2014;245(3):296-301.
- King C, Buffington L, Smith TJ, Grandin T. The effect of a pressure wrap (ThunderShirt) on heart rate and behavior in canines diagnosed with anxiety disorder. J Vet Behav. 2014;9(5):215-221
- 19. Cottam N, Dodman NH, Ha JC. The effectiveness of the anxiety wrap in the treatment of canine thunderstorm phobia: an open-label trial. *J Vet Behav.* 2013;8(3):154-161.
- Ness TJ, Richter HE, Varner RE, Fillingim RB. A psychophysical study of discomfort produced by repeated filling of the urinary bladder. *Pain*. 1998;76(1-2):61-69.
- Dyson DH, Doherty T, Anderson GI, McDonell WN. Reversal of oxymorphone sedation by naloxone, nalmefene, and butorphanol. *Vet Surg.* 1990;19(5):398-403.
- 22. Court MH, Greenblatt DJ. Pharmacokinetics and preliminary observations of behavioral changes following administration of midazolam to dogs. *J Vet Pharmacol Ther.* 1992;15(4):343-350.
- Stegmann GF, Bester L. Some clinical effects of midazolam premedication in propofol-induced and isoflurane-maintained anaesthesia in dogs during ovariohysterectomy. J S Afr Vet Assoc. 2001;72(4):214-216.
- 24. Gardos G. Disinhibition of behavior by antianxiety drugs. *Psychosomatics*. 1980;21(12):1025-1026

- Posner LP, Burns P. Sedative agents: tranquilizers, alpha-2 agonists, and related agents. In: Riviere JE, Papich MG, eds. *Veterinary Pharmacology & Therapeutics*. 9th ed. Wiley-Blackwell; 2009:356-365.
- Mathus-Vliegen EMH, de Jong L, Kos-Foekema HA. Significant and safe shortening of the recovery time after flumazenil-reversed midazolam sedation. *Dig Dis Sci.* 2014;59(8):1717-1725.
- 27. Costa RS, Karas AZ, Borns-Weil S. Chill protocol to manage aggressive & fearful dogs. *Clinician's Brief.* 2019;17(5):63-65.

AUTHOR

Renata S. Costa

DVM, MPhil, MANZCVS, GradDipEd, DACVAA Midwestern University, Glendale, Arizona

Renata S. Costa, DVM, MPhil, MANZCVS, GradDipEd, DACVAA, is an assistant professor of anesthesiology at Midwestern University in Glendale, Arizona. She earned her DVM from Federal University of Minas Gerais in Belo Horizonte, Brazil, and her MPhil and graduate diploma in education from Murdoch University in Perth, Australia. Dr. Costa completed an internship at Murdoch University and an anesthesia residency at Cummings School of Veterinary Medicine at Tufts University.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found here.

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. For questions or inquiries please contact us.

Page 12 of 13

14

clinician's brief

Top 5 Tips for Sedation & Anesthesia in Fractious Dogs

Katherine Bennett, DVM, University of Tennessee Christine Egger, DVM, MVSc, CVA, CVH, DACVAA, University of Tennessee

ANESTHESIOLOGY & PAIN MANAGEMENT NOVEMBER 2018 PEER REVIEWED



FIGURE 1 A long extension set directly connected to the catheter, which is placed in the lateral saphenous vein. An injection port is accessible (out of frame).

Aggression represents over 50% of behavior-related problems in dogs,¹ and

Page 1 of 13

fractious animals pose an inherent risk to veterinary staff. Behavior management is the ideal long-term solution for aggressive or fractious animals; however, some surgical or diagnostic procedures require relatively immediate attention and preclude most recommended behavior modifications. Precautions should be taken to ensure both patient and team safety when sedating or anesthetizing these patients.

Following are the authors' tips for safe handling of a sedated or anesthetized fractious dog presented for diagnostic or surgical procedures.

Owner Communication

Communication with the pet owner ahead of the scheduled appointment is critical. Discussion should include current medications, patient behavior at home, and whether the owner is comfortable medicating the patient at home. Owner involvement can help facilitate a team-based approach to safe and effective patient sedation.² In addition, a thorough risk assessment should be explained to the owner, as many sedative medications can have adverse effects on patients with underlying diseases, particularly cardiovascular disease. Patients with underlying systemic disease may require dose alterations and/or alternative drug protocols to account for comorbidities.

Preappointment Preparation

At-home administration of one or more sedatives (eg, trazodone, clonidine, dexmedetomidine, acepromazine, alprazolam; **Table 1**) the day before and the day of the scheduled visit allows for multimodal anxiolysis and can facilitate delivery of additional sedatives in the clinical setting. Caution should be taken when prescribing multiple serotonin-altering medications, as serotonin syndrome is a potentially lethal side effect (see **Serotonin Syndrome**).³ Combining different medications or introducing new serotonin-altering medications to a dog's treatment protocol can have deleterious effects; owners should be informed that, although uncommon, disinhibition of behavioral tendencies⁴ and/or development of aggression⁵ can occur at home. If adverse behavioral effects or signs of serotonin syndrome do not occur, the dose can be gradually increased over 1 to 2 days until the desired dose is reached or the desired effect is achieved.⁶ Alternatively, medications that do not alter serotonin levels (eg, α_2 agonists, benzodiazepines, gabapentin) can be used.

Serotonin Syndrome

Serotonin syndrome, defined as a group of clinical signs associated with administration of serotoninaltering medications (eg, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, antidepressants), although rare in veterinary medicine, can occur when multiple serotonin-altering medications are coadministered.¹⁸ Clinical signs of serotonin syndrome include altered mental status, agitation, nervousness, myoclonus, hyperreflexia, tremors, diarrhea, incoordination, increased heart rate and blood pressure, and hyperthermia.¹⁹ If a patient is already receiving medications for behavior alteration or other reasons, slow introduction of additional medications at lower doses is recommended. Any signs of agitation, restlessness, or myoclonus may suggest serotonin syndrome, and cessation of any additional serotonin-altering medications is recommended.

Common at-home administration protocols include administering oral trazodone, gabapentin, and alprazolam the day before the appointment and on the morning of the scheduled appointment or administering oral acepromazine, gabapentin, and alprazolam, potentially coadministered with maropitant (2 mg/kg PO q24h) to decrease the risk for vomiting after later administration of injectable sedatives

(especially those that contain a pure μ opioid).⁷

TABLE 1

PERIOPERATIVE ANXIOLYTIC & SEDATIVE DOSAGES IN DOGS¹⁵⁻¹⁷

Drug (Drug Category)	Dosage*
Acepromazine (phenothiazine)	0.5-2 mg/kg PO q8h
Alprazolam (benzodiazepine)	0.02-0.04 mg/kg PO q6h
Clonidine (α ₂ agonist)	0.01-0.05 mg/kg PO q12h
Dexmedetomidine gel (a ₂ agonist)	Refer to product insert
Diazepam (benzodiazepine)	1-2 mg/kg PO q8h
Gabapentin (anticonvulsant, neuropathic pain analgesic)	5-10 mg/kg PO q8-12h
Trazodone** (serotonin antagonist and reuptake inhibitor)	2-10 mg/kg PO q8-12h

*Some dosages are anecdotal based on those used in the authors' facility.

**Indicates commonly prescribed medications that, when combined with other serotoninaltering drugs, may place the patient at risk for serotonin syndrome. Careful and controlled introduction of medication combinations can help mitigate risks for serotonin syndrome development.

Sedation Administration

Top 5 Tips for Sedation & Anesthesia in Fractious Dogs | Clinician's Brief

Many patients may become more stressed in the hospital waiting area, making it

more difficult for sedative medications to reach full efficacy. The owner should be advised to place a muzzle and/or Elizabethan collar on the patient before or just after arrival, if possible. If available, other parts of the hospital (eg, parking lot, grassy relief area, barn) can be used as an environmental distraction for the patient during handling, waiting, and/or sedative administration.⁸ Because dogs use multiple cues (eg, visual, auditory, olfactory) to influence their behavior and/or reactions to their environment,⁹ soft and calm voices and limited personnel involvement are recommended. Pheromone sprays can help reduce anxiety but have not been shown to consistently reduce aggression in dogs.¹⁰

White coat syndrome (ie, the increase in a patient's sympathetic response to stress due to the appearance of medical personnel in white coats or similar clothing) has been well documented in human medicine.¹¹⁻¹³ To reduce the perceived threat of medical personnel, staff members who interact with the patient should avoid wearing white coats or similar hospital clothing while initially handling the patient (ie, from arrival to administration of injectable sedation). Typically, a coat or other outerwear is recommended to be worn over hospital clothing.^{11,12}

Administering sedation via an intramuscular injection (**Table 2**) is preferable and can be done while the patient is walking on a leash, provided the person handling the patient and the person administering the drugs are both experienced enough for a rapid pelvic limb injection and subsequent patient reaction. These drugs are typically used in combination to provide deep sedation and/or general anesthesia. Combining different drug classes (**Table 3**) allows for a dose reduction in all agents, thereby potentially limiting negative adverse effects.

TABLE 2

SEDATIVE DOSAGES IN DOGS¹⁵⁻¹⁷

Drug	Dosage*	Duration of Full Effect**	
Acepromazine	0.01-0.03 mg/kg IM	6-8 hours	
Alfaxalone	1-3 mg/kg IM 15-20 minutes		
Butorphanol	0.1-0.4 mg/kg IM	30-60 minutes	
Dexmedetomidine	1-10 μg/kg IM (not to exceed 10 30-60 minutes μg/kg)		
Hydromorphone	0.05-0.1 mg/kg IM	4-6 hours	
Ketamine	3-10 mg/kg IM 30-60 minutes		
Midazolam	0.1-0.5 mg/kg IM 20-40 minutes		
Tiletamine/zolazepam	1-4 mg/kg IM 30-60 minutes		

*Some dosages are anecdotal based on those used in the authors' facility.

**Most drugs have a dose-dependent duration of effect (ie, higher doses usually prolong the effect); however, higher doses can also increase the frequency of adverse events.

TABLE 3

SEDATIVE COMBINATIONS & DOSAGE RECOMMENDATIONS IN DOGS¹⁵⁻¹⁷

Drug Combination* Dosage**

Effect

Combination 1

https://www.cliniciansbrief.com/article/top-5-tips-sedation-anesthesia-fractious-dogs

Butorphanol	0.4 mg/kg IM	High level of sedation with mild analgesia	
Dexmedetomidine	5 μg/kg IM		
Tiletamine/zolazepam	3 mg/kg IM		
Combination 2			
Hydromorphone [†]	0.1 mg/kg IM	Higher degree of analgesia with good	
Dexmedetomidine	5 μg/kg IM	sedation	
Ketamine	2 mg/kg IM		
Combination 3			
Butorphanol	0.4 mg/kg IM	Dissociative anesthetics or α_2 agonists are not	
Alfaxalone	2 mg/kg IM	recommended in patients with questionable	
Midazolam	0.5 mg/kg IM	cardiac disease or significant comorbidities	

*Opioids can be substituted within their drug class (eg, butorphanol substituted for hydromorphone) if goals for pain management require a different opioid.

Doses can be adjusted based on recommended dosing ranges (Table 2**). Some dosages are anecdotal based on those used in the authors' facility.

[†]Any opioid can be substituted for hydromorphone based on availability.

Other handling techniques involve using a half-wall or chain link fence as a barrier between the patient and the injector/handler. An ideal sedative protocol, as recommended in human medicine, is rapid-acting with minimal side effects, although, without physical examination, adverse effects are difficult to predict in fractious patients.¹³ Of note, most anesthetic drugs are associated with some degree of risk¹⁴; this risk is increased in patients that are unable to be assessed for pre-existing comorbidities (eg, heart disease). Reversible drugs (eg, α_2 agonists, opioids) are preferable, as their adverse effects can be mitigated with reversal agents if necessary.

Some patients may become sedate enough to lose airway protection. Supplies for intubation and appropriate ventilation should always be available for patients that show signs of requiring a protected airway or ventilatory support (eg, cyanosis,

1. in

1 :-

Top 5 Tips for Sedation & Anesthesia in Fractious Dogs: Clinician's Brief

shallow breathing, regurgitation).

 $x = (X_{i} - X_{i})$

Patient Handling While Hospitalized

1. 标识

Fractious patients may require additional precautions for handling and drug administration while hospitalized. Standard monitoring procedures are recommended with the patient sedated or anesthetized. Hospitalization of fractious animals typically requires planning.

Placement of an IV catheter in a pelvic limb can be advantageous, as it provides more room between the patient's head and the injection site. If pelvic limb catheter placement is not feasible, additional placement of long extension sets attached to the IV catheter (Figure 1, top of page) can facilitate semi-remote drug administration and provides an additional level of safety for the patient and staff.

An Elizabethan collar and/or basket muzzle can be used to provide additional safety for aggressive patients, and allowing patients to wear a harness with an attached leash while in a cage can be helpful when removing them from the confined space (Figure 2). Floor-level cages or runs are preferred, as they prevent the need for the handler to lift the patient out of the cage and onto the floor or into a carrier. Muzzles with connections suitable for oxygen delivery are also helpful for providing flow-by oxygen to aggressive patients.

Page 8 of 13



FIGURE 2 To ensure patient and staff safety, an Elizabethan collar and a harness are used on the patient, with the leash attached to the harness and placed toward the cage door.

Recovery & Discharge

For outpatient procedures (eg, outpatient surgery, diagnostic procedures) requiring sedatives/anesthetic drugs, a basket muzzle can be modified so that the endotracheal tube can be removed through the muzzle, which allows the muzzle to be placed on the patient prior to extubation and be in place at the end of the procedure (**Figure 3**). This facilitates safety in the recovery period while still allowing the patient to be closely monitored.

della , tan is

1.0



FIGURE 3 Basket muzzle modified to facilitate extubation (A). Placement of the pilot balloon and endotracheal tube ties through the end of the muzzle is necessary to avoid difficulty extubating the patient (B).

Intravenous catheters can be removed just before discharge. With all tape removed and a bandage left over the catheter, the extension line, which is attached to the catheter hub, can be pulled, thus removing the catheter while keeping the bandage in place for hemostasis (see **Step-by-Step Catheter Removal Video**). Sedatives can be administered intravenously just before catheter removal at the time of discharge and can facilitate a smooth transition from the hospital to the transportation vehicle. The owner should be made aware of the expected nature and duration of the sedation protocol.

Conclusion

Careful planning, communication, and preparation can facilitate a safe and productive appointment for fractious patients that need to be sedated or anesthetized. Multimodal pharmacologic restraint, along with modified approaches to drug administration and patient handling, can mitigate most of the issues encountered with aggressive patients in the hospital setting.

a 52's set 42 of 0

REFERENCES

- Fatjó J, Amat M, Mariotti VM, Luis Ruiz de la Torre J, Manteca X. Analysis of 1040 cases of canine aggression in a referral practice in Spain. J Vet Behav Clin App Res. 2007;2(5):158-165.
- 2. Sueda KL, Malamed R. Canine aggression toward people: a guide for practitioners. *Vet Clin North Am Small Anim Pract*. 2014;44(3):599-628.
- Boyer EW, Shannon M. The serotonin syndrome. N Engl J Med. 2005; 352(11):1112-1120.
- Gruen ME, Sherman BL. Use of trazodone as an adjunctive agent in the treatment of canine anxiety disorders: 56 cases (1995-2007). *J Am Vet Med Assoc*. 2008;233(12):1902-1907.
- Gilbert-Gregory SE, Stull JW, Rice MR, Herron ME. Effects of trazodone on behavioral signs of stress in hospitalized dogs. *J Am Vet Med Assoc*. 2016;249(11):1281-1291.
- 6. Thomas DE, Lee JA, Hovda LR. Retrospective evaluation of toxicosis from selective serotonin reuptake inhibitor antidepressants: 313 dogs (2005-2010). J Vet Emerg Crit Care (San Antonio). 2012;22(6):674-681.
- Hay Kraus BL. Efficacy of maropitant in preventing vomiting in dogs pre-medicated with hydromorphone. *Vet Anaesth Analg.* 2013;40(1):28-34.
- 8. Hsu Y, Sun L. Factors associated with aggressive responses in pet dogs. *Appl Anim Behav Sci.* 2010;123(3-4):108-123.
- Luescher AU, Reisner IR. Canine aggression toward familiar people: a new look at an old problem. *Vet Clin North Am Small Anim Pract*. 2008;38(5):1107-1130, vii.
- Mills DS, Ramos D, Estelles MG, Hargrave C. A triple blind placebocontrolled investigation into the assessment of the effect of Dog Appeasing Pheromone (DAP) on anxiety related behaviour of problem

dogs in the veterinary clinic. Appl Anim Behav Sci. 2006;98(1):114-126.

- 11. Pickering TG, James GD, Boddie C, Harshfield GA, Blank S, Laragh JH. How common is white coat hypertension? *JAMA*. 1988;259(2):225-228.
- Wang XX, Shuai W, Peng Q, et al. White coat effect in hypertensive patients: the role of hospital environment or physician presence. *J Am Soc Hypertens*. 2017;11(8):498-502.
- Moore G, Pfaff JA. Assessment and emergency management of the acutely agitated or violent adult. UpToDate. https://www.uptodate.com/contents/assessment-and-emergencymanagement-of-the-acutely-agitated-or-violent-adult. Updated October 2, 2017. Accessed September 12, 2018.
- Brodbelt DC, Flaherty D, Pettifer GR. Anesthetic risk and informed consent. In: Grimm KA, Lamont LA, Tranquilli WJ, Greene SA, Robertson SA, eds. *Veterinary Anesthesia and Analgesia*. 5th ed. Ames, IA: John Wiley & Sons; 2015:11-22.
- 15. Crowell-Davis SL, Seibert LM, Sung W, Parthasarathy V, Curtis TM. Use of clomipramine, alprazolam, and behavior modification for treatment of storm phobia in dogs. *J Am Vet Med Assoc*. 2003;222(6):744-748.
- Grimm KA, Lamont LA, Tranquilli WJ, Greene SA, Robertson SA, eds. *Veterinary Anesthesia and Analgesia: The Fifth Edition of Lumb and Jones.* Ames, IA: John Wiley & Sons; 2015.
- Plumb DC. *Plumb's Veterinary Drug Handbook*. 9th ed. Hoboken, NJ: Wiley-Blackwell; 2018.
- 18. Haberzettl R, Bert B, Fink H, Fox MA. Animal models of the serotonin syndrome: a systematic review. *Behav Brain Res.* 2013;256:328-345.
- Crowell-Davis SL, Poggiagliolmi S. Understanding behavior serotonin syndrome. *Compend Contin Educ Vet.* 2008;30(9):490-493.

For global readers, a calculator to convert laboratory values, dosages, and other measurements

to SI units can be found here.

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. For questions or inquiries please contact

us.



clinician's brief

Splenectomy: Hilar Ligation Technique

W. Alex Fox-Alvarez, DVM, DACVS-SA, University of Florida J. Brad Case, DVM, MS, DACVS, University of Florida

SURGERY, SOFT TISSUE APRIL 2018 PEER REVIEWED



The spleen has a diverse set of functions, including hematopoiesis, RBC filtration and storage, and immune surveillance. Despite its many functions, removal of the spleen is commonly performed in dogs and cats with rarely observed long-term adverse sequelae. Splenectomy is indicated in cases of splenic neoplasia, trauma, torsion, and infiltrative disease and, occasionally, as treatment for immune-mediated disorders. It is also commonly performed on an emergency basis for hemoabdomen of splenic origin.

Spleen Anatomy

Clinicians should have an understanding of the splenic and regional vascular anatomy before performing splenectomy. The spleen is located on the left side of the body. The head of the spleen is the craniodorsal-most portion and is attached to the greater curvature of the stomach via the gastrosplenic ligament, in which the short gastric arteries and veins are located. The tail of the spleen is the larger, caudal, more mobile portion that sweeps across the ventral midline, with a loose terminal attachment to the greater omentum.

The main blood supply to the spleen comes from the splenic branch of the celiac artery. This splenic artery runs along the left limb of the pancreas, giving off pancreatic branches before spreading into the vessels supplying the splenic parenchyma. It is important to avoid ligating the splenic vessels proximal to these pancreatic branches to avoid damaging pancreatic blood supply.



 FIGURE Splenic and regional vascular anatomy showing the splenic artery (A), gastroepiploic artery (B), short gastric arteries (C), and omental arteries (D)

The head of the spleen is supplied by the short gastric arteries, which arise from the dorsal branch of the splenic artery and anastomose with the branches of the left gastric artery. The majority of the spleen is supplied by the ventral branch of the splenic artery and its numerous intermediate branches into the hilus. The ventral splenic artery continues as the left gastroepiploic artery supplying the greater curvature and fundic portion of the stomach. Ideally, this continuation should be preserved; however, it was shown that sacrifice of the left gastroepiploic vessel did not compromise gastric blood flow or the integrity of the gastric wall in healthy dogs.¹ At the terminal portion of the tail of the spleen, the vessels continue as branches to the omentum.

Surgical Approach

The least complicated anatomic approach to splenectomy that ensures no inadvertent ligation of the pancreatic or left gastroepiploic vessels is the hilar ligation technique. With this technique, the vessels are ligated as they terminate into the spleen. The speed of this technique varies depending on the manner of ligation used, with the use of a vessel-sealing device being the fastest, followed by a staple or clip device, and lastly suture ligation. Some devices can seal vessels up to 7 mm in diameter, whereas hemostatic clips are appropriate for vessels up to 3 mm in diameter. With the appropriate size and material, hand ligation with suture can be used in any size vessel for splenectomy. The following describes the hilar approach to splenectomy.

Of note, one study evaluating the relationship between gastric dilatation volvulus and previous splenectomy found dogs with a previous splenectomy to be 5.3 times more likely to develop gastric dilatation volvulus than were dogs without splenectomy.² Other studies have reported development of gastric dilatation volvulus in atypical breeds (eg, bichon frise, beagle) after splenectomy, which suggests splenectomy may be a potential predisposing factor.³ Thus, some surgeons may recommend prophylactic gastropexy be performed in dogs undergoing splenectomy.

STEP-BY-STEP

SPLENECTOMY: HILAR LIGATION TECHNIQUE

WHAT YOU WILL NEED

- Standard general surgery pack including needle holders, thumb forceps, Metzenbaum scissors, suture scissors, and hemostatic forceps (8-12 inches [20-30 cm])
- Balfour retractor
- Abdominal laparotomy sponges
- Suction device and Poole suction tip
- Electrosurgery handpiece (helpful, but not required)
- ▶ Suture for ligation (generally 2-0 to 3-0 size, depending on patient and pedicle

size)

- +/- Hemostatic clip or staple applicator (optional alternative or supplement to sutures)
- +/- Vessel sealing device (optional alternative or supplement to sutures)

STEP 1

Position the patient in dorsal recumbency (**A**), and prepare the abdomen with a standard aseptic technique. Drape the patient from xiphoid to pubis (**B**). In male dogs, maintain the penis out of the sterile field.



STEP 2

Make a ventral midline abdominal incision from the xiphoid to 2 to 3 cm caudal to the umbilicus (**A**). The incision can be extended caudally if the size of the mass requires. Using electrosurgical instruments or ligation, remove the falciform fat en bloc to improve exposure (**B**). In rare cases, extension from midline into a paracostal incision may be indicated for removal of larger splenic masses.



STEP 3

Perform a methodical exploration of the abdomen. If hemoabdomen is present, use suction to remove the hemorrhage and improve visualization. Carefully inspect the liver and the remaining abdominal viscera to monitor for presence of gross metastasis. A liver biopsy is indicated in cases of suspected malignancy regardless of gross appearance (see **Liver Biopsy**). Gently manipulate the spleen out of the body and onto moistened laparotomy sponges. A diseased spleen is often friable and should be carefully handled to prevent rupture. If the omentum is adhered to a splenic mass, divide the adhesions using electrosurgical devices or ligation. Digital dissection is not recommended, as rupture of the splenic mass may occur.

STEP 4

The hilar vessels can be visualized as they enter the splenic parenchyma (**A**). Using hemostatic forceps, bluntly isolate the vessels (**B**). Using 3-0 absorbable suture, circumferentially double ligate the hilar pedicles (**C** and **D**). Before transecting the vessel, place hemostatic forceps on the pedicle close to the spleen (**E**); this will help prevent splenic bleeding. Repeat this step for all vessels along the splenic hilus until the spleen is removed (**F**).







https://www.cliniciansbrief.com/article/splenectomy-hilar-ligation-...f+Newsletter&utm_campaign=Online+210414&oly_enc_id=067412232356E8U Page 8 of 12





Author Insights

As an alternative to suture ligation, splenic hilar vessels can be ligated using a vessel-stapling apparatus or a vessel-sealing device.⁴

To speed up splenectomy, a surgical assistant can work on isolating the splenic hilar vessels using hemostatic forceps while the surgeon ligates and divides the isolated vessels.

One veterinary study demonstrated no difference in clinical outcome between splenectomy performed using a vessel-sealing device versus a stapler; however, the sealing device yielded significantly shorter procedure times.⁵ Another study found the bursting strength of the sealing device to be greater than 300 mm Hg (ie, \approx 3 times systolic pressure).⁶

STEP 5

After removing the spleen, biopsy any other grossly abnormal tissue. Check the splenic pedicles and biopsy sites for appropriate hemostasis, then gently lavage with warm sterile saline and evacuate the fluid. Perform routine abdominal closure.

Submit the spleen and tissue for histopathologic evaluation.

Postoperative Care & Monitoring

IV fluids should be continued postoperatively and matched to meet the patient's needs. Ongoing monitoring should include serial packed cell volume checks, continuous ECG for assessment of changes in heart rate and rhythm, twice-daily urine output assessment, body weight monitoring, and serial venous blood gas and lactate monitoring. IV opioid analgesics should be administered for at least 24 to 48 hours before weaning or switching to oral analgesic medications. Perioperative antibiotics should not be required for longer than 24 hours unless splenectomy was performed for splenic abscess, in which case antibiotics should be chosen based on results of culture and susceptibility testing and administered

for 10 to 14 days.

REFERENCES

- Hosgood G, Bone DL, Vorhees WD III, Reed WM. Splenectomy in the dog by ligation of the splenic and short gastric arteries. *Vet Surg.* 1989;18(2):110-113.
- Sartor AJ, Bentley AM, Brown DC. Association between previous splenectomy and gastric dilatation-volvulus in dogs: 453 cases (2004-2009). J Am Vet Med Assoc. 2013;242(10):1381-1384.
- Grange AM, Clough W, Casale SA. Evaluation of splenectomy as a risk factor for gastric dilatation-volvulus. *J Am Vet Med Assoc*. 2012;241(4):461-466.
- 4. Monarski CJ, Jaffe MH, Kass PH. Decreased surgical time with a vessel sealing device versus a surgical stapler in performance of canine splenectomy. *J Am Anim Hosp Assoc.* 2014;50(1):42-45.
- Blake JS, Trumpatori BJ, Mathews KG, Griffith EH. Carotid artery bursting pressure and seal time after multiple uses of a vessel sealing device. *Vet Surg.* 2017;46(4):501-506.
- 6. Eick S, Loudermilk B, Walberg E, Wente MN. Rationale, bench testing and in vivo evaluation of a novel 5 mm laparoscopic vessel sealing device with homogeneous pressure distribution in long instrument jaws. *Ann Surg Innov Res.* 2013;7:15.

AUTHORS

W. Alex Fox-Alvarez

DVM, DACVS-SA University of Florida

W. Alex Fox-Alvarez, DVM, is a small animal surgical resident and

incoming assistant professor at University of Florida, where he also earned his DVM. Dr. Fox-Alvarez completed a small animal emergency and zoo animal rotating internship at VCA Valley Animal Hospital and Emergency Center in Tucson, Arizona. His interests are minimally invasive surgery, surgical instrument design, and exotic animal surgery.

J. Brad Case

DVM, MS, DACVS University of Florida

J. Brad Case, DVM, MS, DACVS, is an associate professor and small animal surgeon at University of Florida and serves as president of the Veterinary Endoscopy Society. He earned his DVM from University of California, Davis, and his MS from Colorado State University, where he also completed a residency. Dr. Case's primary clinical research interests are in developing minimally invasive and vascular interventional procedures.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units **can be found here.**

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. For questions or inquiries please contact us.



clinician's brief

Helping Cats Give Insulin the Boot

Callie Harris, DVM, Veterinary Communications Manager, Nestlé Purina PetCare

 NUTRITION
 SPONSORED

 Print/View PDF

Sponsored by Nestlé Purina Company

Studies have shown remission rates for cats with diabetes mellitus can run from 15 percent to 100 percent.¹ The earlier we implement appropriate medical and dietary management, the more likely the diabetic cat is to respond favorably to eventual withdrawal from insulin.²

Achieving remission depends on several factors. Is the patient overweight? Does he or she have concurrent diseases? Will the owner be compliant with medication and diet? Administering insulin is a must to stabilize diabetic patients. It's important for clinic staff to educate clients about the correct way to store insulin, how to handle a syringe and how to inject insulin properly.

Another critical factor is the extent of damage to pancreatic beta cells. Cats diagnosed late in the disease process may have cell damage so severe that insulin may be required indefinitely. Cats with conditions such as acromegaly, chronic

Page 1 of 3
renal disease, thyroid disease and chronic pancreatitis are likewise poor candidates for remission.

Nutritional Management

The goal with any feline diabetic patient is to stabilize glucose levels. In addition to determining the appropriate insulin dose, we need to ascertain what nutritional regimen will work best. High-protein, low-carbohydrate diets have been shown to be optimal for cats with diabetes,³ as well as for promoting retention of lean body mass.⁴ Intake of carbohydrates should be limited because they may contribute to hyperglycemia and glucose toxicity.

Many diabetic cats are also obese — a factor that further impairs the cats' ability to achieve remission. I believe weight loss should be prioritized in feline patients with a body condition score of 8 or greater on a 9-point scale.

According to AAHA guidelines, the optimal food for a diabetic cat in any body condition is a formula that is high in protein, low in carbohydrates and low in fiber.¹ With this in mind (and remembering that every patient is unique), I'll most often recommend Purina^{*} Pro Plan^{*} Veterinary Diets DM Dietetic Management^{*} Canned Feline Formula for my diabetic patients. If I have a patient that is overweight as well as diabetic, I'll strive to maintain control of the diabetes with any of the DM formulas after a healthier weight is achieved. My goal is to help reduce insulin requirements by providing more appropriate glycemic control.

Once the patient is at a healthier weight and responding well to insulin therapy with a series of stable glucose curves, I can begin the process of slowly weaning the cat off of insulin — always with close monitoring and the support of a compliant owner — to see if this option works for them.

REFERENCES

1. Behrend E, Holford A, et al. 2018 AAHA Diabetes Management

EXHIBIT 7 - 201

Guidelines for Dogs and Cats. J Am Anim Hosp Assoc. 2018;54:1-21.

- Roomp K, Rand J. Intensive blood glucose control is safe and effective in diabetic cats using home monitoring and treatment with glargine. J Feline Med Surg. 2009 Aug;11(8):668-82.
- Zoran D, Rand J. The role of diet in the prevention and management of feline diabetes. *Vet Clin North Am Small Anim Pract*. 2013 Mar;43(2):233-43.
- Laflamme D, Hannah S. Increased Dietary Protein Promotes Fat Loss and Reduces Loss of Lean Body Mass During Weight Loss in Cats. *Intern J Appl Res Vet Med.* 2005;3(2):62–68.

AUTHOR

Callie Harris

DVM

Veterinary Communications Manager, Nestlé Purina PetCare

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found here.

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. **For questions or inquiries please contact us.**



clinician's brief

Differential Diagnosis: Hypokalemia

Julie Allen, BVMS, MS, MRCVS, DACVIM (SAIM), DACVP (Clinical), Durham, North Carolina

INTERNAL MEDICINE | OCTOBER 2019 | PEER REVIEWED



Editor's note: A previous version of this article incorrectly listed hyperkalemic periodic paralysis in Burmese cats as a differential diagnosis. This has been corrected as of February 2020.

Following are differential diagnoses, listed in order of

Feedbac

likelihood, for patients presented with hypokalemia.

- Increased loss
 - Through the kidney (most common)
 - Chronic kidney disease
 - Loop and thiazide diuretics
 - Postobstructive diuresis (cats affected more than dogs)
 - Renal tubular disease
 - Osmotic diuresis
 - Acute metabolic acidosis secondary to lactic acid or ketone excretion
 - Primary metabolic alkalosis
 - Diuresis secondary to hyperadrenocorticism; some patients with adrenocortical tumors also produce excess aldosterone
 - High dietary sodium intake
 - Primary hyperaldosteronism, usually due to an adrenal tumor or hyperplasia
 - Excessive mineralocorticoid administration (eg, overdose of desoxycorticosterone pivalate or fludrocortisone)
 - Administration of certain drugs (eg, penicillins, carbonic anhydrase inhibitors, amphotericin B)
 - Through the GI tract
 - Vomiting
 - Chronic diarrhea
 - Ileus
 - Third-spacing (eg, loss in peritoneal fluid)

- Transcellular shifts
 - Insulin release or administration
 - Increased endogenous catecholamines (eg, pheochromocytoma) or epinephrine administration
 - Primary respiratory or metabolic alkalosis
 - Hyperthyroidism, likely due to transcellular shifts
 - Endotoxemia
 - Refeeding syndrome
 - Hypomagnesemia
 - Treatment with or toxicosis from β_2 agonists (eg, albuterol, terbutaline)
 - Hyperinsulinemia secondary to xylitol toxicosis, which stimulates the activity of the Na+/K+-ATPase pump, which catalyzes transfer of potassium in the cells
 - Hypothermia
 - Periodic hypokalemic polymyopathy (Burmese cats)
- Decreased intake
 - Administration of low-/no-potassium intravenous fluids
 - Low-potassium diets, often acidifying diets
 - Severe anorexia (usually a confounding factor and not a primary cause)
 - Ingestion of clay cat litter containing bentonite, which binds potassium in the GI tract

Pseudohypokalemia; occurs secondary to lipemia and marked hyperglobulinemia*

*Only when measured by indirect potentiometry, the method used by most chemistry analyzers; blood gas analyzers using direct potentiometry are unaffected.

REFERENCES

- 1. DiBartola SP, de Morais HA. Disorders of potassium: hypokalemia and hyperkalemia. In: DiBartola SP, ed. *Fluid, Electrolyte, and Acid-Base Disorders*. 4th ed. St Louis, MO: Elsevier Saunders; 2012:92-108.
- George JW, Zabolotosky SM. Water, electrolytes and acid base. In: Latimer KS, ed. Duncan and Prasse's Veterinary Laboratory Medicine: Clinical Pathology. 5th ed. Ames, IA: Wiley-Blackwell; 2011:158-162.
- 3. Hornfeldt CS, Westfall ML. Suspected bentonite toxicosis in a cat from ingestion of clay cat litter. *Vet Hum Toxicol*. 1996;38(5):365-366.
- Kardalas E, Paschou SA, Anagnostis P, Muscogiuri G, Siasos G, Vryonidou A. Hypokalemia: a clinical update. *Endocr Connect*. 2018;7(4):R135-R146.
- 5. Kogika MM, de Morais HA. A quick reference on hypokalemia. *Vet Clin North Am Small Anim Pract.* 2017;47(2):229-234.
- 6. Malik R, Musca FJ, Gunew MN, et al. Periodic hypokalaemic polymyopathy in Burmese and closely related cats: a review including the latest genetic data. *J Feline Med Surg.* 2015;17(5):417-426.
- 7. Murphy LA, Dunayer EK. Xylitol toxicosis in dogs: an update. *Vet Clin North Am Small Anim Pract.* 2018;48(6):985-990.
- 8. Nemzek JA, Kruger JM, Walshaw R, Hauptman JG. Acute onset of hypokalemia and muscular weakness in four hyperthyroid cats. *J Am Vet Med Assoc.* 1994;205(1):65-68.
- Stockham SL, Scott MA. Monovalent electrolytes and osmolality. In: Stockham SL, Scott MA. *Fundamentals of Veterinary Clinical Pathology*. 2nd ed. Ames, IA: Blackwell Publishing; 2008:511-516.
- 10. Thiessen CE, Tofflemire KL, Makielski KM, Ben-Schlomo G, Whitley RD, Allbaugh RA. Hypokalemia and suspected renal tubular acidosis associated with topical carbonic anhydrase inhibitor therapy in a cat. *J*

Vet Emerg Crit Care (San Antonio). 2016;26(6):870-874.

11. Xia Z, He Y, Yu J. Experimental acute toxicity of xylitol in dogs. *J Vet Pharmacol Ther.* 2009;32(5):465-469.

AUTHOR

Julie Allen

BVMS, MS, MRCVS, DACVIM (SAIM), DACVP (Clinical) Durham, North Carolina

Julie Allen, BVMS, MS, MRCVS, DACVIM (SAIM), DACVP (Clinical), is a former clinical assistant professor of clinical pathology at Cornell University. She earned her veterinary degree from University of Glasgow and her MS from Iowa State University, where she completed a rotating internship in small animal medicine and surgery and a residency in small animal internal medicine. She also completed a residency in clinical pathology at North Carolina State University. Dr. Allen focuses on cachexia/anorexia, endocrinology, and hepatobiliary and pancreatic disease and has committed her career to improving the diagnosis of disease.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found here.

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, ELC. For questions or inquiries please contact us.

Canine Polyuria/Polydipsia: When Is Testing for Hyperadrenocorticism Indicated?



ENDOCRINOLOGY & METABOLIC DISEASES SPONSORED

Print/View PDF



Sponsored by Dechra Veterinary Products

Abby, a 9-year-old female spayed miniature poodle, was presented for polyuria/polydipsia (PU/PD) of several weeks' duration. Abby had been drinkin more, asking to go out more frequently, and urinating larger volumes, which ha the owner concerned about a possible UTI. Abby was up to date on vaccines (i¢ rabies, *Bordetella bronchiseptica*, leptospirosis, distemper/adenovirus/ parainfluenza/parvovirus) and parasite prevention. Her medical history was unremarkable, except for a history of medial patellar luxation. She had not received any medications except parasite prevention in the preceding months.

CBC, serum chemistry, total thyroxine (T_4), and urinalysis were recommended based on examination findings and the presence of PU/PD. Abby's owner expressed financial constraints but authorized the urinalysis, saying she would consider the cost of further testing.

A urine sample was collected via cystocentesis. Urinalysis revealed a urine specific gravity of 1.006 and inactive sediment. Culture was performed to rule out occult infection and was negative.

After receiving these results, Abby's owner authorized the additional recommended tests. One week la Abby returned for fasting bloodwork. CBC was unremarkable, and T₄ was within normal limits. Serum chemistry profile revealed increased ALP, ALT, and cholesterol.

Differentials for Canine Polyuria/Polydipsia

Considering Abby's blood work and urinalysis results, her veterinarian began to work through the long of differentials for PU/PD.¹ Based on Abby's laboratory results, examination findings, and medical hist many of the differentials could be ruled out, leaving the following as remaining differentials:

- Hyperadrenocorticism
- Atypical Cushing's disease (hyperaldosteronism)
- Hypoadrenocorticism
- Liver disease
- Neoplasia
- Central diabetes insipidus
- Primary nephrogenic diabetes insipidus
- Renal medullary washout
- Acute kidney injury
- Pheochromocytoma
- Psychogenic polydipsia

After reviewing this list, Abby's veterinarian strongly suspected hyperadrenocorticism. Her signalment appropriate (ie, a middle-aged miniature poodle) and she also had characteristic laboratory (ie, increa ALP/ALT and hypercholesterolemia) and examination findings (ie, pendulous abdomen).

Diagnostic Tests for Cushing's Disease

There are several tests that can be used to diagnose hyperadrenocorticism, each with their own unique advantages and disadvantages. The urine cortisol:creatinine ratio can be used to help rule out Cushing

addition, the LDDS test can serve as a differentiating test, distinguishing between adrenal-dependent a pituitary-dependent disease in $\leq 60\%$ of cases.³ If a nonadrenal illness is present, however, the LDDS te may produce a false-positive result.³

The LDDS test can serve as a differentiating test, distinguishing between adrenal-dependent and pituitary-dependent disease in ≤60% of cases.

The ACTH stimulation test is another comp diagnostic test for Cushing's disease. It is n effective in diagnosing iatrogenic hyperadrenocorticism than the LDDS test has a higher specificity.¹ However, it canno differentiate pituitary-dependent from adrenal-dependent Cushing's disease, thu requiring follow-up testing for a positive re

Abby's veterinarian elected to perform the LDDS test. This was a good option for Abby because of the terelatively low cost, lack of evidence of nonadrenal illness, and the fact that it can serve as a differentiati test.

Abby was brought in for an all-day visit to the clinic. The veterinary team collected a baseline blood sar administered dexamethasone (0.01-0.015 mg/kg IV), and collected blood samples 4 and 8 hours after dexamethasone injection. Abby's cortisol levels were as follows:

- Before dexamethasone injection: 10 ug/dL
- 4 hours postinjection: 4 ug/dL
- 8 hours postinjection: 10 ug/dL

These results show suppression of cortisol production at 4 hours, followed by an escape of suppression hours. This pattern is diagnostic for pituitary-dependent Cushing's disease. Based on these results, Abl veterinarian contacted the owner to recommend trilostane treatment.

Conclusion

When middle-aged dogs are presented for PU/PD, the top 3 differentials should generally be hyperadrenocorticism, diabetes mellitus, and chronic renal disease. However, it is important to also th through other differential diagnoses for PU/PD. Some of these differentials can be ruled out based on examination/laboratory findings and history, whereas others require more advanced testing. The diagnostic investigation of PU/PD requires veterinarian discretion in determining when to look for Cushing's disease with specific tests such as the LDDS test or begin investigation for other differentials

By thinking through this case critically and considering other differentials for Abby's PU/PD, Abby's veterinarian avoided LDDS testing until there was a high clinical index of suspicion. This not only minimized the likel: hood of stressing hilly and her owner with unnecessary resp https://www.cliniciansbrief.com/article/canine-polyuria-polydipsia-when-testing-hyperadrenocorticism-indicated Page 3 of 6

But also ensured recipionsible use of the owner's available frexiliality soundes

Internal Medicine. Elsevier Saunders; 2017:180.

- 2. Smiley LE, Peterson ME. Evaluation of a urine cortisol:creatinine ratio as a screening test for hyperadrenocorticism in dogs. *J Vet Intern Med.* 1993;7(3):163-168.
- Greco D. Cushing disease (pituitary-dependent hyperadrenocorticism) in animals. Merck Veterinary Manual website. https://www.merckvetmanual.com/endocrine-system/thepituitary-gland/cushing-disease-pituitary-dependent-hyperadrenocorticism-in-animals. Updated August 2019. Accessed March 18, 2021.
- 4. Mooney CT. How to interpret tests for canine hyperadrenocorticism. Paper presented at: 2008 World Small Animal Veterinary Association World Congress. Dublin, Ireland; 2008.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units **can be found** All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not ref recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission c Educational Concepts, LLC. For questions or inquiries please contact us.

https://www.cliniciansbrief.com/article/canine-polyuria-polydipsia-when-testing-hyperadrenocorticism-indicated

https://www.cliniciansbrief.com/article/canine-polyuria-polydipsia-when-testing-hyperadrenocorticism-indicated

EXHIBIT 7 - 213

clinician's brief



Left-Sided Congestive Heart Failure

Jessica McGinnis, DVM, University of Florida College of Veterinary Medicine Amara Estrada, DVM, DACVIM (Cardiology), University of Florida

JANDARY / FEBRUARY 2018 | SEER REVIEWED



Left-sided congestive heart failure (L-CHF) is a life-threatening condition caused venous congestion secondary to increased left atrial pressure. This pressure occurs when the left ventricle is unable to adequately fill with or eject blood because of a primary structural or functional cardiac condition.1

L-CHF patients may initially show no clinical signs; however, those that present with acute dyspnea mu.

SIDED CONGESTIVE HEART FAILURE IN DOGS & CATS

Condition	Effect	Species & Breed
Myxomatous mitral valve disease	Increased left atrial pressure	 Cavalier King Charles spaniel Chihuahua Miniature pinschers Yorkshire terrier Other small-breed dogs
Dilated cardiomyopathy ^{4,16}	Increased left atrial pressure	 Doberman pinscher Boxer Great Dane German shepherd dog Labrador retriever Other large- & giant-breed dog
Hypertrophic cardiomyopathy ¹	Thickening of the left ventricle	 Cats¹⁷ Maine coon Persian American domestic shorthat

Clinical Signs

Cats and dogs may appear clinically normal in the early compensatory phase of L-CHF. Monitoring sleeping respiratory rates (SRR) at home can help detect early L-CHF in patients with known cardiac disease. A sustained SRR of more than 30 breaths per minute may be indicative of potential decompensated CHF.² As the disease progresses and the patient reaches the decompensated phase of L

EXHIBIT 7 - 215

absence of these findings, however, does not rule out the presence of L-CHF. Cats, for example, do not breathe deeply enough to manifest obvious pulmonary crackles even with severe dyspnea. Decreased rectal temperature, pale mucous membranes, and prolonged capillary refill time because of vasoconstriction and decreased peripheral perfusion may also be observed, and cardiac arrhythmias m be present, depending on the underlying condition.^{1,3} Coughing does not always indicate that a dog wit cardiac disease has L-CHF, as small dogs frequently have a paroxysmal-to-sustained cough related to compression of the mainstem bronchus secondary to cardiac enlargement.⁴ In these patients, thoracic radiography is needed to establish the diagnosis and guide treatment.

Patients with acute dyspnea should undergo aggressive stabilizing treatment before any ancillary diagnostic testing is performed.

Diagnosis

If clinical signs are not immediately life-threatening, at a minimum, a lateral thoracic radiograph should obtained. Thoracic radiography is the gold standard for diagnosing pulmonary edema and venous congestion secondary to L-CHF.^{3,5} If the patient is not in distress, a 3-view study with a ventrodorsal or dorsoventral (VD/DV) view and opposite lateral thoracic views is ideal. Characteristic findings of cardiogenic pulmonary edema include increased interstitial-to-alveolar infiltrates of the perihilar and/c caudodorsal lung field in dogs.^{3,5} (See **Figures 1A** and **1B**.)



FIGURE 1 (A) L-CHF in a Cavalier King Charles spaniel with mitral valve disease. Enlarged cranial lobar vessels are marked by the arrows. Enlarged left atrium is marked with an asterisk. (B) DV projection shows a caudal interstitial-to-alveolar pattern with air bronchograms (arrow). Images courtesy of University of Florida Small Animal Hospital

In cats, a ventral or diffuse interstitial-to-alveolar pattern may be present^{3,5}; pleural effusion is indicated pleural fissure lines, retraction of the lung lobes, and effacement of the cardiac silhouette.⁶ (See **Figure** : Dyspneic cats with evidence of pulmonary infiltrates should receive a presumptive diagnosis of cardiog pulmonary edema until proven otherwise (often by a clinical diuretic trial).



 FIGURE 2 L-CHF in a cat with cardiomegaly and pleural effusion with visible pleural fissure line (arrow).

Left atrial enlargement is typically present in both cats and dogs with L-CHF. In dogs, left atrial enlargement typically appears in radiographs as a rounded increased opacity caudal to the carina in the perihilar region on the lateral projection. (See **Figure 1A**.) Generalized cardiomegaly is identified by measuring vertebral heart score (VHS).^{3,5} (See **Figure 3**.) In cats, both generalized cardiomegaly and lef atrial enlargement are more difficult to assess because of their more subtle radiographic changes; they a characterized by a VHS score greater than 8 and the presence of a valentine-shaped heart on the VD/DV projection, respectively. However, normal left atrial size on thoracic radiography does not rule out the presence of L-CHF in dyspneic cats.¹ Once acute L-CHF has been identified and treated, evaluation by a cardiologist is recommended, but stabilization of the patient is the first priority.



 FIGURE 3 VHS of 10.5 in a cat. Normal VHS for cats and dogs is less than 8.0 and less than 10.5, respectively. Note the diffuse interstitial-to-alveolar lung pattern, which most likely represents cardiogenic pulmonary edema.

Additional initial diagnostics include blood pressure measurement and renal and electrolyte studies to

Nevertheless, a positive NT-proBNP SNAP test can raise clinical suspicion of L-CHF and prompt the practitioner to treat accordingly.

Treatment

Acute L-CHF is treated with oxygen supplementation and diuretic therapy.^{1,3,7,9} (See **Figure 4**.) Oxygen be administered via flow-by, oxygen cage, or nasal oxygen cannulas and should be provided until the patient is eupneic in room air (ie, 21% oxygen).^{1,3} In cats, empiric treatment with an albuterol inhaler ca also be considered; however, this should be avoided if proven that it adds extra stress to the patient.



 FIGURE 4 Algorithm for recognizing, diagnosing, and treating feline CHF.

Furosemide is the initial diuretic of choice and should be administered at 2 to 4 mg/kg IV.^{1,3,7} If IV acces not possible because of patient distress, furosemide can be administered IM.⁹ Maximal effect is expecte within 30 minutes of IV administration and within 1 to 2 hours of IM administration.^{7,9} Diuretic therapy should aim to relieve respiratory distress. Repeat bolus doses can be administered every 30 minutes unt the desired effect is achieved. Ideally, the total daily dose of furosemide should not exceed 12 mg/kg.¹

If repeat bolus doses are required, a furosemide CRI at a rate of 0.66 to 1.0 mg/kg/h may be considered.¹ Thoracocentesis is recommended in cats with clinically significant pleural effusion.¹ Because azotemia is hypokalemia may develop with the use of a loop diuretic (eg, furosemide), renal and electrolyte values should be monitored daily in hospitalized patients receiving treatment for acute L-CHF. These values

EXHIBIT 7 - 219

dogs with stage B2 and C myxomatous mitral valve disease and dogs with dilated cardiomyopathy. Pimobendan has been shown to prolong the time to onset and recurrence of L-CHE.¹⁰⁻¹³ No prospective literature supports the use of pimobendan in cats, but retrospective studies have suggested a potential benefit of this drug in cats with hypertrophic cardiomyopathy and L-CHF, especially those with systolic dysfunction and without systolic anterior motion of the mitral valve.^{14,15}

Conclusion

L-CHF is often a life-limiting disease. However, patients who receive an initial diagnosis of L-CHF have : approximate survival-to-discharge rate of 80%, and patients typically have a good quality of life during treatment of compensated L-CHF.¹ (See **Resource**.)

In a well-managed patient nave to previous cardiac medications, the average survival time with L-CHF i to 12 months.^{1,11} SRR is a valuable parameter for owners to measure at home and, when increased, indicates the need for prompt treatment.² Continued follow-up care, including repeat measurement of renal and electrolyte values, thoracic radiography (if indicated), and echocardiography is an important aspect of L-CHF management.



REFERENCES

Resource

▶ Cardiac Education Group.

- 3. Mazzaferro EM. Emergency management of congestive heart failure [published online October 1, 2005]. *Veterinary Medicine*. 2005;100(10):734-741.
- 4. Atkins C, Bonagura J, Ettinger S, et al. Guidelines for the diagnosis and treatment of canine chronic valvular heart disease. *J Vet Intern Med.* 2009;23:1142-1150.
- 5. Guglielmini C, Diana A. Thoracic radiography in the cat: identification of cardiomegaly and congestive heart failure. *J Vet Cardiol*, 2015;17(suppl 1):S87-S101.
- 6. Stillion JR, Letendre JA. A clinical review of the pathophysiology, diagnosis, and treatment of pyothorax in dogs and cats. *J Vet Emerg Crit Care (San Antonio)*. 2015;25(1):113-129.
- 7. Gordon SG, Ct E. Pharmacotherapy of feline cardiomyopathy: chronic management of heart failure. *J Vet Cardiol.* 2015;17(suppl 1):S159-S172.
- 8. Harris AN, Beatty SS, Estrada AH, et al. Investigation of an N-terminal prohormone of brain natriuretic peptide point-of-care ELISA in clinically normal cats and cats with cardiac disease. *J Vet Intern Med.* 2017;31(4):994-999.
- 9. Harada K, Ukai Y, Kanakubo K, et al. Comparison of the diuretic effect of furosemide by different methods of administration in healthy dogs. *J Vet Emerg Crit Care (San Antonio)*. 2015;25(3):364-371.
- Boswood A, Hggstrm J, Gordon G, et al. Effect of pimobendan in dogs with preclinical myxomatous mitral valve disease and cardiomyopathy: the EPIC studya randomized clinical trial. J Vet Intern Med. 2016;30(6):1765-1779.
- 11. Hggstrm J, Boswood A, OGrady M, et al. Effect of pimobendan or benazepril hydrochloride on survival times in dogs with congestive heart failure caused by naturally occurring myxomatous mitral valve disease: the QUEST study. *J Vet Intern Med.* 2008;22(5):1124-1135.
- 12. OGrady MR, Minors SL, OSullivan ML, Horne R. Effect of pimobendan on case fatality rate in Doberman pinschers with congestive heart failure caused by dilated cardiomyopathy. *J Vet Intern Med.* 2008;22(4):897-904.
- 13. Summerfield NJ, Boswood A, OGrady MR, et al. Efficacy of pimobendan in the prevention of congestive heart failure or sudden death in doberman pinschers with preclinical dilated cardiomyopathy (the PROTECT study). *J Vet Intern Med.* 2012;26(6):1337-1349.
- 14. Gordon SG, Saunders AB, Roland RM, et al. Effect of oral administration of pimobendan in cats with heart failure. *J Am Vet Med Assoc.* 2012;241(1):89-94.
- 15. Reina-Doreste Y, Stern JA, Keene BW, et al. Case-control study of the effects of pimobendan on survival time in cats with hypertrophic cardiomyopathy and congestive heart failure. *J Am Vet Med Assoc.* 2014;245(5):534-539.
- 16. Simpson S, Edwards J, Ferguson-Mignan TFN, Cobb M, Mongan NP, Rutland CS. Genetics of human and canine dilated cardiomyopathy. *Int J Genomics*. 2015;2015:204823.

DVM

University of Florida College of Veterinary Medicine

Jessica McGinnis, DVM, is currently an intern in emergency medicine and critical care with a special focus in cardiology at University of Florida. She earned her DVM from Michigan State University. Following graduation, she completed a 1-year rotating internship at Red Bank Veterinary Hospital. She has a special interest in arrhythmias and arrhythmogenic cardiomyopathy.

FUN FACT: When not at work, Jessica enjoys kayaking and river tubing.

Amara Estrada

DVM, DACVIM (Cardiology) University of Florida

Amara Estrada, DVM, DACVIM (Cardiology), is a professor of cardiology and the associate chair for instruction in the department of small animal clinical sciences at University of Florida, where she also earned her DVM. Dr. Estrada completed a cardiology residency at Cornell University. She frequently speaks at continuing education meetings nationally and internationally. Her research interests include inherited cardiomyopathies and interprofessional education.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found I All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not refle recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. For questions or inquiries please contact us.



clinician's brief

Monitoring Blood Glucose in Patients with Diabetes Mellitus

Thomas Schermerhorn, VMD, DACVIM (SAIM), Kansas State University

ENDOCRINOLOGY & METABOLIC DISEASES NOVEMBER 2016 PEER REVIEWED



A long-term patient monitoring strategy that is clinically sound, practical, and effective should be developed for every patient

with diabetes mellitus (DM). A close clinician–pet owner relationship is critical to success, as the pet owner provides daily care and performs most day-to-day monitoring. Owners should be educated to recognize early signs of problems with DM management and to communicate their observations to the veterinary team. Routine physical examinations and laboratory testing are also critical and present opportunities to discuss progress, troubleshoot problems, and assess quality of life. Restoring and maintaining patient quality of life is a paramount concern of most owners^{1,2} and should be a foundational goal of any monitoring strategy.

Optimal glycemic control requires appropriate insulin therapy to control hyperglycemia and avoid hypoglycemia and other complications. Various laboratory tests and clinical tools are available and appropriate for monitoring^{3,4}; however, no single method or combination has been shown to have clear, significant clinical benefits. Therefore, the monitoring program should be practical and the components tailored to meet individual patient needs and owner abilities, circumstances, and treatment goals. Recommendations for DM monitoring in dogs and cats are typically based on expert advice and experience, and published consensus guidelines are available.⁵ Elimination of clinical signs of DM is an acceptable and achievable goal for most patients, but various monitoring strategies can be used to achieve acceptable glycemia. Interventions should be performed frequently enough to be effective but not so often that they are impractical or inconvenient for the owner.

Monitoring Methods

Monitoring DM involves several direct and indirect methods for assessing glycemic control (**Table 1**). Direct monitoring uses a quantitative method to determine blood glucose (BG; eg, spot or random BG sampling, BG curve, interstitial glucose monitoring [IGM]). Indirect monitoring evaluates a subjective (eg, physical examination findings, clinical signs) or objective (eg, quantitative measurements of hemoglobin A1c [HbA1c] or fructosamine) parameter influenced by BG rather than glucose itself. Monitoring for the typical DM patient should incorporate several methods, each with advantages and disadvantages (**Table 2**).

TABLE 1

DIABETES MELLITUS MONITORING METHODS

Method	Monitoring Test/Procedure	Information Provided
Direct	BG curve IGM Spot BG determination	Quantitative BG concentration
Objective indirect	HbA1c Serum fructosamine Urine glucose measurement	Retrospective information about BG concentration
Subjective indirect	Clinical signs Physical examination	Glycemic control inferred from history and physical examination

Assessment of Clinical Signs

Polydipsia and polyuria are commonly observed clinical signs of DM that are directly related to the magnitude of hyperglycemia but are of limited sensitivity and specificity. Hyperglycemia results in plasma hypertonicity, which stimulates thirst and promotes volume loss via osmotic diuresis and glucosuria once the renal threshold for glucose reabsorption is exceeded.

Appetite, body weight, and body condition can also provide clues to glycemic control. Appetite persists in most diabetic dogs and cats, but body weight and condition are abnormal in many patients at the time of diagnosis; they may be improved through insulin therapy and glycemic control. Poor glycemic control should be suspected if a patient's weight/condition does not improve or begins to decline during therapy. The monitoring strategy must detect deviations from a patient's normal condition (see **Benefits of Monitoring for Clinical Signs**). Owners should be made aware of signs of poor glycemic control and instructed to observe water consumption, voiding habits, and appetite, along with body condition, weight, and overall health. Concerning trends or indicators should be shared with the clinician.

BENEFITS OF MONITORING FOR CLINICAL SIGNS

The usefulness of monitoring for clinical signs caused by hyperglycemia is 2-fold:

- ► A significant disturbance in BG can be inferred from the persistence or emergence of clinical signs during treatment (the renal threshold for glucose is ≈200 mg/dL in dogs and ≈250 mg/dL in cats).⁵
- Evidence shows a positive correlation between objective measures (ie, serum fructosamine and mean 8-hour BG concentration) and owner assessment of control based on clinical signs.²⁵

Careful, frequent evaluation of clinical signs is an important part of monitoring BG and protecting overall health.²⁵ DM is a primary cause of cataracts in dogs and a cause of peripheral neuropathy in dogs and cats.^{26,27} Thus, signs of these conditions and other common diabetic complications or concurrent disorders (eg, pancreatitis, renal failure, endocrinopathy, neoplasia) should be included in monitoring.²⁶⁻²⁸

Urine Monitoring

Urine testing for glucose and ketones in DM is used to detect changes in health status before clinical signs appear. Abrupt changes in the magnitude of glucosuria or emergence of ketonuria can signal a recent disruption in glycemic control, but this advantage may not be realized in practice, as outward clinical signs often precede detection of altered urine glucose or ketone concentrations in urine. In addition, urine testing can have several drawbacks (eg, difficulty in obtaining a sample for testing, leading to poor compliance).⁶ Overall, this method is not recommended for DM monitoring; it may be useful in some circumstances but must be interpreted in context of other findings.⁶

TABLE 2

ADVANTAGES & DISADVANTAGES OF DIABETES MELLITUS MONITORING METHODS

Monitoring Method	Advantages	Disadvantages
ASSESSMENT OF CLINICAL SIGNS	Easy to use frequently Can correlate at-home and in-clinic observations Involves owner in pet's care Absence of signs associated with improved quality of life	Subjective; interpretation vulnerable to bias/expectations Chronic, mild/moderate BG disturbances may be missed.
GLYCATED PROTEIN MEASUREMENT	Provides time- averaged BG information Monitoring is periodic; requires only a single blood sample Reliable commercial	Information is retrospective. Serial sampling is more helpful than a single test result. Precise target ranges/therapeutic endpoints are undefined. Frequent testing increases cost to owners.

	assays available for HbA1c and fructosamine	Patient factors/concurrent disorders influence results.
Fructosamine	Reflects average BG for ≈2 weeks preceding test	Does not reflect long-term changes in BG status Does not correlate well with other glycemic assessments in some patients
HbA1c	Small volume sample required (several drops of blood) Reflects average BG for 70 days (cats) or 120 days (dogs) preceding test	Less sensitive to short-term changes in BG Can be influenced by factors that affect Hb concentration/turnover
BG MEASUREMENT	Provides pharmacodynamic information about response to insulin Immediate, real-time measurement of BG	Normal biologic variability may have substantial impact on results. Substantial cost
BG curve	Traditional, familiar technique Uses simple, reliable technology (glucometer) Can be performed in the clinic or at home	Time consuming; practical considerations limit time period over which curve can be performed. Requires multiple blood samples May not be predictive of future insulin needs
IGM (flash or continuous)	Provides timely information about	Changes in interstitial glucose lag behind changes in BG.

	insulin action Provides real-time and retrospective data Well tolerated; suitable for at-home use Daily data can be monitored/collected over several weeks.	No approved veterinary IGM units; some manufacturers may not make technology/equipment available to clinicians.
Spot BG measurement (capillary or venous blood sample)	Useful for documenting hypoglycemia	Randomly timed BG measurements have little value for patient assessment or guiding therapy.
URINE GLUCOSE MONITORING	Allows for simultaneous testing for urine glucose and ketones May be only option for home testing for some owners	Results are semiquantitative and lag behind blood changes. Glucosuria does not correlate closely with BG. Samples may be difficult to obtain for some owners.

Glycated Proteins

Proteins exposed to glucose are altered via a nonenzymatic chemical reaction. The concentration of these glycated proteins in blood increases with the circulating BG concentration. Because glycated proteins are metabolized in the same manner as nonglycated proteins, their concentration in the circulation reflects the average BG over the lifespan of the parent protein. Serum fructosamine and HbA1c are the major glycated proteins in dogs and cats; monitoring these blood concentrations can provide insight about glycemic control and response to insulin.

Fructosamine values represent the concentrations of several glycated serum proteins, but glycated albumin makes up the largest portion.⁷ In dogs and cats, fructosamine concentration is frequently used to monitor DM and is interpreted to reflect average glycemia over the previous 2 weeks, which is the approximate lifespan of serum albumin. HbA1c is a specific glycated hemoglobin moiety used extensively for monitoring glycemia in humans with DM but is used less frequently in veterinary medicine. Due to hemoglobin's longer serum lifetime, HbA1c levels reflect average serum glucose over the erythrocyte lifespan in circulation (dogs, ≤ 120 days; cats, ≈ 70 days).⁸ Although HbA1c represents glycemia over a substantially longer time than fructosamine, acute, short-term disruptions in glycemic control affect fructosamine sooner than HbA1c (see **Drawbacks of Glycated Protein Monitoring**). A reduction in fructosamine and HbA1c concentrations is expected with successful insulin therapy.^{7,9}

Clinicians have traditionally relied on fructosamine measurement rather than other moieties partly due to the widespread commercial availability of fructosamine assays. However, recent studies have underscored the possible advantage of HbA1c for assessing glycemic control in dogs,¹⁰⁻¹³ and commercial assays are available for assessing canine and feline HbA1c.

DRAWBACKS OF GLYCATED PROTEIN MONITORING

Medical conditions that alter concentrations of the parent protein also affect the glycated versions. Fructosamine reduction occurs in nondiabetic dogs with hypoproteinemia or hypoalbuminemia and in those with hyperlipidemia and/or azotemia.²⁹ Fructosamine is also reduced in cats as a consequence of increased protein turnover associated with concurrent hyperthyroidism,³⁰ although it may remain within the reference range.³¹ Many of the conditions affecting fructosamine also affect HbA1c, but HbA1c concentration is also altered by anemia and other conditions that influence RBC turnover.³²

Blood Glucose

Direct determination of BG is the gold standard for immediate and real-time assessment of glycemia. In diabetic patients, BG monitoring over time reflects pharmacodynamic actions of insulin and can provide information about onset, peak activity, and duration of action, as well as its overall effectiveness in controlling glycemia. The BG curve has been the traditional approach used to document patient insulin response, but IGM has become more commonplace. Randomly timed, single determinations of BG concentration (ie, spot measurement) have little interpretive value and are not recommended when making decisions about insulin dose.

The Blood Glucose Curve

This method involves sampling and testing every 1 to 2 hours over a defined time

(usually 12 hours but sometimes longer) to plot BG, typically using a portable glucometer. Venous or capillary blood samples from various sites (eg, small vein, ear tip, paw pad) are obtained manually using a needle or lancet. The number of points on the curve is determined by the sampling frequency. The BG curve is most often performed in clinic, but some clinicians recommend owners learn to do it at home. A review of the background, method, and interpretation of the BG curve is available.¹⁴

Interstitial Glucose Monitoring

IGM allows for measurement of glucose concentration in interstitial fluid over days to weeks.¹⁵ IGM includes both continuous and flash glucose monitoring (FGM) methods. Continuous glucose monitoring automatically displays each glucose measurement for users in real time and can integrate with insulin pump systems to adjust insulin dosing, whereas FGM displays a single value result only when the sensor is interrogated by the reader (see **Interstitial Glucose Monitoring Systems**). IGM provides values for glucose that differ from those of capillary or venous blood.¹⁶ The gradient between blood and interstitial glucose, which can range from 20% to 110%,¹⁶ is greatest when large fluctuations in BG (increasing or decreasing) occur and there is a lag (minutes) before the 2 compartments equilibrate. Thus, IGM may underreport rapid changes in BG, which is particularly important when there is risk for development of hypoglycemia.

Monitoring performed by pet owners is a viable way for the clinician to obtain BG information.^{17,18} In a study, \approx 85% of owners were successful with long-term home BG monitoring that required frequent blood sampling to produce curves.¹⁹ Anecdotal reports indicate owners and clinicians are willing to use IGM to perform at-home monitoring; this is especially true when an FGM device is used, as these systems do not require frequent calibration and data can be easily retrieved and analyzed. A particular advantage of FGM systems is that daily glycemic data can help facilitate treatment to achieve clinical goals rather than just elimination of clinical signs. For example, insulin treatment can be adjusted more frequently based on glycemic data and metabolic targets (eg, desired range for

average daily glucose).

INTERSTITIAL GLUCOSE MONITORING SYSTEMS

IGM has been used in veterinary medicine for >15 years.³³ Several systems studied have proven useful in dogs and cats.³⁴ Advances in technology have rendered IGM systems more user friendly and better suited for veterinary applications. A newer FGM system has shown promise in veterinary medicine, although published information is limited to a single study.³⁵ All commercial IGM systems involve similar components and operating principles.¹⁵ The basic unit consists of a disposable sensor that combines a serum chemical detection system with a transmitter and receiver that collect, store, and display BG data. A stylet introduces the sensor through the skin and positions the tip to contact the interstitial fluid. The body of the sensor, which contains the transmitter, is affixed to shaved skin using a mild adhesive (Figure 1). An incorporated chemical reaction platform metabolizes interstitial glucose to generate an electrical signal that is proportional to its concentration.¹⁵ A description of the use of an FGM device in small animals is available.³⁶

https://www.cliniciansbrief.com/article/monitoring-blood-glucose-...+Newsletter&utm_campaign=Online+210701&oly_enc_id=0674i2232356E8U Page 12 of 21



▲ FIGURE 1 A sensor unit from a flash device adhered to the skin of a diabetic cat. A manufacturerprovided device easily applies the small sensor unit (35-mm diameter × 5-mm height) to the shaved area. The sensor uses a flexible filament in contact with the interstitial fluid to measure BG every 60 seconds and data storage capacity to record BG data. Wireless technology transfers BG data stored in the sensor unit to a handheld reader unit.

Interventional vs Dose Monitoring

When considering methods of glucose monitoring, it is worth drawing distinctions between BG monitoring performed to determine a patient's global response to a particular dose of insulin (ie, dose monitoring) and monitoring performed to determine whether a patient's immediate glycemic status requires correction (ie, interventional monitoring). Both can be accomplished through available techniques, have the same advantages and disadvantages, and can be used in making therapeutic decisions. In practice, however, these are very different approaches to managing glycemia (**Figure 2**).

Monitoring BG in veterinary patients generally serves to assess the larger picture of insulin response and BG control over the day rather than as a guide for day-today changes in therapy. Dose monitoring can be useful and provide helpful information, but the use of interventional monitoring should be considered cautiously. Although some pet owners may be interested in and eager to attempt interventional monitoring and make insulin adjustments, the author does not recommend it, as there has been little evidence to show that the effort and expense actually improve long-term outcomes or reduce complications, and the very stringent targets for BG control involve increased risk for hypoglycemic events in human and, probably, veterinary patients. Studies addressing these concerns are limited. In a small group of cats receiving at-home monitoring to achieve tight BG control, complication rate was low,²⁰ but constant care and anxiety regarding hypoglycemia are common concerns among pet owners and chronic or recurrent hypoglycemia can lead to increased patient morbidity and poor quality of life.^{1,2} Some clinicians use a modified approach to interventional monitoring described above by having owners check BG immediately before an insulin dose and use the information to modify the dose as necessary. An advantage of this approach is the opportunity to reduce the likelihood of hypoglycemia, but the clinician must provide the owner with clear goals and guidelines for making dose decisions.


FIGURE 2 Effects of different monitoring strategies on the BG curve. The red line shows a theoretical BG curve following an insulin injection at the 0hour mark. Within 6 hours of injection, BG returned to the preinsulin level. At this point (A), no action occurs if the dose monitoring strategy is used. However, if the interventional monitoring strategy is used, an additional insulin injection is indicated, as BG exceeds the desired target range (≤250 mg/dL). The subsequent response (gray line) brings BG into an acceptable range. At the 12-hour mark (B), the patient with dose monitoring (red line) received a scheduled second insulin injection, but the patient with interventional monitoring received no insulin, as BG values were in the target range. Without additional intervention, both patient curves were similar (black line) for the remainder of the day. Adopting a strict interventional monitoring strategy requires additional insulin be provided at the 16-hour mark when BG again exceeded the target range.

Regardless of the method used to obtain a BG curve, comparison with other measures used to assess BG control (eg, clinical evaluation, markers of long-term glycemic control) can help validate results. The BG curve is especially helpful in detecting hypoglycemic events during testing. Hypoglycemia typically reflects an excess of insulin and should prompt dose reduction. Curve analysis can also demonstrate persistent hyperglycemia, which is consistent with poor glycemic control. Troubleshooting persistent hyperglycemia is more difficult than troubleshooting hypoglycemia, as the former can have numerous causes (eg, poor compliance, problems with insulin administration, underdosing, insulin

resistance).

A major limitation of the BG curve is imposed by biologic variability that impacts day-to-day insulin action. Depending on insulin type and formulation used, absorption and activity in humans under experimental conditions can vary from 15% to 50% day to day.²¹ Variability is typically greater in clinical patients,²² with inconsistent or unpredictable changes in glycemia even after administration of equivalent doses of the same insulin. Numerous factors, including the patient's emotional state (eg, stress or anxiety), exercise, body temperature, and comorbidities, among others, may contribute to variability.²³

The veterinary literature contains examples of the effect of biologic variability on BG curve data. In a study, dogs receiving the same insulin type and dose showed marked variability in routinely determined BG curve parameters, including minimum, maximum, and mean BG concentrations and time to nadir, on 12-hour BG curves obtained 24 hours apart.²⁴ In that study, curve analysis resulted in a different insulin treatment recommendation in nearly 45% of paired curves and treatment recommendations were frequently opposite (ie, one curve of the pair indicated a need for a dose increase and the other indicated a need for a dose decrease).

Conclusion

No single monitoring tool or combination has been shown to provide significant, measurable advantages in diabetic dogs or cats. Reliance on a single tool is discouraged. Effective monitoring should incorporate several methods that assess different aspects of glycemic control. A flexible and practical monitoring program that aims to provide objective information while balancing patient and owner needs can engage the pet owner as a primary caregiver, enhance compliance, and strengthen the clinician-pet owner relationship.

REFERENCES

 $https://www.cliniciansbrief.com/article/monitoring-blood-glucose-...+Newsletter \& utm_campaign=Online+210701\&oly_enc_id=067412232356E8U$

Page 16 of 21

- 1. Niessen SJ, Powney S, Guitian J, et al. Evaluation of a quality-of-life tool for dogs with diabetes mellitus. *J Vet Intern Med.* 2012;26(4):953-961.
- 2. Niessen SJ, Powney S, Guitian J, et al. Evaluation of a quality-of-life tool for cats with diabetes mellitus. *J Vet Intern Med.* 2010;24(5):1098-1105.
- 3. Bennett N. Monitoring techniques for diabetes mellitus in the dog and cat. *Clin Tech Small Anim Pract.* 2002;17(2):65-69.
- 4. Cook AK. Monitoring methods for dogs and cats with diabetes mellitus. *J Diabetes Sci Technol*. 2012;6(3):491-495.
- Behrend E, Holford A, Lathan P, Rucinsky R, Schulman R. 2018 AAHA diabetes management guidelines for dogs and cats. *J Am Anim Hosp Assoc.* 2018;54(1):1-21.
- 6. Schaer M. A justification for urine glucose monitoring in the diabetic dog and cat. *J Am Anim Hosp Assoc.* 2001;37(4):311-312.
- 7. Reusch CE, Liehs MR, Hoyer M, Vochezer R. Fructosamine: a new parameter for diagnosis and metabolic control in diabetic dogs and cats. *J Vet Intern Med.* 1993;7(3):177-182.
- Miller E. Long-term monitoring of the diabetic dog and cat: clinical signs, serial blood glucose determinations, urine glucose, and glycated blood proteins. *Vet Clin North Am Small Anim Pract.* 1995;25(3):571-584.
- Davison LJ, Podd SL, Ristic JM, Herrtage ME, Parnham A, Catchpole B. Evaluation of two point-of-care analysers for measurement of fructosamine or haemoglobin A1c in dogs. *J Small Anim Pract*. 2002;43(12):526-532.
- 10. Goemans AF, Spence SJ, Ramsey IK. Validation and determination of a reference interval for canine HbA1c using an immunoturbidimetric assay. *Vet Clin Pathol*. 2017;46(2):227-237.
- 11. Elliott DA, Nelson RW, Reusch CE, Feldman EC, Neal LA. Comparison of serum fructosamine and blood glycosylated hemoglobin concentrations for assessment of glycemic control in cats with diabetes

mellitus. J Am Vet Med Assoc. 1999;214(12):1794-1798.

- Oikonomidis IL, Tsouloufi TK, Soubasis N, Kritsepi-Konstantinou M. Validation, reference intervals and overlap performance of a new commercially available automated capillary electrophoresis assay for the determination of the major fraction of glycated haemoglobin (HbA1c) in dogs. *Vet J.* 2018;234:48-54.
- Kim NY, An J, Jeong JK, et al. Evaluation of a human glycated hemoglobin test in canine diabetes mellitus. *J Vet Diagn Invest*. 2019;31(3):408-414.
- Schermerhorn T. The role of the glucose curve. *Clinician's Brief*. 2010;8(11):23-25.
- 15. Ajjan R, Slattery D, Wright E. Continuous glucose monitoring: a brief review for primary care practitioners. *Adv Ther.* 2019;36(3):579-596.
- Cengiz E, Tamborlane WV. A tale of two compartments: interstitial versus blood glucose monitoring. *Diabetes Technol Ther*. 2009;11(Suppl 1):S11-S16.
- 17. Casella M, Wess G, Reusch CE. Measurement of capillary blood glucose concentrations by pet owners: a new tool in the management of diabetes mellitus. *J Am Anim Hosp Assoc*. 2002;38(3):239-245.
- Mathes MA. Home monitoring of the diabetic pet. *Clin Tech Small Anim Pract*. 2002;17(2):86-95.
- Casella M, Wess G, Hassig M, Reach CE. Home monitoring of blood glucose concentration by owners of diabetic dogs. *J Small Anim Pract*. 2003;44(7):298-305.
- 20. Roomp K, Rand J. Intensive blood glucose control is safe and effective in diabetic cats using home monitoring and treatment with glargine. *J Feline Med Surg.* 2009;11(8):668-682.
- Heinemann L. Insulin pharmacology. In: Pickup JC, Williams G, eds. *Textbook of Diabetes*. 3rd ed. Oxford, UK: Blackwell Science; 2003:42.1-42.15.

- 22. Heise T, Nosek L, Rønn BB, et al. Lower within-subject variability of insulin detemir in comparison to NPH insulin and insulin glargine in people with type 1 diabetes. *Diabetes*. 2004;53(6):1614-1620.
- 23. Guerci B, Sauvanet JP. Subcutaneous insulin: pharmacokinetic variability and glycemic variability. *Diabetes Metab.* 2005;31(4 Pt 2):4S7-4S24.
- 24. Fleeman LM, Rand JS. Evaluation of day-to-day variability of serial blood glucose concentration curves in diabetic dogs. *J Am Vet Med Assoc.* 2003;222(3):317-321.
- 25. Briggs CE, Nelson RW, Feldman EC, Elliot DA, Neal LA. Reliability of history and physical examination findings for assessing control of glycemia in dogs with diabetes mellitus: 53 cases (1995-1998). *J Am Vet Med Assoc*. 2000;217(1):48-53.
- Fracassi F. Canine diabetes mellitus. In: Ettinger SJ, Feldman EC, Cote E, eds. *Textbook of Veterinary Internal Medicine*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2017:1767-1781.
- Rand J, Gottlieb SA. Feline diabetes mellitus. In: Ettinger SJ, Feldman EC, Cote E, eds. *Textbook of Veterinary Internal Medicine*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2017:1781-1795.
- Hess RS, Saunders HM, Van Winkle TJ, Ward CR. Concurrent disorders in dogs with diabetes mellitus: 221 cases (1993-1998). *J Am Vet Med Assoc.* 2000;217(8):1166-1173.
- 29. Reusch CE, Haberer B. Evaluation of fructosamine in dogs and cats with hypo- or hyperproteinaemia, azotaemia, hyperlipidaemia and hyperbilirubinaemia. *Vet Rec.* 2001;148(12):370-376.
- 30. Reusch CE, Tomsa K. Serum fructosamine concentration in cats with overt hyperthyroidism. *J Am Vet Med Assoc.* 1999;215(9):1297-1300.
- 31. Gal A, Trusiano B, French AF, Lopez-Villalobos N, MacNeill AL. Serum fructosamine concentration in uncontrolled hyperthyroid diabetic cats is within the population reference interval. *Vet Sci.* 2017;4(1):E17.

https://www.cliniciansbrief.com/article/monitoring-blood-glucose-...+Newsletter&utm_campaign=Online+210701&oly_enc_id=067412232356EBU

- 32. Radin MS. Pitfalls in hemoglobin A1c measurement: when results may be misleading. *J Gen Intern Med.* 2014;29(2):388-394.
- 33. Wiedmeyer CE, DeClue AE. Continuous glucose monitoring in dogs and cats. *J Vet Intern Med*. 2008;22(1):2-8.
- 34. Surman S, Fleeman L. Continuous glucose monitoring in small animals. *Vet Clin North Am Small Anim Pract*. 2013;43(2):381-406.
- Corradini S, Pilosio B, Dondi F, et al. Accuracy of a flash glucose monitoring system in diabetic dogs. *J Vet Intern Med.* 2016;30(4):983-988.
- Wilson S. FreeStyle libre glucose monitor FAQ. Veterinary Information Network website. https://www.vin.com/doc/?id=9001847&pid=11200.
 Published March 7, 2019. Accessed September 9, 2019.

AUTHOR

Thomas Schermerhorn

VMD, DACVIM (SAIM) Kansas State University

Thomas Schermerhorn, VMD, DACVIM (SAIM), is a professor of small animal medicine and the Morgan K "Al" Jarvis Chair of Veterinary Medicine at Kansas State University, where his laboratory focuses on cellular and molecular endocrinology, particularly the study of diabetes mellitus and related metabolic disorders in dogs and cats. Dr. Schermerhorn completed a medical internship at South Shore Veterinary Associates in South Weymouth, Massachusetts, and a residency in small animal internal medicine at Cornell University, where he also received research training as a graduate fellow in the department of molecular medicine. His clinical interests include canine and feline endocrinology, particularly diabetes mellitus.

For global readers, a calculator to convert laboratory values, dosages, and other measurements



clinician's brief

Disseminated Intravascular Coagulation Diく

Julien Guillaumin, DVM, DACVECC, DECVECC, The Ohio State University

EMERGENCY MEDICINE & CRITICAL CARE | OCTOBER 2019 | PEER REVIEWED



Disseminated intravascular coagulation (DIC) is a clinical syndrome that occurs as a complication of systemic disease and creates a hypercoagulable state, usually through crosstalk between inflammation and hemostasis.¹ This activation of

Page 1 of 11

blood coagulation generates intravascular thrombin and fibrin, resulting in thrombosis of small-to-medium vessels, and can lead to multiorgan dysfunction syndrome if not appropriately controlled.² Disseminated thrombus formation consumes platelets, clotting factors, and regulation factors (eg, antithrombin) and may progress to overt DIC.¹ DIC can occur in several phases: a subclinical phase, an organ failure phase, and/or an overt (ie, bleeding) phase.

Thrombin, a product of hemostasis, exerts inflammatory mediation through the thrombin-thrombomodulin complex.³ Hemostasis is regulated by 3 antithrombotic systems, including antithrombin, which is most relevant to DIC pathogenesis. Antithrombin has important anticoagulant and anti-inflammatory effects, and its cofactor heparin makes it much more active.⁴ Although DIC can increase morbidity and mortality in affected patients, treating the underlying disease can generally control and reverse its physiologic consequences.

Historical Findings & Clinical Signs

There are no specific historical findings for DIC. In the overt phase, bleeding can be present, but subclinical DIC is also common. In cases of subclinical DIC, any history and clinical signs will be due to the primary disease that is causing DIC (eg, sepsis, immune-mediated hemolytic anemia, trauma, heat stroke; **Table 1**).⁵ Because of the association between inflammation and risk for development of DIC, clinicians should look for signs of systemic inflammatory response syndrome or sepsis, including tachycardia, tachypnea, increase in temperature, and signs of severe tissue trauma.

The DIC continuum is initiated by a prothrombotic, hypercoagulable condition. Clinical signs vary based on the phase. Affected patients may have no overt signs of DIC (eg, bleeding, petechiae), have signs of organ dysfunction due to microthrombi, or may progress to a hypocoagulable bleeding phase, ^{1,2} as clotting factors are consumed by the generalized activation of hemostasis that is central to the syndrome. Although DIC can be chronic and progress over several days, it can also be self-limiting and self-resolving and never progress to a bleeding phase.

TABLE 1

POSSIBLE CAUSES OF DISSEMINATED INTRAVASCULAR COAGULATION⁵

Type of Cause	Condition
Infectious inflammatory	BacterialSevere localized infection
	Sepsis
	Viral Canine parvovirus
	► FIP
	Fungal
	Fulminating systemic fungal disease
Noninfectious inflammatory	Tissue trauma and/or ischemiaGastric dilatation volvulus
	Pancreatitis
	▶ Trauma
	► Heatstroke
	Envenomation

https://www.cliniciansbrief.com/article/disseminated-intravascular-...f+Newsletter&utm_campaign=Online+210705&oly_enc_id±0674l2232356E8U Page 3 of 11 EXHIBIT 7 - 245 Successful cardiopulmonary resuscitation

Immune-mediated causes

Immune-mediated hemolytic anemia

Neoplasia

- Hemangiosarcoma
- Acute leukemia

Diagnosis

Diagnosis of DIC can be challenging. DIC is a dynamic state of hemostasis imbalance that can result in concurrent hyper- and hypocoagulable states, depending on the organs affected. Scoring systems to determine the phase of DIC can be useful due to the absence of pathognomonic signs or laboratory abnormalities. Scoring systems also allow for a more objective characterization of the syndrome and can help identify patients with subclinical DIC, particularly for clinicians not expert in the disease; the more overt the signs of DIC are, the clearer the diagnosis. Several scoring systems have been developed and tested in both human and veterinary medicine.^{1,2,6-9}

The Wiinberg scoring system is a mathematical model that considers expert evaluations to be the gold standard. If a predisposing disease is present, clinicians can use this scoring system, which includes fibrinogen levels, D-dimer levels, prothrombin time (PT), and activated partial thromboplastin time (aPTT). In a study, the scoring system had a positive predictive value of 80% and a negative predictive value of 81%, therefore missing 20% of patients that experts believed had DIC.⁹ Thrombocytopenia or hypercoagulable thromboelastographic tracing can also be present in patients with DIC.¹⁰

The ability of various scoring systems to predict mortality has also been investigated. A study has compared several scoring systems, including a modification of the International Society on Thrombosis and Haemostasis human DIC scoring system (**Table 2**), the Wiinberg scoring system, and results of individual hemostasis assays.¹

TABLE 2

HUMAN SCORING SYSTEM FOR DISSEMINATED INTRAVASCULAR COAGULATION*

Points	0	1	2	3
Platelets (×10 ³ /µL)	>100	>50	<50	
D-dimers (ng/mL)	<1000		1000-5000	>5000
Fibrinogen (mg/dL)	>100	<100		
Prothrombin index [†]	>70%	40%-70%	<40%	

*The human scoring system is presented as suggested by the International Society of Thrombosis and Haemostasis,⁶ Scores range from 0 to 8. A score \geq 5 is compatible with overt DIC.

[†]Prothrombin index = (PT control plasma ÷ PT patient plasma) × 100

A 78% accuracy for mortality was identified when 3 of 6 individual hemostasis assays (ie, PT, aPTT, fibrinogen, antithrombin, D-dimer, platelet count) were outside the reference range; this was found to be a superior predictor of mortality as compared with previously reported scoring systems.¹ Due to the limited availability of some diagnostic tests (eg, D-dimer) in practice, DIC may often be diagnosed based on the presence of a compatible primary disease (**Table 1**) and changes in classic hemostatic tests (**Table 3**).

Treatment & Management

Treatment of DIC can be complex and controversial. The only therapeutic approach recognized to be of benefit is treatment of the primary disease process (eg, administration of antibiotics and source control in septic patients).^{2,8} When the underlying disorder is properly managed, DIC may resolve spontaneously prior to development of overt clinical bleeding, although some cases may require supportive treatment aimed at the coagulation system (**Table 3**).²

Plasma therapy is recommended to correct active hemorrhage and/or for perioperative stabilization. Several guidelines and consensus statements in humans recommend administration of platelet concentrate and fresh frozen plasma (FFP) in DIC patients with active bleeding and in patients at high risk for bleeding that would require further invasive procedures.² FFP should not be used to correct abnormal coagulation parameters or increase antithrombin levels, as FFP contains only minimal antithrombin; however, FFP can replace other coagulation proteins that were consumed in the DIC process and may help control clinical signs of bleeding. An initial FFP dose of 15 mL/kg is recommended, although higher doses may be required.²

TABLE 3

RECOMMENDED DIAGNOSTIC TESTS & TREATMENTS FOR PHASES OF DISSEMINATED INTRAVASCULAR COAGULATION²

	Subclinical Phase	Organ Failure Phase	Bleeding Phase
DIAGNOSTIC TEST			
PT	Normal	Normal	Increased

https://www.cliniciansbrief.com/article/disseminated-intravascular-...f+Newsletter&utm_campaign=Online+210705&oly_enc_id=0674I2232356E8U Page 6 of 11

EXHIBIT 7 - 248

aPTT	Normal	May be slightly increased	Increased
Platelet count	Normal to slightly decreased (>150,000/μL)	May be slightly decreased	Decreased
TREATMENT			
Of primary disease, if known	Recommended	Recommended	Recommended
With blood transfusion	No specific recommendation	No specific recommendation	Recommended
With heparin	Recommended	No specific recommendation	Not recommended

Although use of unfractionated heparin in the treatment of DIC is controversial in human medicine, most of the aforementioned guidelines recommend unfractionated heparin or low-molecular-weight heparin (LMWH) to treat subclinical DIC. Experimental studies have shown that heparin can partially inhibit the activation of coagulation in DIC,¹¹ but its impact on mortality or other clinically relevant outcomes in humans and veterinary patients is unknown. A low unfractionated heparin dose of 7-10 units/kg/hr has been shown to be safe in humans with sepsis-associated DIC,^{12,13} but these doses are much lower than the dose commonly recommended in veterinary medicine for thromboprophylaxis (150-300 units/kg SC q6-8h).¹⁴ LMWH can be used at doses of 0.8-1 mg/kg SC q6-8h for enoxaparin or 150 units/kg SC q8h for dalteparin.¹⁴ The impact of heparin therapy on the inhibition of the coagulation system in veterinary medicine is unclear, with conflicting results available in dogs.^{15,16}

Prognosis & Prevention

Prognosis depends on the phase of the syndrome. Specific mortality rates for

nonbleeding patients with DIC are lacking, but a recent study showed a 60% mortality rate in dogs with DIC in the bleeding phase.¹

Preventive measures may not be needed, as DIC can resolve spontaneously when the underlying disorder improves. However, the recommendation for nonbleeding humans with DIC is use of either unfractionated heparin or LMWH.²

Clinical Follow-Up & Monitoring

In DIC patients with diseases that predispose to DIC (**Table 1**), inflammatory signs (eg, temperature, heart rate, respiratory rate, leukocytes, band neutrophils) should be monitored. If inflammatory signs are improving and the patient is clinically improving, progression of DIC is generally halted. Similarly, laboratory data pertinent to DIC diagnosis (eg, PT, aPTT, d-dimer levels, platelet count) should be regularly (eg, daily) monitored. Because DIC is a dynamic process, changes can occur rapidly and clinical decisions may change if the syndrome progresses.

aPTT = activated partial thromboplastin time, DIC = disseminated intravascular coagulation, FFP = fresh frozen plasma, LMWH = low-molecular-weight heparin, PT = prothrombin time

REFERENCES

- Goggs R, Mastrocco A, Brooks MB. Retrospective evaluation of 4 methods for outcome prediction in overt disseminated intravascular coagulation in dogs (2009-2014): 804 cases. J Vet Emerg Crit Care (San Antonio). 2018;28(6):541-550.
- Wada H, Matsumoto T, Yamashita Y. Diagnosis and treatment of disseminated intravascular coagulation (DIC) according to four DIC guidelines. *J Intensive Care*. 2014;2(1):15.
- 3. Ito T, Kakihana Y, Maruyama I. Thrombomodulin as an intravascular

safeguard against inflammatory and thrombotic diseases. *Expert Opin Ther Targets*. 2016;20(2):151-158.

- Levy JH, Sniecinski RM, Welsby IJ, Levi M. Antithrombin: antiinflammatory properties and clinical applications. *Thromb Haemost*. 2016;115(4):712-728.
- Hopper K, Bateman S. An updated view of hemostasis: mechanisms of hemostatic dysfuntion associated with sepsis. *J Vet Emerg Crit Care*. 2005;15:83-91.
- Angstwurm MW, Dempfle CE, Spannagl M. New disseminated intravascular coagulation score: a useful tool to predict mortality in comparison with Acute Physiology and Chronic Health Evaluation II and Logistic Organ Dysfunction scores. *Crit Care Med.* 2006;34(2):314-320; quiz 328.
- Levi M, Toh CH, Thachil J, Watson HG. Guidelines for the diagnosis and management of disseminated intravascular coagulation. British Committee for Standards in Haematology. *Br J Haematol.* 2009;145(1):24-33.
- 8. Wada H, Thachil J, Di Nisio M, et al. Guidance for diagnosis and treatment of DIC from harmonization of the recommendations from three guidelines. *J Thromb Haemost*. 2013. doi: 10.1111/jth.12155
- 9. Wiinberg B, Jensen AL, Johansson P, et al. Development of a model based scoring system for diagnosis of canine disseminated intravascular coagulation with independent assessment of sensitivity and specificity. *Vet J.* 2010;185(3):292-298.
- Wiinberg B, Jensen AL, Johansson PI, Rozanski E, Tranholm M, Kristensen AT. Thromboelastographic evaluation of hemostatic function in dogs with disseminated intravascular coagulation. *J Vet Intern Med.* 2008;22(2):357-365.
- Pernerstorfer T, Hollenstein U, Hansen J, et al. Heparin blunts endotoxin-induced coagulation activation. *Circulation*. 1999;100(25):2485-2490.

- Jaimes F, De La Rosa G, Morales C, et al. Unfractioned heparin for treatment of sepsis: a randomized clinical trial (The HETRASE Study). *Crit Care Med.* 2009;37(4):1185-1196.
- 13. Wen JM, Sun YX, Pan XH, Chen HS. Effects of low-molecular-weight heparin and unfractionated heparin on traumatic disseminated intravascular coagulation. *Trop J Pharm Res.* 2018;17(5):961.
- Plumb DC, ed. Heparin. *Plumb's Veterinary Drug Handbook*. 8th ed. Stockholm, WI: Wiley-Blackwell; 2015:929.
- Pouzot-Nevoret C, Barthélemy A, Cluzel M, Verwaerde P, Bonnet-Garin JM, Goy-Thollot I. Enoxaparin has no significant anticoagulation activity in healthy beagles at a dose of 0.8 mg/kg four times daily. *Vet J*. 2016;210:98-100.
- Lunsford KV, Mackin AJ, Langston VC, Brooks M. Pharmacokinetics of subcutaneous low molecular weight heparin (enoxaparin) in dogs. J Am Anim Hosp Assoc. 2009;45(6):261-267.

AUTHOR

Julien Guillaumin

DVM, DACVECC, DECVECC The Ohio State University

Julien Guillaumin, DVM, DACVECC, DECVECC, is an associate professor of emergency medicine and critical care at The Ohio State University. He earned his DVM from National Veterinary School of Nantes in Nantes, France, and completed a small animal rotating internship at National Veterinary School of Alfort in Maisons-Alfort, France. Dr. Guillaumin completed a residency at University of California, Davis, and serves on the American College of Veterinary Emergency Critical Care residency training committee and the European College of Veterinary Emergency and Critical Care education committee. His clinical interests are hemostasis, blood banking and blood products, immune-mediated hemolytic anemia, thrombosis, and systemic inflammatory response syndrome, sepsis, and multiple organ dysfunction syndrome.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found here.

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. **For questions or inquiries please contact us.**



Septic shock. - cardionespiratory Amst Critical ILLNESS Rolated conficusteroid Insufficiency

CASE IN POINT

CIRCI

VOMITING & DIARRHEA IN A LETHARGIC DOG

April Summers, DVM, PhD Cornell University Julien Guillaumin, DVM, DACVECC, DECVECC Colorado State University ax, an 8-year-old, 32-lb (14.5-kg), neutered male border collie, was emergently presented for vomiting, diarrhea, and lethargy of 3 days' duration. He was fed a veterinary commercial diet but, when he began vomiting, was transitioned to a bland diet of boneless; skinless boiled chicken and white rice; however, he continued to vomit while on the bland diet.

255

TABLE 1

VENOUS BLOOD GAS RESULTS

Variable	Presenting Value	Reference Range
рН	7.22	7,35-7,47
Partial pressure of carbon dioxide (mm Hg)	46	32-43
Bicarbonate (mEq/L)	13.7	20-25
Sodium (mEq/L)	140	140-150
Potassium (mEq/L)	3.9	3.9-4.9
Chloride (mEq/L)	109	109-120
Calcium (mg/dL)	10	10-12
Magnesium (mEq/L)	1.24	1.04-1.46
Glucose (mg/dL)	40	85-112
Lactate (mg/dL)	110	0-18
BUN (mg/dL)	12	9-33
Creatinine (mg/dL)	0.8	0.7-1.8
Base deficit (mEq/L)	7.2	-4 to 4

TABLE 2

CBC RESULTS

Variable	Presenting Value	Reference Range
Hematocrit (%)	44	37.3-61.7
Total leukocytes (cells/µL)	20,700	5050-16,760
Neutrophils (cells/µL)	17,000	2950-11,640
Bands (cells/µL)	3000	0-100
Lymphocytes (cells/µL)	1000	1050-5100
Monocytes (cells/µL)	1900	160-1120
Eosinophils (cells/µL)	60	60-1230
Basophils (cells/µL)	0	100
Platelet count (×10³/µL)	62	148-484

Max had a previous history of 2 exploratory laparotomies for foreign bodies but had no other major medical history. He was the only dog in the household, had access to a fenced backyard, and had no significant travel history. He was up to date on vaccines and flea, tick, and heartworm prevention.

Physical Examination

On presentation, Max was laterally recumbent, obtunded, and ≈7% dehydrated. He was pyrexic (temperature, 104.5°F [40.3°C]) and tachycardic (150 bpm) with a normal respiratory rate (28 breaths per minute). Mucous membranes were pale, and capillary refill time was prolonged (ie, 3 seconds). He had weak peripheral pulses, and his distal limbs and paw pads were cool to the touch. Harsh lung sounds were auscultated bilaterally throughout all lung fields. He was painful on abdominal palpation, particularly in the cranial abdomen, and had profuse hemorrhagic diarrhea; he also passed pieces of 2 rubber ball toys from his rectum. His owners did not report any foreign material having been passed at home. The remainder of the physical examination was unremarkable.

Diagnosis & Clinical Management

Venous blood gas analysis revealed metabolic acidosis due to hyperlactatemia and hypoglycemia (*Table 1*). ECG revealed sinus tachycardia. Systolic blood pressure was 40 mm Hg (Doppler); an arterial catheter was subsequently placed, and direct arterial blood pressure monitoring was initiated.

Images obtained using abdominal-focused assessment with sonography for trauma revealed no evidence of free fluid. Images obtained using thoracic-focused assessment with sonography for trauma revealed 4 to 5 B lines in the region of the right middle lung lobe; B lines are reverberation artifacts and can be present with interstitial edema as air content decreases. Abdominal radiographs revealed fluid-filled loops of intestine consistent with diffuse ileus; however, there was no evidence of GI obstruction. Abdominal sonograms were suggestive of pancreatitis with focal peritonitis but were otherwise unremarkable. Thoracic radiographs revealed an alveolar pattern in the right middle lung lobe that was suggestive of aspiration pneumonia.

Initial laboratory values revealed leukocytosis characterized by monocytosis and neutrophilia with a left shift (*Table 2*). Max was also thrombocytopenic. Serum chemistry profile revealed decreased albumin and globulin and increased ALT, ALP, and total bilirubin (*Table 3*).

Max was stabilized with crystalloid fluid boluses (lactated Ringer's solution [total, 40 mL/kg IV]), followed by a colloid bolus (6% hydroxyethyl starch in sodium chloride [5 mL/kg IV]) administered over 20 minutes. Of note, the use of synthetic colloids is controversial in humans with sepsis due to increased risk for acute kidney injury. Two 25% dextrose boluses (1 mL/kg IV) were also administered to help treat hypoglycemia. Broad-spectrum antibiotic therapy (ie, ampicillin/sulbactam [30 mg/kg IV], enrofloxacin [10 mg/kg IV]) was initiated within an hour of admission, and oxygen supplementation (100 mL/kg/min increased to a maximum of 4-5 L/min) was provided via nasal cannula.

Because Max's blood pressure did not respond adequately to fluid therapy and had an oscillometric mean of 50 mm Hg, septic shock was diagnosed. Norepinephrine at 0.2 μ g/kg/min CRI was initiated and increased incrementally by 0.1 μ g/ kg/min to 0.8 μ g/kg/min within 45 minutes, at which point vasopressin (0.5 milliUnits/kg/min CRI IV) was initiated.

DIAGNOSIS:

SEPTIC SHOCK WITH SUSPECTED CRITICAL ILLNESS-RELATED CORTICOSTEROID INSUFFICIENCY (CIRCI)

Due to the lack of improvement in blood pressure with increasing doses of vasopressors, CIRCI was

TABLE 3

SERUM CHEMISTRY RESULTS

Variable	Presenting Value	Reference Range
Albumin (g/dL)	2.6	2.9-4.2
Globulin (g/dL)	1.2	2.2-2.9
ALT (U/L)	88	10-55
ALP (U/L)	361	15-120
γ-glutamyl transferase (U/L)	6	<3-6
Total bilirubin (mg/dL)	0.9	0.1-0.4

TREATMENT AT A GLANCE

- Vital parameters and blood work abnormalities should be closely monitored.
- Hypoglycemia and electrolyte abnormalities should be treated as necessary.
- Blood pressure monitoring and response to vasopressor therapy is an important component of identifying potential CIRCI patients.
- Due to the lack of dosage information available for injectable hydrocortisone,⁷ hydrocortisone at 1 mg/kg IV bolus followed by CRI at 0.08 mg/kg/hr can be considered as a modification of the human protocol.^{5,8}
- If injectable hydrocortisone is unavailable, other corticosteroids, including prednisone (0.7-1.4 mg/kg/ day), can be considered.

CIRCI = critical illness-related corticosteroid insufficiency

October 2019

cliniciansbrief.com 69

strongly suspected. Resting cortisol was $6.96 \mu g/dL$ (reference range, $1.8-9 \mu g/dL$), and hydrocortisone sodium succinate (1 mg/kg IV bolus followed by CRI at 0.08 mg/kg/hr) was subsequently initiated to treat possible comorbid CIRCI (see *Treatment at a Glance*, previous page).

Prognosis & Outcome

Despite treatment and supportive care, Max's status continued to decline and he suffered cardiorespiratory arrest 6 hours after presentation. Autopsy confirmed aspiration pneumonia, gastroenteritis, and pancreatitis.

Septic shock is uncommonly reported in veterinary medicine, and prognosis is poor even with treatment. Reported survival rate in dogs with hypotension severe enough to require vasopressor therapy has been reported to be $\approx 10\%$ to 20% as compared with a 40% survival rate in humans.¹⁻³ The prognosis for septic shock for humans and dogs with CIRCI is unknown.

Discussion

CIRCI is defined as inadequate corticosteroid activity in relation to the severity of a patient's illness (see Take-Home Messages).4 CIRCI has been reported to occur in ≈60% of humans with severe sepsis and septic shock.⁵ The cause of hypothalamic-pituitaryadrenal axis dysfunction is poorly understood. Potential factors of this dysfunction include decreased production of adrenocorticotropic hormone (ACTH), corticotropin-releasing hormone, and cortisol; dysfunction of their associated receptors; adrenal damage from infarction or hemorrhage; adrenal suppression from chronic exogenous glucocorticoid administration; and inflammatory cytokines causing systemic inflammation-associated glucocorticoid resistance. No specific guidelines exist in veterinary medicine for diagnosing or treating CIRCI, and only rare case reports exist. The recommendation for treatment of CIRCI in humans is administration of injectable hydrocortisone, preferably as a constant rate infusion.⁶

TAKE-HOME MESSAGES

- ▶ Septic shock is defined as an infection associated with systemic hypotension that occurs despite adequate fluid resuscitation and requires use of vasopressors to maintain a mean arterial blood pressure ≥65 mm Hg.
- Treatment of septic shock is complex and often requires continuous assessment and adjustment based on the dynamic needs of the patient. Early source control and administration of appropriate antibiotics is a critical treatment goal for patients with sepsis.
- CIRCI is a form of adrenal insufficiency in critically ill patients and should be suspected in patients with vasopressorrefractory hypotension. In humans, it is recommended to initiate hydrocortisone therapy without additional tests when there is vasopressor-refractory hypotension.⁴
- Diagnosis of CIRCI in veterinary medicine can be challenging, as CIRCI has no specific diagnostic criteria; however, it should be suspected in any patient with vasopressor-refractory hypotension.
- There has been no agreement on a single test for definitive diagnosis of CIRCI in humans, although a blunted ACTH stimulation test with a Δ-cortisol result <9 µg/dL and/or a resting cortisol level <10 µg/dL have been suggested to be indicative of CIRCI.^{4,7,8} In veterinary medicine, a study in septic dogs found that a Δ-cortisol level <3 µg/dL obtained from a standard 1-hour ACTH stimulation test using 250 µg of cosyntropin was associated with hypotension and decreased survival.⁹
- Prompt recognition of potential CIRCI is important, as earlier shock resolution can lead to lower mortality in patients with septic shock.¹⁰
- Early injectable hydrocortisone administration may be considered as a treatment regimen in septic shock patients with vasopressor-refractory hypotension.^{6,10} []]

STATEMENT OF OWNERSHIP

STATEMENT OF OWNERSHIP, MANAGEMENT, & CIRCULATION

Publication title: *Clinician's Brief* Publication number: 1542-4014 Filing date: 10/1/19 Issue frequency: Monthly Number of Issues published annually: 12 Annual subscription price: \$65 Complete mailing address of known office of publication: 2021 S Lewis Ave, Suite 760, Tulsa, OK 74104 Contact person: Natalie Williams Telephone: 918-710-4631 Full name and complete mailing address of Publisher, Editor, & Managing Editor: Elizabeth Green, 2021 S Lewis Ave, Suite 760, Tulsa, OK 74104; Indu Mani, 2021 S Lewis Ave, Suite 760, Tulsa, OK 74104; Samantha Farley, 2021 S Lewis Ave, Suite 760, Tulsa, OK 74104 **Owner:** Educational Concepts LLC, 2021 S Lewis Ave, Suite 760, Tulsa, OK 74104—Owners: Slegfried Ventures, 1924 S Utica Ave, Tulsa, OK 74104; Elizabeth Green, 2021 S Lewis Ave, Suite 760, Tulsa, OK 74104; John O'Brien, 12118 Nieman Rd, Overland Park, KS 66213; Antoinette Passaretti, 3936 Sawmill Rd, Doylestown, PA 18902; James D. Zielinski, 2403 High Hammock Rd, Seabrook Island, SC 29455; Donald C, Plumb, N 1782 Bogus Rd, Stockholm, WI 54769 Known bondholders, mortgages, and other security holders owning or holding 1 percent or more of total amount of bonds, mortgages, or other securities: None Issue date for circulation data below: September 2019

Auguara Ma

No Conton of

EXTENT & NATURE

	Copies Each Issue During Preceding 12 Months	Single Issue Published Nearest to Filing Date
Total number of copies	49,918	41,201
Paid and/or requested distribution		
(1) Outside-county paid/requested mail subscriptions stated on PS Form 3541	44,007	35,395
(2) In-county paid/requested mail subscriptions stated on PS Form 3541	0	0
(3) Sales through dealers and carriers, street vendors, counter sales, and other non-USPS paid distribution	104	95
(4) Other classes mailed through USPS	0	0
Total paid and/or requested distribution	44,111	35,490
Nonrequested distribution by mail and outside mail		
(1) Outside-county as stated on PS Form 3541	5,475	5,464
(2) In-county as stated on PS Form 3541	0	0
(3) Other classes mailed through USPS	0	0
(4) Nonrequested copies distributed outside the mail	116	0
Total nonrequested distribution	5,591	5,464
Total distribution	49,703	40,954
Copies not distributed	200	233
Total	49,903	41,187
Percent paid and/or requested circulation	88.8%	86.7%

Signature and title of editor, publisher, business manager, or owner: Elizabeth Green, Publisher

I certify that all information furnished on this form is true and complete. I understand that anyone who furnishes false or misleading information on this form or who omits material or information requested on the form may be subject to criminal sanctions (including fines or imprisonment) and/or civil sanctions (including civil penalties).

References

- Kenney EM, Rozanski EA, Rush JE, et al. Association between outcome and organ system dysfunction in dogs with sepsis: 114 cases (2003-2007). J Am Vet Med Assoc. 2010;236(1):83-87.
- Gravelyn TGJ. Clinical features and outcome of septic shock in dogs: 37 cases (2008-2015). Paper presented at: 2016 International Veterinary Emergency and Critical Care Symposium; September 7-11, 2016; Grapevine, TX.
- Ducrocq N, Biferi P, Girerd N, et al. Critical illnessrelated corticosterold insufficiency in cardiogenic shock patients: prevalence and prognostic role. *Shock*. 2018;50(4):408-413.
- Marik PE, Pastores SM, Annane D, et al. Recommendations for the diagnosis and management of corticosteroid insufficiency in critically ill adult patients: consensus statements from an international task force by the American College of Critical Care Mediclne. Crit Care Med. 2008;36(6):1937-1949.
- Annane D, Pastores SM, Rochwerg B, et al. Guidelines for the diagnosis and management of critical illness-related corticosteroid insufficiency (CIRCI) in critically III patients (part I): Society of Critical Care Medicine (SCCM) and European Society of Intensive Care Medicine (ESICM) 2017. Crit Care Med. 2017;43(12):1751-1763.
- Peyton JL, Burkitt JM. Critical illness-related corticosteroid insufficiency in a dog with septic shock. J Vet Emerg Crit Care (San Antonio). 2009;19(3)262-268.
- Martin LG, Groman RP, Fletcher DJ, et al. Pituitaryadrenal function in dogs with acute critical illness. JAm Vet Med Assoc. 2008;233(1):87-95.
- Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med.* 2013;39(2):580-637.
- Burkitt JM, Haskins SC, Nelson RW, Kass PH. Relative adrenal insufficiency in dogs with sepsis. J Vet Intern Med. 2007;21(2):226-231.
- de Jong MF, Beishuizen A, Spijkstra JJ, Girbes AR, Groeneveld AB. Relative adrenal insufficiency: an identifiable entity in nonseptic critically ill patients? *Clin Endocrinol (Oxf)*. 2007;66(5):732-739.

ACTH = adrenocorticotropic hormone CIRCI = critical illness-related corticosteroid insufficiency

October 2019 C

cliniciansbrief.com 71

EXHIBIT 7 - 259



clinician's brief

Atenolol Use in Cats with Subclinical Hypertrophic Cardiomyopathy

Rebecca L. Quinn, DVM, DACVIM (SAIM, Cardiology), Cape Cod Veterinary Specialists, Buzzards Bay, Massachusetts

CARDIOLOGY

Print/View PDF

In the Literature

Coleman AE, DeFrancesco TC, Griffiths EH, et al. Atenolol in cats with subclinical hypertrophic cardiomyopathy: a double-blind, placebo-controlled, randomized clinical trial of effect on quality of life, activity, and cardiac biomarkers. *J Vet Cardiol*. 2020;30:77-91.

FROM THE PAGE...

Hypertrophic cardiomyopathy (HCM) is the most common cardiovascular disorder in cats, affecting up to 29.4% of feline patients.¹ Cats with clinical signs of HCM are often treated with diuretics, angiotensinconverting–enzyme inhibitors, β blockers, or antiplatelet and anticoagulant medications.² However, evidence-based data supporting specific and ideal therapies for subclinical feline HCM are lacking. Diagnostic findings for subclinical HCM include thickened left ventricular walls and left atrial dilation in the absence of other disease (eg, congenital heart disease, hyperthyroidism, systemic hypertension).

This study^{*} evaluated pet owner-perceived quality of life and activity levels in cats with subclinical HCM and lifestyle-matched healthy controls, as well as owner-perceived quality of life, quantitative activity measurements, cardiac biomarkers, and echocardiographic variables in cats with preclinical HCM, with and without atenolol therapy.

A total of 27 healthy cats and 32 cats with subclinical HCM were included. As compared with healthy cats, cats with subclinical HCM had significantly more arrhythmias, higher cardiac troponin. I concentrations,

and higher N-terminal pro-B natriuretic peptide concentrations. There was no difference in overall activity scores or quality of life scores between healthy cats and cats with subclinical HCM.

Of the 32 cats with subclinical HCM, 16 were randomized and given atenolol (6.25 mg PO every 12 hours; dosage was the same regardless of body weight, BCS, or echocardiographic findings) and 16 were given a placebo. All HCM patients were reassessed at baseline and again at 6 months. Cats receiving atenolol had significantly lower heart rate and murmur grades compared with cats receiving a placebo. In cats with subclinical HCM, atenolol treatment did not significantly affect systemic blood pressure, echocardiographic variables, quality of life, or activity levels.

Atenolol has been prescribed by veterinary cardiologists to manage HCM, with the main goal of prolonging the subclinical phase of disease while maintaining a high quality of life. Atenolol use in humans with HCM remains a mainstay therapy, with evidence of improved clinical condition. In the present study, some benefits were noted in cats that had subclinical HCM and were receiving atenolol, but there was no significant improvement in all areas assessed. More significant results may occur in cats with severe subclinical HCM if an alternative survey is offered or if higher doses of atenolol are administered.

... TO YOUR PATIENTS

Key pearls to put into practice:

Cats are often difficult to medicate. There are some benefits to atenolol therapy in cats that have subclinical HCM, but it is important to weigh the pros and cons of treatment and prescribe medications most likely to improve quality of life and longevity. Antiplatelet therapy can be prioritized in some cases.

2

Atenolol therapy may be most useful when given based on the patient's body size and BCS and on the severity of echocardiographic findings.



Baseline diagnostics should be obtained prior to initiating medical therapy in cats with subclinical HCM. Recheck is needed after 6 months, and treatment should be adjusted to maximize positive effects.

This study was funded by a grant fram Marris Animal Foundation with additional support provided by (DEXX Laboratories,

REFERENCES

https://www.cliniciansbrief.com/article/atenolol-use-cats-subclinic...ef+Newsletter&utm_campaign=Online+210914&oly_enc_id=0674I2232356E8U Page 2 of 4

- Fox PR, Keene BW, Lamb K, et al. International collaborative study to assess cardiovascular risk and evaluate long-term health in cats with preclinical hypertrophic cardiomyopathy and apparently healthy cats: the REVEAL study. J Vet Intern Med. 2018;32(3):930-943.
- Luis Fuentes VL, Abbott J, Chetboul V, et al. ACVIM consensus statement guidelines for the classification, diagnosis, and management of cardiomyopathies in cats. *J Vet Intern Med*. 2020;34(3):1062-1077.

AUTHOR

Rebecca L. Quinn

DVM, DACVIM (SAIM, Cardiology) Cape Cod Veterinary Specialists, Buzzards Bay, Massachusetts

Rebecca L. Quinn, DVM, DACVIM (SAIM, Cardiology), is a cardiologist at Cape Cod Veterinary Specialists in Buzzards Bay, Masachusetts. She earned her DVM from Tufts University Cummings School of Veterinary Medicine and completed an internship in small animal medicine and surgery at Veterinary Referral and Emergency Center in Norwalk, Connecticut, as well as residencies in small animal internal medicine and cardiology at Texas A&M University and Angell Animal Medical Center, respectively. Dr. Quinn's interests include managing patients with heart disease and concurrent conditions (eg, renal, GI, liver, or endocrine disease).

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found here.

All Clinician's Brief content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. For questions or inquiries please contact us.



clinician's brief

Gastroesophageal Reflux Disease in Dogs

Tanner Slead, DVM, North Carolina State University M. Katherine Tolbert, DVM, PhD, DACVIM (SAIM), Texas A&M University





EXHIBIT 7 - 265

Episodic clinical signs

TREATMENT

- Consider GABA-derivative muscle relaxant (eg, baclofen) for inhibition of transient LES relaxation^{1,2}
- Consultation with an internist regarding dosing, safety, and monitoring is recommended

Clinical signs worsen at night, evidence of bile reflux on endoscopy

TREATMENT

- Consider bile acid sequestrant (eg, cholestyramine)³
- Consultation with an internist regarding dosing, safety, and monitoring is recommended

Concern for LES disease or megaesophagus based on radiography, fluoroscopy, and breed considerations

TREATMENT

- Consider phosphodiesterase inhibitor (eg, sildenafil) for LES relaxation⁴⁶
- Consultation with an internist regarding dosing, safety, and monitoring is recommended

GABA = γ-aminobutyric acid, GERD = gastroesophageal reflux disease, LES = lower esophageal sphincter, PPI = proton pump inhibitor

REFERENCES

- Wise J, Conklin JL. Gastroesophageal reflux disease and baclofen: is there a light at the end of the tunnel? *Curr Gastroenterol Rep.* 2004;6(3):213-219.
- 2. Lehmann A, Hansson-Brändén L, Kärrberg L. Effects of repeated administration of baclofen on transient lower esophageal sphincter



clinician's brief

Diagnosing Feline Infectious Peritonitis

Matthew Kornya, DVM, ABVP (Feline) Residency Trained, ACVIM (SAIM) Resident, Ontario Veterinary College, The Cat Clinic, Ontario, Canada

INFECTIOUS DISEASE NOVEMBER/DECEMBER 2020 PEER REVIEWED



https://www.cliniciansbrief.com/article/diagnosing-feline-infectlous-peritonitis

EXHIBIT 7 - 267



FECV = feline enteric coronavirus, RT = reverse transcriptase

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units **can be found here.**

All *Clinician's Brief* content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from *Clinician's Brief* may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. **For questions or inquiries please contact us.**

Diagnosing Feline Infectious Peritonitis | Clinician's Brief

https://www.cliniciansbrief.com/article/diagnosing-feline-infectious-peritonitis

EXHIBIT 7 - 269



clinician's brief

Anaphylactic Hemoperitoneum in Dogs

Michelle Goodnight, DVM, MS, DACVECC, Gwinnett Technical College, Lawrenceville, Georgia

EMERGENCY MEDICINE & CRITICAL CARE | NOVEMBER/DECEMBER 2021

Print/View PDF

In the Literature

Hnatusko AL, Gicking JC, Lisciandro GR. Anaphylaxis-related hemoperitoneum in 11 dogs. *J Vet Emerg Crit Care (San Antonio)*. 2021;31(1):80-85.

FROM THE PAGE ...

Common signs of anaphylaxis in dogs include hemorrhagic gastroenteritis, hepatic congestion, gallbladder wall edema, increased liver enzyme activity, hemoconcentration, cutaneous manifestations (eg, hives), and, in severe cases, acute cardiovascular collapse and death.

This retrospective case series describes hemoperitoneum, a less common complication of anaphylaxis. Coagulopathy of anaphylaxis is rare, and patients are

presented with nontraumatic hemoperitoneum. This multifactorial phenomenon is poorly understood and has only been described twice in veterinary and once in human medicine literature.¹⁻³

Eleven previously healthy dogs with acute onset of clinical signs consistent with anaphylaxis and with confirmed hemoperitoneum were presented after collapse or acute weakness. No dogs had cutaneous manifestations or pleural, pericardial, or pulmonary fluid accumulation. Most dogs exhibited concurrent GI signs, 4 dogs had hypoglycemia, and 5 dogs had coagulopathy that was confirmed by blood work.

Treatment varied among patients and included epinephrine, fluid therapy, diphenhydramine, famotidine, and glucocorticoids. Eight dogs received fresh frozen plasma, and 2 dogs required RBC transfusion.

Anaphylactic hemoperitoneum should be considered in cases of nontraumatic hemoperitoneum with no clear cause and concurrent clinical signs of anaphylaxis (eg, distributive shock, elevated ALP, gallbladder halo sign on ultrasound indicative of gallbladder wall edema).

The need for fresh frozen plasma and RBC transfusion in this case series suggests that early identification of anaphylactic coagulopathy and hemoperitoneum can improve treatment decisions and outcome.

... TO YOUR PATIENTS

Key pearls to put into practice:

Approximately 20% of patients presented with anaphylaxis do not show dermal signs⁴; therefore, lack of dermal manifestations should not exclude anaphylaxis as a differential diagnosis in patients with other clinical signs of anaphylaxis.



Nontraumatic hemoperitoneum is a documented complication of anaphylaxis, which should be a differential diagnosis when hemoperitoneum is present along with gallbladder halo sign, elevated ALP, and GI signs.

Medical management of anaphylactic hemoperitoneum consists of epinephrine and fluid therapy. Surgery is contraindicated. Addition of H₁-receptor antagonists (eg, diphenhydramine), H₂-receptor antagonists (eg, famotidine), glucocorticoids, and blood products should be based on individual patient parameters.

SUGGESTED READING

Dowling PM. Anaphylaxis. In: Silverstein DC, Hopper K, eds. Small Animal Critical Care Medicine. 2nd ed. Elsevier Saunders; 2015:807-811.

REFERENCES

- Lisciandro GR. Update on canine anaphylaxis: diagnosis, treatment & medically-treated hemoabdomen & more than gallbladder wall edema. FASTVet website. Published April 3, 2020. Accessed April 19, 2021. https://fastvet.com/wp-content/uploads/2020/04/08-FASTVet-2020-08-FASTVet-SOCHIRAV-AX-GBWE-5-FASTVet-ABVP-Denver-Canine-Anaphylaxis-2019.pdf.
- Caldwell DJ, Petras KE, Mattison BL, Wells RJ, Heffelman VL. Spontaneous hemoperitoneum and anaphylactic shock associated with Hymenoptera envenomation in a dog. J Vet Emerg Crit Care (San Antonio). 2018;28(5):476-482.
- 3. Borahay MA, Harirah HM, Olson G, Kilic GS, Karipcin S, Hankins GDV. Disseminated intravascular coagulation, hemoperitoneum, and
reversible ischemic neurological deficit complicating anaphylaxis to prophylactic antibiotics during cesarean delivery: a case report and review of literature. *AJP Rep.* 2011;1(1):15-20.

4. Shmuel DL, Cortes Y. Anaphylaxis in dogs and cats. J Vet Emerg Crit Care (San Antonio). 2013;23(4):377-394.

AUTHOR

Michelle Goodnight

DVM, MS, DACVECC

Gwinnett Technical College, Lawrenceville, Georgia

Michelle Goodnight, DVM, MS, DACVECC, is a veterinary technology instructor at Gwinnett Technical College in Lawrenceville, Georgia, and a relief veterinarian. She earned her DVM from Virginia-Maryland College of Veterinary Medicine and completed an emergency and critical care residency at The Ohio State University. Dr. Goodnight also served in the US Army, and her military awards include the Bronze Star, Purple Heart, Meritorious Unit Commendation, and Combat Action Badge.

For global readers, a calculator to convert laboratory values, dosages, and other measurements to SI units can be found here.

All Clinician's Brief content is reviewed for accuracy at the time of publication. Previously published content may not reflect recent developments in research and practice.

Material from Clinician's Brief may not be reproduced, distributed, or used in whole or in part without prior permission of Educational Concepts, LLC. For questions or inquiries please contact US.



https://www.cliniciansbrief.com/article/anaphylactic-hemoperitoneu...f+Newsletter&utm_campaign=Online+220126&oly_enc_id=067412232356E8U

EXHIBIT 7 - 273

×

3/31/2022 (27) Unnany Bladdon ulfrasoung Blunder 24 Putm'swar is a blunder Essential of Blunt Trayma @ Essenfials of Blunt Trauma 3/31/2022 h Triage pr. Dr. McGuitty med vet motal status posture gast respiration that rate Mmcolor Blood pressure extremity temperature Actua Blacking obrious wounds or Tractures pain email 2) shock in traums Rebera. McBuitty @medvet, com 3) FAST Scan Thoracia FAST. Abdominal FAST. 4) prognostic Ind. cators Oscoring systems Brecomberg on presentation 3 head traums Hematochezsa preumonia. Hypocakeria. admission base access 5) Trauma Trape fore score o-3 Perfusion vet cot score - plasms lactate, ionized calcium 6) Thoraco centes: s preumotheran 7th-got intercestal space drainair out Possible complication prentrotha (HIBIT 7 - 274

pulmonary contrisions - peak signs 24-48 hrs analgesia. Rimachud. 11 Bronchud: lator ventilator. antibrotic Thoracostomy Tube Autologous Blood patch Rib Fractures Fla: 1 chest. Traumaitic Myscarditis Diaphragmotis Herniq Hemoabdomen Uroabdomen Key point shock resuse. top - thing, orygen. Blood Thoraco entro

pannop FAST SCA. Viscoeladicat monsof

Nocita Aminocaproic Acid -



EXHIBIT 7 - 275

Fluid Resuscitat 10-30 ml Kg over 20-30 minute. shoch poj gow/kg cet 60m/kg) 15m: nut Normosol-R 5-10 ml Vet starch. Lactated Ringers Permissive Hypotension goal SBP-80-gomgHg or 100mgHg Malgessig - Bupranorphine Avoid - NSAIDS & Cortico steroid Butophanul Full assess mont - pray (Thorap, andomen. thoras) Blood test - sometime ALT. Dwner education pulmonauy confusion proumothora Hemorrhage Intracranic so day and pleeding avrhythemts Bilian ruphin Uroabdomen

Breaking the Seal

Emergency Management of Urethral Obstruction in Cats

Stephanie La Plume, DVM Emergency Department Head MedVet Campbell & Mountain View



EXHIBIT 7 - 277

Feline Urethral Obstruction: Chief complaint

- Stranguria
- Frequency in the litter box
- Lethargy
- Anorexia
- Abdominal Pain
- Vomiting
- Collapse/unable to stand
- "Constipation"
- "Meditating"



Feline Urethral Obstruction: Physical exam

- Predominantly male; female UO very rare and typically secondary to calculi
- Turgid, painful urinary bladder that cannot be expressed
- Inability to express the bladder can also be normal in cats so this alone is not diagnostic; corroborate with reported stranguria and/or azotemia
- Abdominal pain
- Dehydration
- Tachycardia or Bradycardia
- Vocalizing
- Hyperemic, bloody, or bruised penis +/- plug at tip
- Collapse



Feline Urethral Obstruction: Risks

- Need to caution owners about potential risks associated with treatment
- Risk of sedation or anesthesia in compromised patient including risk of anesthetic death
- Risk of urethral tear due to inflamed & friable urethra; if tear occurs may require prolonged medical or even surgical management
- Risk of recurrence of UO including immediately after urethral catheter removed, treatment is not always successful & can recur in future
- 90-95% survival rate, with reported recurrence rates of 15-40%.
- Potential for calculi for which cystotomy surgery may be recommended once nonazotemic
- Potential referral for perineal urethrostomy surgery for repeat offenders





Feline UO: Initial Stabilization

- Analgesia & Fluids ASAP
- Treat hyperkalemia
- Urethral catheterization



Stabilization:

- Analgesia
- IV catheter and fluids prior to deobstruction paramount
- Fluid bolus 10-20mL/kg indicated in critical cats
- Balanced electrolyte solutions (NormR, Plasma-lyte) IV allows for more rapid correction of metabolic acidosis and no difference in correction of hyperkalemia compared to 0.9% NaCl
- ECG indicated right away if unstable on presentation



Stabilization: ECG

- Lead II ECG rhythm strip abnormalities secondary to hyperkalemia:
- Tall and spiked T waves
- Widened QRS complexes, lengthened PR intervals
- Flattened P waves
- Atrial standstill
- Ventricular fibrillation
- Asystole





Stabilization and Treatment: Hyperkalemia

- Ultimately, treatment for hyperkalemia should depend on ECG
- Fluids!
- Calcium gluconate 1mL/kg of 10% (= 100mg/kg) IV slow over 10min while monitoring ECG; stop if bradycardia worsens
- Doesn't decrease K+
- Cardioprotective effect lasts 20-30min
- Dextrose IV 1-2mL/kg of 25% (diluted 1:1)
- Regular insulin 1u IV; give with dextrose bolus, need to monitor BG + add dextrose to ongoing IV fluids

TABLE.

Cats with Urethral Obstruction: Degrees of Hyperkalemia

DEGREEROF (YPERFCARE)/A	сарын ногасанын сонсентентон	
Mild hyperkalemia	< 6 mEq/L	Dilutional fluid therapy (10–20 mL/ kg/H), with rate adjusted as patient stabilizes
Moderate hyperkalemia	6-8 mEq/L	 IV administration of: Dextrose (50% solution [1 mL/kg] diluted to final concentration of 10%-20%) Regular insulin (1 U)
Severe hyperkalemia	> 8 mEq/L	Całcium gluconate (0.5–1 mL/kg IV), followed by regular insulin and dextrose IV





Feline UO: Diagnostic Workup

- Bloodwork
- Radiographs
- Urinalysis



Diagnostics: Bloodwork

- Bloodwork prior to sedation
- Hyperkalemia
- Azotemia
- Metabolic acidosis
- Hemoconcentration
- Recheck bloodwork q24 hours for azotemic patients or those with severe postobstructive diuresis; sooner if severe hyperkalemia



Diagnostics: Radiographs



Diagnostics: Radiographs preferable to ultrasound

- MUST include entire urethra to rule out calculi!
- Prior to deobstruction can be valuable to diagnose calculi prior to procedure if stable enough for concurrent cystotomy
- Post-deobstruction (preferred) valuable to assess urinary catheter placement
- Decreased serosal detail in neck of bladder common
- Ultrasound still useful to detect free fluid on presentation
- Ultrasound cannot detect calculi in pelvic urethra which the catheter may pass around
- Artifact secondary to alcohol from ECG leads visible in this radiograph



Diagnostics: Urinalysis, no culture needed

- · Must include sediment
- Obtain catheter sample at time of urethral catheterization
- Urine culture NOT necessary on presentation for routine UO, though recommended if repeat urinary catheterization
- 2019 OSU Study of 34 male cats presenting for UO
- No urine cultures yielded growth at presentation (0/34)
- Culture recommended if recent history of urinary catheterization
- Incidence of bacteriuria at presentation and resulting from urinary catheterization in feline urethral obstruction

Cooper E.S.^[1], Lasley E.^[1], Daniels J.B.^[1], et al. Journal of Veterinary Emergency and Critical Care. volume 29 issue 5 pages 472-477. September 2019



Feline Urethral Obstruction: Chief complaint

- Stranguria
- Frequency in the litter box
- Lethargy
- Anorexia
- Abdominal Pain
- Vomiting
- Collapse/unable to stand
- "Constipation"
- "Meditating"



Feline Urethral Obstruction: Physical exam

- Predominantly male; female UO very rare and typically secondary to calculi
- Turgid, painful urinary bladder that cannot be expressed
- Inability to express the bladder can also be normal in cats so this alone is not diagnostic; corroborate with reported stranguria and/or azotemia
- Abdominal pain
- Dehydration
- Tachycardia or Bradycardia
- Vocalizing
- Hyperemic, bloody, or bruised penis +/- plug at tip
- Collapse



Feline Urethral Obstruction: Risks

- Need to caution owners about potential risks associated with treatment
- Risk of sedation or anesthesia in compromised patient including risk of anesthetic death
- Risk of urethral tear due to inflamed & friable urethra; if tear occurs may require prolonged medical or even surgical management
- Risk of recurrence of UO including immediately after urethral catheter removed, treatment is not always successful & can recur in future
- 90-95% survival rate, with reported recurrence rates of 15-40%.
- Potential for calculi for which cystotomy surgery may be recommended once nonazotemic
- Potential referral for perineal urethrostomy surgery for repeat offenders





Feline UO: Initial Stabilization

- Analgesia & Fluids ASAP
- Treat hyperkalemia
- Urethral catheterization



Stabilization:

- Analgesia
- IV catheter and fluids prior to deobstruction paramount
- Fluid bolus 10-20mL/kg indicated in critical cats
- Balanced electrolyte solutions (NormR, Plasma-lyte) IV allows for more rapid correction of metabolic acidosis and no difference in correction of hyperkalemia compared to 0.9% NaCl
- ECG indicated right away if unstable on presentation



Stabilization: ECG

- Lead II ECG rhythm strip abnormalities secondary to hyperkalemia:
- Tall and spiked T waves
- Widened QRS complexes, lengthened PR intervals
- Flattened P waves
- Atrial standstill
- Ventricular fibrillation
- Asystole





Stabilization and Treatment: Hyperkalemia

- Ultimately, treatment for hyperkalemia should depend on ECG
- Fluids!
- Calcium gluconate 1mL/kg of 10% (= 100mg/kg) IV slow over 10min while monitoring ECG; stop if bradycardia worsens
- Doesn't decrease K+
- Cardioprotective effect lasts 20-30min
- Dextrose IV 1-2mL/kg of 25% (diluted 1:1)
- Regular insulin 1u IV; give with dextrose bolus, need to monitor BG + add dextrose to ongoing IV fluids

TABLE.

Cats with Urethral Obstruction: Degrees of Hyperkalemia

		Therease Controles
Mîtd hyperkalemia	< 6 mEq/L	Dilutional fluid therapy (10–20 mL/ kg/H), with rate adjusted as patient stabilizes
Moderate hyperkalemia	6–8 mEq/L	IV administration of: • Dextrose (50% solution [1 mL/kg] diluted to final concentration of 10%–20%) • Regular insulin (1 U)
Severe hyperkalemia	> 8 mEq/L	Calcium gluconate (0.5–1 mL/kg IV), followed by regular insulin and dextrose IV





Feline UO: Diagnostic Workup

- Bloodwork
- Radiographs
- Urinalysis



Diagnostics: Bloodwork

- Bloodwork prior to sedation
- Hyperkalemia
- Azotemia
- Metabolic acidosis
- Hemoconcentration
- Recheck bloodwork q24 hours for azotemic patients or those with severe postobstructive diuresis; sooner if severe hyperkalemia



Diagnostics: Radiographs



Diagnostics: Radiographs preferable to ultrasound

- MUST include entire urethra to rule out calculi!
- Prior to deobstruction can be valuable to diagnose calculi prior to procedure if stable enough for concurrent cystotomy
- Post-deobstruction (preferred) valuable to assess urinary catheter placement
- Decreased serosal detail in neck of bladder common
- Ultrasound still useful to detect free fluid on presentation
- Ultrasound cannot detect calculi in pelvic urethra which the catheter may pass around
- Artifact secondary to alcohol from ECG leads visible in this radiograph



Diagnostics: Urinalysis, no culture needed

- Must include sediment
- Obtain catheter sample at time of urethral catheterization
- Urine culture NOT necessary on presentation for routine UO, though recommended if repeat urinary catheterization
- 2019 OSU Study of 34 male cats presenting for UO
- No urine cultures yielded growth at presentation (0/34)
- Culture recommended if recent history of urinary catheterization
- Incidence of bacteriuria at presentation and resulting from urinary catheterization in feline urethral obstruction

Cooper E.S.^[1], Lasley E.^[1], Daniels J.B.^[1], et al. Journal of Veterinary Emergency and Critical Care. volume 29 issue 5 pages 472-477. September 2019





Feline UO: Treatment

- Analgesia
- Fluids
- Urethral catheterization
- Alpha 2 antagonists



Stabilization and Treatment: Analgesia & Sedation

- Anesthesia for immobilization & urethral relaxation
- May not be necessary in critically ill cats; analgesia is
- Buprenorphine or other opioid
- Diazepam 0.2-0.5mg/kg IV minimal hypotensive effect & aids urethral relaxation
- Ketamine 2-5mg/kg IV -or-
- Alfaxan 1-4mg/kg IV -or-
- Dexmedetomidine 0.05-0.2mL IV

Coccygeal epidural



Stabilization: Urethral catheterization

- Buster Easy Slide open ended or Slippery Sam personal preference for both unblocking + indwelling, only need a single catheter, 10 & 14cm 3.5Fr; PTFE
- Other options: Mila small animal urinary catheter, 3.5-5Fr red rubber, Argyle; IV catheter without stylet/needle to flush distal urethra
- Polypropylene tomcat can be used for unblocking but should not be left indwelling- too uncomfortable and irritating to urethra, better options available
- Open ended aids flushing urethra



Stabilization: Urethral catheter choice

- Retrospective evaluation of urinary indwelling catheter type in cats with urethral obstruction (January 2014 to December 2014): 91 cases. <u>Davidow</u> <u>E.B.^[1] Journal of Veterinary Emergency and Critical Care. volume 30 issue 2 pages 239-242. March 2020
 </u>
- Retrospective, 91 cats; 3.5Fr Argyle vs 3.5Fr red rubber, no difference in recurrence

Initial treatment factors associated with feline urethral obstruction recurrence rate: 192 cases (2004-2010). Hetrick P.F.^[1] and Davidow E.B. Journal of the American Veterinary Medical Association. volume 243 issue 4 pages 512-9, 8/15/2013

- Retrospective; Recurrence in 24h higher with 5Fr than 3.5Fr u. cath



Stabilization: Decompressive cystocentesis-Safe prior to catheterization

- Association of abdominal effusion with a single decompressive cystocentesis prior to catheterization in male cats with urethral obstruction. Gerken K.K.^[2], <u>Cooper</u> <u>E.S.^[2]</u>, Butler A.L.^[1], <u>et al.</u> Journal of Veterinary Emergency and Critical Care. volume 30 issue 1 pages 11-17. January 2020
- A single decompressive cystocentesis prior to catheterization did NOT lead to development of clinically significant abdominal effusion
- Abdominal effusion may be found at presentation in cats with urethral obstruction. The significance of this effusion remains to be determined.



Stabilization: Decompressive cystocentesis-Safe prior to catheterization

- Outcome of male cats managed for urethral obstruction with decompressive cystocentesis and urinary catheterization: 47 cats (2009-2012). Hall J.[1], Hall K., Powell L.L., et al. Journal of veterinary emergency and critical care (San Antonio, Tex. : 2001). volume 25 issue 2 pages 256-62, 2015
- Decompressive cystocentesis, in cats with urethral obstruction, followed by placement of an indwelling urinary catheter, did not result in a diagnosis of bladder rupture in any cat.



Stabilization: Decompressive cystocentesis-Safe, but not beneficial

- Multicenter evaluation of decompressive cystocentesis in the treatment of cats with urethral obstruction. Reineke E.L., Cooper E.S., Takacs J.D., et al. Journal of the American Veterinary Medical Association. volume 258 issue 5 pages 483-492. 3/1/2021
- Prospective randomized trial
- Decompressive cystocentesis prior to unblocking- no difference in ease or time to place urethral catheter in 88 male cats
- No difference in abdominal effusion between groups immediately & 4h after procedure


- Clip + Aseptic Prep
- Very careful sterile technique
- Can use glove paper or fenestrated drape for sterility
- Especially hard to avoid contamination when placing longer catheters (like red rubbers) without a drape
- Dorsal recumbency with hindlimbs pulled cranially eases extrusion of the penis





- More positioning...
- Hold penis by preputial reflection
- Straighten urethral sigmoid flexure by pulling penis caudally



- Sterile lube on tip of catheter; can also try mixing lube with saline for flush
- Pulsating saline retropulsion is key
- Vibration is the key to unlock any mechanical system
- Dilates urethra and loosens and flushes obstructing material retrograde into the bladder
- Gentle hand, tap gently at the blockage while pulsating saline until it gives way. Patience!



- Other tricks... be gentle, and keep trying!
- Change size of syringe attached to extension set for pulsating saline- 35, 20, 12cc
- Back the catheter completely out of urethra and reinsert (gently) multiple times, by removing may allow some grit to come out of urethra
- Massage penis gently to break up plug or manipulate debris out distally
- Deeper sedation/analgesia
- Use nylon IVC (no stylet) and pass suture into bladder, can use suture as stylet to guide u.cath into bladder
- If unable, then decompressive cystocentesis & referral is indicated



- Stay sutures to attach u.cath-more comfortable for patient, easier to remove, and able to re-use the sutures in case urinary catheter needs to be changed or adjusted
- Sterile collection set: if sterilized IV bags + drip set- remove clamps & not micro drip; or commercially available closed urine collection set
- Tape line to tail with enough room to lift tail but not get a hindlimb through
- Hard plastic E-collar ALWAYS
- Ongoing analgesia- buprenorphine







- Flushing the bladder after catheter passed not shown to prevent recurrent UO
- 2019 study showed urinary bladder lavage at the time of urethral catheterization had no significant effect on in-hospital recurrence rate of the condition, duration of urinary catheter retention, or duration of hospitalization
- Effect of urinary bladder lavage on in-hospital recurrence of urethral obstruction and durations of urinary catheter retention and hospitalization for male cats. Dorsey T.I., Monaghan K.N., Respess M., et al. Journal of the American Veterinary Medical Association. Volume 254 issue 4 pages 483-486. 2/15/2019



- Hospitalization with indwelling catheter shown to prevent recurrent UO relative to outpatient care after passing a catheter
- Typically in place between 24-48 hours until urine clear and nonazotemic; average in our hospital 36h
- Removal of an indwelling catheter before urine appears grossly normal may be associated with development of RUO
- One-time catheterization with outpatient care was inferior to the standard care protocol but was successful in many cats and may be a reasonable alternative when clients cannot pursue standard care.
- Evaluation for association between indwelling urethral catheter placement and risk of recurrent urethral obstruction in cats. Seitz M.A., Burkitt-Creedon J.M. And Drobatz K.J. Journal of the American Veterinary Medical Association, volume 252 issue 12 pages 1509-1520, 6/15/2018.



Treatment: Fluids!

- Post-obstructive diuresis (>2mL/kg/h UOP) reported in 87% of cats with UO
- Need to monitor ins and outs or severe dehydration can occur
- Replace insensible losses 20mL/kg/day in addition to matching hourly urine production in euhydrated patients; dehydrated patients need even higher fluid rates
- Need to assess hydration & perfusion parameters to determine if more fluids needed
- Commonly start fluids around ~5mL/kg/h
- If low UOP, check hydration status, bladder palpation and catheter patency; check cage for urine; also consider AKI



Treatment: Alpha-1 antagonists- Prazosin

- Use of of Alpha-1 antagonists is intended to relax urethral sphincter smooth muscle
- Prazosin, Acepromazine, Phenoxybenza mine
- Initial treatment factors associated with feline urethral obstruction recurrence rate: 192 cases (2004-2010). Hetrick P.F.[1] and Davidow E.B. Journal of the American Veterinary Medical Association . volume 243 issue 4 pages 512-9, 8/15/2013
- Lower recurrence rate in 24h and 30d with Prazosin than with Phenoxybenzamine



Treatment: Alpha-1 antagonists- Prazosin

- Though commonly used, evidence in support of antispasmodics is limited and further prospective investigation is needed.
- Effect of prazosin on feline recurrent urethral obstruction. <u>Hanson K.R.^[2]</u>, Rudloff E.^[2], Yuan L.^[1] et al. Journal of feline medicine and surgery. v23 issue 12 pages 1176-1182. December 2021
- The effect of prazosin on outcome in feline urethral obstruction. Erica L Reineke¹, Emily K Thomas¹, Rebecca S Syring¹, Jennifer Savini¹, Kenneth J Drobatz¹ J Vet Emerg Crit Care. 2017 Jul;27(4):387-396.
- Both double blinded prospective studies, found no difference between Prazosin & placebo in recurrence of UO



Treatment: Analgesia

- Need ongoing analgesia both hospitalized and after discharge
- Buprenorphine my top choice
- Gabapentin may also have value and some anxiolytic properties
- However, liquid gabapentin is bitter, higher volume, and hence harder to administer & more unpleasant to cats than buprenorphine



Treatment: Meloxicam- not recommended

- A prospective randomized study of efficacy of 2 treatment protocols in preventing recurrence of clinical signs in 51 male cats with obstructive idiopathic cystitis. <u>Nivy</u> <u>R., Segev G.</u>, Rimer D., <u>et al.</u> Journal of Veterinary Internal Medicine . volume 33 issue 5 pages 2117-2123, 2019.
- Compared phenoxybenzamine + alprazolam with & without meloxicam; no difference between groups.
- Considering this and concern for potential renal compromise, not recommended



Treatment: Prescription diets

- Recommended for all cats with UO, canned preferable to dry
- Common history on presentation- recent diet change within past 1 month, and for recurrent UO especially discontinuing RX urinary diet
- Hill's c/d & Royal Canin Urinary SO are what we carry
- Cats who eat canned food have lower USG and consume more total water than those who eat dry alone
- Kruger et al. (2015) described the effect of consistently feeding a therapeutic urinary food (Hill's Prescription Diet c/d Multicare Feline Dry). Results showed a significant reduction in recurrence of FIC episodes of 89% over 12 months.



Treatment: Without catheterization

- A protocol for managing urethral obstruction in male cats without urethral catheterization. <u>Cooper</u>, et al J Am Vet Med Assoc. 2010 Dec 1; 237(11): 1261–1266.
- Acepromazine (0.25 mg, IM, or 2.5 mg, PO, q 8 h), buprenorphine (0.075 mg, PO, q 8 h), and medetomidine (0.1 mg, IM, q 24 h) and decompressive cystocentesis
- SQF PRN
- Cats were placed in a quiet, dark environment to minimize stress. Treatment success was defined as spontaneous urination within 72 hours and subsequent discharge from the hospital.
- Success in 11/15; 4 cats failed uroabdomen or hemoabdomen
- Could be considered if no other options; transient urethral catheterization still vastly preferred and safer



Common Pitfalls:

- Withholding IV fluids until unblocked
- Not giving analgesia right away if sufficiently stable
- Forcibly pushing through the obstruction with urinary catheter rather than flushing
- Keeping tomcat polypropylene catheter in place
- Failure to recognize and treat postobstructive diuresis
- Insufficient sterility & iatrogenic infection

- Lack of closed collection set, open u.cath provides route of entry for bacteria
- Failure to remove clamps from fluid lines to sterile collection set
- Use of micro-drip set in urinary collection set
- Not supplementing dextrose when insulin given
- Radiograph not including entire urethra

Summary

- Immediate analgesia paramount
- Stabilize by starting IV fluids, check ECG & address hyperkalemia prior to unblocking
- Hospitalization optimal, yet even outpatient treatment preferable over euthanasia
- Patience, pulsating saline retropulsion during urethral catheterization, dorsal recumbency with legs forward and extending penis caudally key for unblocking success.
- Alpha-1 antagonist such as prazosin commonly used with minimal risk but still lack solid evidence



Thank you!

- Thank you for attending, I hope you've gained some clinically relevant information
- Thank you to the incredible veterinary staff, they are the heroes to our patients and truly indispensible!
- Thank you to my Medical Director, Dr. Monica Clare, for her mentorship in this presentation
- Many thanks to my husband for supporting me as an emergency veterinarian, a profession which often isn't easy on our partners and families



EXHIBIT 8

Loma Linda Animal Hospital

Leonard Sigdestad, DVM 2605 S Waterman Avenue San Bernardino, Ca 92408 (909) 825-3144 Fax (909) 824-5145

June 20, 2022

Veterinary Medical Board Department of Consumer Affairs

1747 North Market Boulevard, Suite 230 Sacramento, CA 95834-2987

To Whom It May Concern:

I have known Dr Hong Park as a neighboring colleague for 30 years. Since losing his Veterinary License he has been diligent in keeping his continuing education. I can personally say that I have seen him at all of our Orangebelt Veterinary Association meetings. I would recommend that Dr Park have his Veterinary License reinstated.

"I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct."

Sincerely,

Leonard Sigdestad, DVM

Veterinary Medical Board 1747 N Market BLVD, #230 Sacramento, CA 95834

To Whom It May Concern:

This letter is in support of Dr. Hong Rak Park's application for his California Veterinary Medical license.

As the records indicate, Dr. Park first received his Veterinary Medical license on July 24, 1978, and voluntarily surrendered his CA Veterinary license on 7/22/19. He subsequently sold his practice of almost 40 years. Since that time, he has been actively maintaining his clinical knowledge by participating in many continuing education seminars and attending local veterinary meetings with the Orange Belt Veterinary Medicine Association and joining a Christian Veterinary mission trip to Nicaragua for 10 days in 2019.

Dr. Park has been a veterinarian for over 40 years. He was an outstanding member of his community, and skilled clinician. At this point in his career, Dr. Park will not return to full time practice but would like to have his California Veterinary license reinstated so he can do parttime relief work or locums.

I strongly support his application. Please let me know if you have any questions.

I declare under penalty of perjury un the law of the State of California that the foregoing is true and correct.

EA License # 2416 Albert M. Brojdich

Date:

Veterinary Medical Board 1747 N Market BLVD, #230 Sacramento, CA 95834

To Whom It May Concern:

This letter is in support of Dr. Hong Rak Park's application for his California Veterinary Medical license.

As the records indicate, Dr. Park first received his Veterinary Medical license on July 24, 1978, and voluntarily surrendered his CA Veterinary license on 7/22/19. He subsequently sold his practice of almost 40 years. Since that time, he has been actively maintaining his clinical knowledge by participating in many continuing education seminars and attending local veterinary meetings with the Orange Belt Veterinary Medicine Association and joining a Christian Veterinary mission trip to Nicaragua for 10 days in 2019.

Dr. Park has been a veterinarian for over 40 years. He was an outstanding member of his community, and skilled clinician. At this point in his career, Dr. Park will not return to full time practice but would like to have his California Veterinary license reinstated so he can do part-time relief work or locums.

I strongly support his application. Please let me know if you have any questions.

I declare under penalty of perjury un the law of the State of California that the foregoing is true and correct.

Marion Hammarlund, DVM

atel

Leonard Sigdestad, DVM

Marshall Scott, DVM

Date:

Date:

Date:

5-1-22

I declare under penalty of perjury under the laws of the State of CA. that the foregoing is true and correct. I have known Der Park for more than 30 years. He is a good small animal veterinarian. I recommend he receive his license

Sincerely. M. a. Hammarlund, DUM CA-3972

EXHIBIT 9

STATE OF CALIFORNIA IICA BOIS (Rev. 04/2020)	Reset Form DEPARTMENT OF JUSTICE PAGE 1 of 4
REQUEST FOR LIVE SCAN SERVICE	
Applicant Submission	
A-D-133 ORI (Code assigned by DOJ)	Authorized Applicant Type
Type of License/Certification/Permit OR Working Title (Maximum 30 character	rs - f assigned by DOJ, use exact title exeigned)
Contributing Agency Information:	
Agency Authorized to Receive Criminal Record Information	Mail Code (five-digit code assigned by DOJ)
Street Address or P.O. Box	Contact Name (mandatory for all school submissions)
City State ZIP Code	Contact Telephone Number
Applicant Information: PARK Last Name	HONG R First Name Middle Initial Suffix
Other Name: (AKA or Alias)	
Last Name Sex Male Female Date of Birth Height Weight Eve Color Hair Color	First Name Suffix Driver's License Number Billing Number
Place of Birth (State or Country) Social Security Number	(Agency Billing Number) Misc. Number (Other Identification Number)
Home <u>3/0/ F/:ntr:dgr pr</u> Address Street Address or P.O. Box	Eullerton CA 92835 City State ZIP Code
I have received and read the included Privacy Notic	e, Privacy Act Statement, and Applicant's Privacy Rights.
Your Number: OCA Number (Agency Identifying Number)	Level of Service: DOJ FBI (If the Level of Service Indicates FBI, the fingerprints will be used to check the criminal history record information of the FBI.)
If re-submission, list original ATI number: (Must provide proof of rejection) Original ATI Number	
Employer (Additional response for agencies specified by statu	te):
Employer Name	
Street Address or P.O. Box	Telephone Number (optional)
City State	ZIP Code Mail Code (five digit code assigned by DOJ)
Name of Operator	Data 7/11/22 1911
Certifix Transmitting Adency LSID EP9	ATI Number Amount Collected/Billed

EXHIBIT 9 - 001