Estimated antimicrobial dispensing frequency and preferences for lactating cow therapy by Ontario dairy veterinarians

A comparison between maropitant and metoclopramide for the prevention of morphine-induced nausea and vomiting in dogs

Comparison of complication rates of unilateral, staged bilateral, and single-session bilateral surgery for the treatment of bilateral medial patellar luxation in dogs

Analysis of canine urolith submissions to the Canadian Veterinary Urolith Centre, 1998–2014

Evaluation of toxicity of a chronic alternate day metronomic cyclophosphamide chemotherapy protocol in dogs with naturally occurring cancer

Validation de la version francophone d’une échelle composite multidimensionnelle pour l’évaluation de la douleur postopératoire chez les chats

Follicular dynamics and ovulation time in gilts and post-weaning sows

Feasibility of quantitative contrast ultrasound imaging of bladder tumors in dogs

Nasal carriage of methicillin-resistant Staphylococcus pseudintermedius in dogs treated with cephalaxin monohydrate

Primary frontal sinus squamous cell carcinoma in a dog treated with surgical excision

Suspected immune-mediated neutropenia and corticosteroid responsive pancytopenia in a Portuguese water dog
Professional Liability • Life & Disability • Business Insurance

Available exclusively to members of the Canadian Veterinary Medical Association, the specialized CVMA Insurance Program offers the most comprehensive and cost-effective insurance protection for you, your practice and your employees.

Members save an average of 10% when joining either the Commercial Insurance or Employee Benefits programs!

866-860-CVMA (2862)
www.cvmainsurance.com
Deliberately Different

Accelerated Hydrogen Peroxide® Disinfectants for Infection Control & Biosecurity

PREvail® over tough germs and harsh chemicals with AHP®

What makes Accelerated Hydrogen Peroxide® (AHP®) disinfectants so different? Formulating a disinfectant that kills pathogens is easy, formulating a disinfectant that kills AND is less toxic is difficult. Our Prevail™ surface disinfectants were deliberately designed to be effective against a broad-spectrum of hard to kill pathogens while remaining gentle for users, animals, materials and the environment. Using Prevail™ improves both animal and human health while protecting your assets by reducing the risk of exposure to harsh chemicals and deadly pathogens.

That’s why we are not just different from what you’re currently using, we are Deliberately Different™.

ViroxAnimalHealth.com

Contact Virox Animal Health for product distribution information.

Contact Virox Animal Health for product distribution information.

Virox is proud to be an Emerald Member of the AAHA Strategic Alliance Program.
KNOWING MAKES ALL THE DIFFERENCE
An early diagnosis could save my life.

You can be the difference between “I wish we could have done something” and “I’m so glad we caught this soon enough...”

Visit IDEXX.ca/preventivecare to learn more
# Contents

## SCIENTIFIC RUBRIQUE SCIENTIFIQUE

<table>
<thead>
<tr>
<th>Page</th>
<th>Article Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>Estimated antimicrobial dispensing frequency and preferences for lactating cow therapy by Ontario dairy veterinarians</td>
<td>David F. Léger, Nathalie C. Newby, Richard Reid-Smith, Neil Anderson, David L. Pearl, Kerry D. Lissimore, David F. Kelton</td>
</tr>
<tr>
<td>35</td>
<td>A comparison between maropitant and metoclopramide for the prevention of morphine-induced nausea and vomiting in dogs</td>
<td>Augusto M. Lorenzutti, Manuel Martín-Flores, Nicolás J. Litterio, Martín A. Himelfarb, Sergio H. Invaldi, María P. Zarazaga</td>
</tr>
<tr>
<td>39</td>
<td>Comparison of complication rates of unilateral, staged bilateral, and single-session bilateral surgery for the treatment of bilateral medial patellar luxation in dogs</td>
<td>Bronwyn A. Fullagar, Päivi Rajala-Schultz, Bianca F. Hettlich</td>
</tr>
<tr>
<td>45</td>
<td>Analysis of canine urolith submissions to the Canadian Veterinary Urolith Centre, 1998–2014</td>
<td>Doreen M. Houston, Heather E. Weese, Nick P. Vanstone, Andrew E.P. Moore, J. Scott Weese</td>
</tr>
<tr>
<td>51</td>
<td>Evaluation of toxicity of a chronic alternate day metronomic cyclophosphamide chemotherapy protocol in dogs with naturally occurring cancer</td>
<td>Arata Matsuyama, J. Paul Woods, Anthony J. Mutsaers</td>
</tr>
<tr>
<td>56</td>
<td>Validation de la version francophone d’une échelle composite multidimensionnelle pour l’évaluation de la douleur postopératoire chez les chats</td>
<td>Paulo V.M. Steagall, Beatriz P. Monteiro, Anne-Marie Lavoie, Diane Frank, Eric Troncy, Stelio P.L. Luna, Juliana T. Brondani</td>
</tr>
<tr>
<td>65</td>
<td>Follicular dynamics and ovulation time in gilts and post-weaning sows</td>
<td>Sara I. Williams, R. Luzbel de la Sota</td>
</tr>
<tr>
<td>70</td>
<td>Feasibility of quantitative contrast ultrasound imaging of bladder tumors in dogs</td>
<td>Rachel E. Pollard, Katherine D. Watson, Xiaowen Hu, Elizabeth Ingham, Katherine W. Ferrara</td>
</tr>
<tr>
<td>73</td>
<td>Nasal carriage of methicillin-resistant Staphylococcus pseudintermedius in dogs treated with cephalaxin monohydrate</td>
<td>Punpichaya Fungwithaya, Pattrarat Chanchaithong, Nathita Phumthanakorn, Nuvee Prapasarakul</td>
</tr>
<tr>
<td>79</td>
<td>Primary frontal sinus squamous cell carcinoma in a dog treated with surgical excision</td>
<td>Janet A. Grimes, Candace J. Pagano, Bonnie B. Boudreaux</td>
</tr>
<tr>
<td>83</td>
<td>Suspected immune-mediated neutropenia and corticosteroid responsive pancytopenia in a Portuguese water dog</td>
<td>Ellen B. Denstedt</td>
</tr>
</tbody>
</table>

**CASE REPORT RAPPORT DE CAS**

| 79   | Primary frontal sinus squamous cell carcinoma in a dog treated with surgical excision | Janet A. Grimes, Candace J. Pagano, Bonnie B. Boudreaux |

**STUDENT PAPER COMMUNICATION ÉTUDIANTE**

| 83   | Suspected immune-mediated neutropenia and corticosteroid responsive pancytopenia in a Portuguese water dog | Ellen B. Denstedt |

**QUIZ CORNER TEST ÉCLAIR**

*FOR PERSONAL USE ONLY*
No fleas. No ticks. No mess.

Monthly, soft beef-flavoured NexGard for dogs is easy for owners to give and provides strong and consistent efficacy against both fleas and ticks all month long.1

Safe and efficacious for puppies eight weeks of age or older.1
## Contents  Table des matières

### FEATURES  RUBRIQUES SPÉCIALES

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors/Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>LETTER TO THE EDITOR COURRIER DES LECTURES</td>
<td>Emergency care after-hours — Comments on an ethicists remarks Bernard Vallée</td>
</tr>
<tr>
<td>13</td>
<td>PRESIDENT’S MESSAGE LE MOT DU PRÉSIDENT</td>
<td>Bill C-246 dies on House floor Le projet de loi C-246 est défait à la Chambre des communes Troy Bourque</td>
</tr>
<tr>
<td>15</td>
<td>VETERINARY MEDICAL ETHICS DÉONTOLOGIE VÉTÉRINAIRE</td>
<td>Attracting new clients with the first phone call/Recruter des clients lors du premier appel téléphonique Terra Shastri</td>
</tr>
<tr>
<td>87</td>
<td>VETERINARY PRACTICE MANAGEMENT GESTION D’UNE CLINIQUE VÉTÉRINAIRE</td>
<td>Lynne S. Sandmeyer, Bianca S. Bauer, Marina L. Leis, Bruce H. Grahn</td>
</tr>
<tr>
<td>69</td>
<td>BOOK REVIEW COMPTE RENDU DE LIVRE</td>
<td>Clinical Veterinary Advisor: Dogs and Cats, 3rd edition Janeen Junaid</td>
</tr>
<tr>
<td>14</td>
<td>ERRATUM</td>
<td></td>
</tr>
<tr>
<td>78</td>
<td>INDUSTRY NEWS</td>
<td></td>
</tr>
<tr>
<td>86</td>
<td>INDEX OF ADVERTISERS</td>
<td></td>
</tr>
<tr>
<td>95</td>
<td>Classfieds Petites annonces</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>NEWS NOUVELLES</td>
<td>Heather Broughton, Isabelle Vallières</td>
</tr>
</tbody>
</table>

---

**Contributors**

“Instructions for authors” are available online (www.canadianveterinarians.net).

The Canadian Veterinary Journal
La Revue vétérinaire canadienne

339 rue Booth Street
Ottawa, Ontario K1R 7K1
Telephone: (613) 236-1162
Fax: (613) 236-9681
E-mail: hbroughton@cvma-acvm.org
Website/Site Web: www.canadianveterinarians.net
www.veterinairescanada.net

© Canadian Veterinary Medical Association 2017
L'Association canadienne des médecins vétérinaires 2017

The Canadian Veterinary Journal is indexed or abstracted in:
La Revue vétérinaire canadienne est indexée ou ses articles sont résumés dans :
AGRICOLA, Biological Abstracts, Capsule Report, Current Contents — Agriculture,
Current Veterinary Drug File, EMBASE/Excerpta Medica,
Index Veterinarius, Index Medicus, Quarterly Index, Science Citation Index, Small

Printed by/Imprimé par
AN Design Communications
339 rue Booth Street
Ottawa, Ontario
ISSN 0008-5286

Photo by/Photo de : Shutterstock

Typesetting/Typographie
AN Design Communications
Printed by/Imprimé par
The Lowe-Martin Group
Ottawa, Ontario

Return undeliverable Canadian addresses to:
339 rue Booth Street
Ottawa, Ontario K1R 7K1
e-mail: hbroughton@cvma-acvm.org

Subscriptions (2017). Annual: Canada $205 + applicable GST or HST; foreign
$220 US, institutional $275. Express subscriptions available. Single issue/back issue:
$25 each, institutional single issue = $50.00 + GST or HST, if applicable. (All prices
subject to change.) Missing issues will be replaced if the Subscriptions Office is
notified within 6 months (for requests within Canada) and 1 year (for requests from
abroad) of the issue date. The publisher expects to supply missing issues only when
losses have been sustained in transit and when the reserve stock will permit. Telephone
(613-236-1162) or (1-800-567-2862) and fax (613-236-9681) orders accepted with
a valid Visa or MasterCard number. Please advise the publisher of address changes
promptly.

Abonnements (2017). Annuel : Canada 205 $ + GST ou TVH en vigueur; pays
étranger 220 $ É-U ; prix d’une institution 275 $. Abonnement express disponible. Anciens
numéros (chacun) : 25 $, ancien numéro d’institution 50 $ + TVH ou GST en vigueur. Les prix sont sujets à change
ment sans préavis. Les numéros qui ne sont pas reçus seront remplacés si l’éditeur en est infor
mé dans les 6 mois (pour les demandes venant du Canada) et 1 an (pour les demandes venant
de l’étranger) suivant la date de parution. L’éditeur s’engage à remplacer les numéros manquants seulement lorsque
les pertes ont été subies en transit et lorsque ses réserves le permettent. On peut payer son
abonnement par téléphone (613-236-1162) ou (1-800-567-2862), par téléphone
(613-236-9681) ou par carte de crédit (Visa ou MasterCard). Veuillez aviser le bureau
de l’éditeur de tout changement d’adresse.

Editorial policy: All published articles including editorials and letters reflect the
opinions of the authors and do not necessarily reflect the opinion of the publisher.
Publication of an advertisement does not necessarily imply that the publisher agrees
with or supports the claims therein.

Éditeur en chef : Carlton Gyles, Guelph, Ontario
Assistants éditeurs : Wayne McDonell, Guelph, Ontario
Jane Bajwa, Burnaby, British Columbia
Bruce Grahn, Saskatoon, Saskatchewan

Managing Editor/Directrice de la rédaction
Heather Broughton, Ottawa, Ontario

Assistant Managing Editor/Directrice adjointe de la rédaction
Linda Chow, Ottawa, Ontario

Advertising Manager/Gérante de la publicité
La Revue vétérinaire canadienne est indexée ou ses articles sont
présentés : Index Veterinarius, Index Medicus, Quarterly Index, Science Citation Index, Small

Student Subscriptions/Abonnements des étudiants

The editors and staff of The Canadian Veterinary Journal are pleased to have as readers student
veterinarians at Canadian veterinary colleges! The production and distribution of student
subscriptions is made possible through the generous sponsorship of
Scotiabank
Banque Scotia

Les rédacteurs et le personnel de La Revue vétérinaire canadienne sont heureux de compter les étudiants
e en médecine vétérinaire des collèges vétérinaires au Canada au nombre de leurs lecteurs. La production et
la distribution des abonnements des étudiants ont été rendues possible grâce au généreux soutien de
Banque Scotia
Scotiabank

Your CVMA membership means MORE...

**INFLUENCE**
ADVANCING YOUR ISSUES, YOUR CONCERNS AND YOUR PROFESSIONAL INTERESTS.
The CVMA looks at policy matters in terms of their potential impact on the profession. Our role as an advocate for animal welfare and veterinary medicine at the national level influences your access to critical drugs, contributes to the development of responsible animal welfare policies, mitigates decisions that could adversely affect your delivery of veterinary care, and fosters a wider appreciation of the role of veterinarians in the One Health concept.

As a CVMA member you benefit from...
- Engagement with Government and key stakeholders to influence policy decisions
- International relations to provide the Canadian veterinary perspective
- Media and public relations to provide balanced and trustworthy information and to promote veterinary professionals
- Position statements on animal welfare and national veterinary issues
- Codes of practice for Canadian kennel and cattery operations, and for the care and handling of farm animals
- Member consultations and online discussions on key veterinary issues

**KNOWLEDGE**
KEEPING YOU CURRENT ON VETERINARY SCIENCE AND PRACTICE, RESEARCH, INNOVATION AND TRENDS TO ENHANCE YOUR CAREER DEVELOPMENT AND LIFELONG LEARNING.
The CVMA provides you with the latest news, information, and clinical and non-clinical continuing professional development. Our role as a knowledge provider enables you to broaden your knowledge and skills and maintain your competence to the highest professional standards.

As a CVMA member you benefit from...
- The Canadian Veterinary Journal
- Canadian Journal of Veterinary Research
- Clinician’s Brief™ (free global digital edition)
- CVMA national convention
- CVMA Veterinary Summit
- CVMA Emerging Leaders Program
- CVMA Canadian Veterinary Reserve
- Member e-newsletter ‘Online from 339’
- CVMA online continuing education portal
- VetFolio® online educational resources (subscription discount)

**RESOURCES**
SUPPORTING OUR MEMBERS THROUGH EVERY STAGE OF THEIR CAREER WITH ACCESS TO A RANGE OF EXCLUSIVE PRACTICE TOOLS AND RESOURCES.
The CVMA provides members access to professional resources, veterinary economic reports, practice management solutions, client education resources, and exclusive online content to support you and your practice team in the effective delivery of veterinary services.

As a CVMA member you benefit from...
- MyVetStore.ca™ - CVMA’s web store solution for clinics
- Practice owner’s economic survey
- Individual practice diagnostic and valuation report
- Provincial suggested fee guide
- Associate compensation and benefits report
- Compensation report for non-DVM staff
- Compensation report for DVMs outside private practice
- Practice management articles and resources
- CVMA group insurance program
- CVMA mentoring program
- VetLaw Online™ legal advice column
- CVMA Green Veterinary Practice and self-audit tool
- Antimicrobial SmartVet mobile app
- Veterinarian health and wellness resources
- Early career DVM web resource hub
- Guidelines for the successful employment of new veterinary graduates
- Sedative, anaesthetic and pain management protocols posters
- Guidelines for the legitimate use of compounded drugs in veterinary practice
- Antimicrobial prudent use guidelines for beef cattle, dairy cattle, poultry and swine
- Therapeutic decision cascade poster
- Animal abuse resources for practitioners faced with this issue
- Preventive healthcare, nutritional assessment and client education tools and resources
- Animal health week annual public awareness campaign

**SAVINGS**
PUTTING MONEY IN YOUR POCKET AND DELIVERING MORE VALUE TO INCREASE YOUR PROFITABILITY.
The CVMA uses its national purchase power and strategic partnerships so that you can benefit from discount rates and money-saving services.

As a CVMA member you benefit from...
- Hotel discounts worldwide
- National and Enterprise Rent-a-Car discounts
- The Personal Insurance home and auto group savings
- Scotiabank® business banking and lending solutions
- The CVJ classified ads discount
- Staples Advantage™ business products
- Adtel® telephone hold service and digital signage
- Petro-Canada SuperPass™ fuel/diesel/car wash discount
- WSAVA World Congress (registration discount)
- WVA Congress (registration discount)
- Plumb’s Veterinary Drugs™ (subscription discount)

Visit canadianveterinarians.net or contact the CVMA at 1-800-567-2962 for information about the many benefits and privileges of membership.
Leba III is on your side, tartar will tap out.

Cleans Teeth with the Ease of a Spray

THE LEBA III DIFFERENCE

LEBA III works with the saliva. No brushing required. Spray in the mouth, not on the teeth. Used daily, it stimulates good flora and combats bad bacteria keeping the teeth clean and the gums healthy.

Pets ingest dental products, they cannot rinse. They can become subject to the side effects of the chemical components. LEBA III contains no Grapefruit Seed Extract, no chlorides or chemical agents.

Used by veterinarians since 1994.

100% response in Double Blind Trials. See the results on www.lebalab.com

BLUEWATER BRIDGE, ON, CA & MI, USA
Photo by David J Sullivan

To Order, Call 1 (866) 532-2522
Questions? Call 1 (519) 542-4236 | www.lebalab.com | tellus@lebalab.com
Letter to the Editor  Courrier des lecteurs

Emergency care after-hours — Comments on an ethicist's remarks

Dear editor,

My comment is regarding “An ethicist’s commentary on a dog requiring emergency care after-hours” (Can Vet J 2016;57: 683–685). Bernard E. Rollin, PhD, allegedly inspired by “some of the wisdom that may be found in the writings of Plato,” inputs that “For the veterinarian in this case to start talking money even before looking at the animal is at the very least sleazy and borders on obscene.”

Many of us will disagree with this judgment, since I believe it is only fair, not to say essential, to provide callers with at least some idea of the potential initial costs for seeing the animal. This is a case-by-case situation where I trust most veterinarians to be able to discuss the potential financial impact of medical care while keeping in mind their primary obligation to the patients. However this is not my main concern with the ethicist’s commentary.

Further down, in case of a client’s inability to pay for the animal’s care, Dr. Rollin suggests that “As a worst-case, the veterinarian can suggest that the owner surrender the animal, and then he or she can treat the animal and adopt it out… (he) can then provide the newspapers or other media with a touching human interest story that will buy him far more favorable publicity than he could acquire in any other way.”

And then, the original owner hears about his surrendered animal, treated at no charge by the veterinarian in exchange of free publicity, now owned by someone else. Let’s revisit what is “sleazy and obscene,” as defined and supported by this ethicist’s commentary.

I am appalled by the conclusion that evokes wisdom and recognition of opportunities. In my interpretation of Plato, tactfully discussing the cost of veterinary care is only transparent and professional. Diverting an animal from his legitimate owner in exchange of free publicity would be a major and obscene fault.

Bernard Vallée, DMV
455, rue Lacroix
Nicolet (Québec)
J3T 1K4
e-mail : bernard.vallee@sogetel.net

Constructive and professional comments made in the spirit of intellectual debate are welcomed by the Editor. Writers are expected to be respectful of others and to ensure that letters are considerate and courteous. The Editor reserves the right to remove comments deemed to be inflammatory or disrespectful.

Animal Health Information Sources

Below is a list of several links to Canadian sources of information on animal health and disease. Our goal is to provide current information while not duplicating existing efforts. We hope that this contact information will be of assistance to veterinarians across the country.

1. Canadian Animal Health Coalition (CAHC/CCSA) newsletter
http://service.meltwaternews.com/mnews-ws/resources/pastnewsletter/latestHtml?n=MTUwNTUz&f=MTUyNyQz

2. Alberta Animal Health Source (ABVMA) site:
http://www.albertaanimalhealthsource.ca/

3. Animal Health Laboratory — University of Guelph
http://www.guelphlabservices.com/ahl/

http://www2.gov.bc.ca/gov/content/industry/agriculture-seafood/animals-and-crops/animal-health/animal-health-centre/newsletter

5. Prairie Diagnostic Services Inc. (Animal Health Perspectives newsletter)
http://pdsc.ca/


7. University of PEI — Diagnostic Services (Newsletter)
http://www.upei.ca/avc/diagnostic-services/newsletters
April 21 – 23, 2016
Halifax Marriott Harbourfront Hotel
Halifax, NS
www.apvc.ca

Veterinarians

Dr. Etienne Côté
- Update on HCM Pulmonary Thromboembolisms
- Mgmt. of Incidentally Detected Heart Murmurs
- Coughing, a New Approach
- Cardiac Drugs: Overview and Apps
- Cardiorenal Syndrome: Seeking the Perfect Balance
- Treating CHF in 2017

Dr. Judy Rochette
- Cats are Not Small Dogs... But it Sure Feels Like it Sometimes
- Oral Pathology: Is it Normal? Do We Treat?
- Should this Tooth be Extracted?
- Complicated Extractions and Complications from Extractions
- It’s Not Always Black and White: Radiographic Interpretation
- Oral Masses. Benign or Otherwise
- Dental Emergencies: What We See and How to Treat

Dr. Lynne Seibert
- Simple Steps for Managing Behaviour Cases
- Psychopharmacology. When Do Drugs Help?
- Fears and Phobias. What’s to be Afraid of?
- Canine Aggression.
- Feline Social Behaviour and Inter Cat Aggression
- The Scoop! Managing Feline House Soiling

Dr. Julie Churchill
- Setting up for Success - First Year of Life
- Mobility 2.0: Feeding Recommendations for OA
- The Golden Years: New Tricks for Feeding Old Dogs
- Raw Diets: Doing IT Right
- Cats with Kidney Disease: Can Nutrition Help?
- Feeding Hospitalized Patients: Satisfying NO Appetite

Dr. Gary Conboy
- Lungworm: If You’re Not Seeing It, You’re Missing It
- Lyme Disease and Ixodes Scapularis in the Atlantic Provinces

Dr. Andre Shih
- Anaesthesia for Critical Patients, Keeping Them Safe
- How to Treat Refractory Hypotension, Keeping it Up
- Newest CPR Guidelines
- Perioperative Antibiotic Therapy. Picking the Best

Dry Lab (Veterinarians):

Dr. Etienne Côté
- What’s Wrong with that Rhythm? ECG Based Case Studies

Dry Lab (Animal Health Technicians):

Dr. Andre Shih
- Anaesthetic Monitoring. Staying in Tune

Dr. Etienne Côté
- ECG, What Does the Technician See?
- Top Questions Technicians have Asked

David Liss
- Sweet & Sour: The Diabetic Patient
- All About Kidney Disease
- Case Detectives: Abdominal X-rays
- Case Detectives: Thoracic X-rays
- Critical Care Nursing 101
- Shock, Triage and Hands-on Patient Care
- It’s a Bloat!
- Basic Cheap ER Blood Tests
- Red, White and Blue, Transfusion
- Punched in the Gut. Acute Pancreatitis
- Endocrine Case-tastrophies!
- The Dreaded Blocked Cat

Join more than 850 other delegates, exhibiting companies and a world class list of speakers in an environment of true maritime hospitality
**A COMPLETE PACKAGE FOR THE ENTIRE VETERINARY TEAM**

**Dr. Lynne Seibert**
- Behaviour-friendly Practice Strategies
- Humane Handling During Veterinary Procedures
- Preventing Behaviour Problems in Dogs and Cats
- Improving Compliance with Behaviour Modification Plans

**Dr. Judy Rochette**
- Dental Radiograph Techniques and Equipment Maintenance Tips and Tricks
- Techs Guide to Oral Pathology

**Wet Lab (Techs):**
**Dr. Gary Conboy**
- Species in the Feces

**Support Staff/Mgr.**
**Dr. Peter Weinstein**
- Missions, Values, Standards of Care and Creating the Client Experience
- Operations and Working ON the Practice
- Teamwork, It Makes the Dream Work

**Business Management**
**Eric Garcia**
- New Tools and Tips to Manage Your Online Reputation
- Developing the Ultimate Facebook Marketing Strategy
- Optimizing Your Digital Presence Real Case Studies
- 25 Electronic Tools/Apps that will Rock Your Veterinary Practice

**Dr. Peter Weinstein**
- Working ON, Not Just IN Your Practice.
- Vision, Mission and Values
- Client Experience. The People Org. Chart
- Systems, Operations, Processes
- KPIs, Planning and Wrap-up

<table>
<thead>
<tr>
<th>Role</th>
<th>Name</th>
<th>Topics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mgr./Vet</td>
<td>Tim Banker</td>
<td>New Perspective on Stress</td>
</tr>
<tr>
<td>Support Staff</td>
<td>Dr. Lynne Seibert</td>
<td>Behaviour-friendly Practice Strategies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Humane Handling During Veterinary Procedures</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Preventing Behaviour Problems in Dogs and Cats</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Improving Compliance with Behaviour Modification Plans</td>
</tr>
<tr>
<td></td>
<td>Dr. Julie Churchill</td>
<td>Deciphering Fact from Fiction - Helping Clients Select Pet Foods</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Communicating with Clients - Answering Crazy Questions About Food</td>
</tr>
<tr>
<td>Full Team</td>
<td>Dr. Julie Churchill</td>
<td>Nutritional Team Approach - It Takes a Village</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Top Five Tips for Good Nutrition</td>
</tr>
</tbody>
</table>

**Fees**

<table>
<thead>
<tr>
<th>Role</th>
<th>Full</th>
<th>Partial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veterinarians</td>
<td>$425</td>
<td>$225</td>
</tr>
<tr>
<td>Technicians &amp; Vet’s Assistants</td>
<td>$225</td>
<td></td>
</tr>
<tr>
<td>Managers</td>
<td>$325</td>
<td></td>
</tr>
<tr>
<td>Support Staff</td>
<td>$175</td>
<td></td>
</tr>
</tbody>
</table>

**For further information contact:**
Dr. Courtney Sherlock, *Chair*
APVC Committee on Arrangements
PO Box 310
Eastern Passage, NS, B3G 1M6
902-483-2034
Email: cgsherlock@hotmail.com
WVC is dedicated to providing quality year-round continuing education to the veterinary community through an array of learning styles and environments.

To register and see the full year’s calendar of events, visit wvc.org

Knowledge You Can Use Now
President’s Message
Le mot du président

Bill C-246 dies on House floor
Le projet de loi C-246 est défait à la Chambre des communes

Bill C-246 (The Modernization Animal Protection Act) passed first reading in the spring of 2016. This private member’s Bill was brought forward by liberal Member of Parliament, Mr. Nathaniel Erskine-Smith (Beaches-East York). Its aim was to improve and update specific sections pertaining to animal protection found in the Criminal Code, Fisheries Act, Textile Labelling Act, Wild Animal and Plant Protection and Regulation of International and Interprovincial Trade Act, and the Canada Consumer Product Safety Act.

Bill C-246 would have closed loopholes; it would have put a ban on importing cat and dog fur and shark fins. It called for tougher rules on puppy mills and animal fighting. Also, with the Supreme Court decision earlier this year that narrowly defines bestiality as penetration involving a person and animal in the Criminal Code, Mr. Erskine-Smith’s Bill was looking to expand that definition to include any sort of sexual activity between people and animals.

On October 5, 2016 the Parliament of Canada voted not to send the Bill to the Committee of Justice and Human Rights for further consideration. The vote was 198 Nays to 84 Yeas. If passed the Committee would have studied the Bill further but with the no vote the Bill is dead.

The CVMA strongly supported this Bill. The government defeated the Bill because they thought a better way to address the issue was to review the Acts when an overall review of justice legislation occurs. This is something the government is committed to doing.

This ends for now Mr. Erskine-Smith’s attempt to update federal legislation to increase animal protection. Progress, however, has been made. It is now part of the liberal government mandate to make changes to the Criminal Code when the review of justice legislation occurs. Between 1999 and 2005, 4 similar Criminal Code amendments introduced to the House died when Parliament was dissolved.

For almost 20 years, the CVMA has been involved in efforts to modernize and strengthen protection for animals under the

Use of this article is limited to a single copy for personal study. Anyone interested in obtaining reprints should contact the CVMA office (hbroughton@cvma-acmv.org) for additional copies or permission to use this material elsewhere.

L’usage du présent article se limite à un seul exemplaire pour étude personnelle. Les personnes intéressées à se procurer des réimpressions devraient communiquer avec le bureau de l’ACMV (hbroughton@cvma-acmv.org) pour obtenir des exemplaires additionnels ou la permission d’utiliser cet article ailleurs.
Veterinarians are often the first professionals to examine an abused animal. Effective legislation is an important tool to help those who deal with abused animals, including humane societies and law enforcement agencies. Furthermore, there is overwhelming evidence of a direct link between animal abuse and violence toward people, especially family members. Legislation that deals more effectively with cruelty to animals may help play a role in breaking the cycles of violence that occur in some communities.

The CVMA feels that animal cruelty laws should use scientific language and be a stand-alone section of the Criminal Code, rather than simply a type of property offence. The laws should recognize that animals are more than just property.

Animal agriculture, hunting, and fishing exemptions will likely need to be explored with any new legislation. In 2004 under Justice Minister Irwin Cotler there was consensus with 30 animal-based sector groups supporting amendments to the Criminal Code. The concerns of agriculture, hunting, and fishing groups were also addressed in Bill C-246. Erskine-Smith was looking to get back to the consensus the justice minister was able to reach in 2004. Erskine-Smith spoke to 3 previous justice ministers and went through the debates of the older Bills. He also reviewed the concerns expressed in submissions by animal-use groups at the time, and incorporated language from both in Bill C-246.

This is a bad news, good news story. Liberals now have a mandate before them much earlier than they would have. Mr. Erskine-Smith stated after the Bill was defeated, “It wasn't a victory for Bill C-246, but it is a victory for animals.” The CVMA, along with allied organizations, will continue to lobby for changes in the Criminal Code. A meeting with the federal justice minister's office is already being planned. We really need to get these archaic animal cruelty laws updated while still protecting animal use.

Troy Bourque

Erratum

Can Vet J 2016;57:1062–1066

The second author's name was submitted to us in the original manuscript with an incorrect middle initial. A request has been made to change the initial for Jennifer Morrissey from an “F” to a “K.” This author's name should now read Jennifer K. Morrissey.
Ethical question of the month — January 2017

Welfare audits are becoming a common component of quality assurance programs. In addition, welfare audits are demanded by processors and retailers when videos are released that imply animal welfare abuse on farms supplying products to these processors or retailers. Should welfare audits be performed by the herds’ own veterinarians? If a third party audit is specifically requested by a processor or retailer, does a veterinarian need to be licensed in the province where they perform the third party welfare audit? Are there advantages to having all welfare audits performed by non-veterinarians?

Les vérifications de bien-être deviennent un élément courant des programmes d’assurance de la qualité. De plus, des vérifications de bien-être sont exigées par les transformateurs et les détaillants lorsque des vidéos publiées laissent sous-entendre qu’il s’est produit de la violence envers les animaux dans des fermes fournissant des produits à ces transformateurs ou à ces détaillants. Ces vérifications devraient-elles être réalisées par les vétérinaires affectés aux troupeaux? Si une vérification par un tiers est spécifiquement demandée par un transformateur ou un détaillant, un vétérinaire devrait-il détenir un permis dans la province où il effectue la vérification de bien-être de tierce partie? Enfin, y aurait-il des avantages à la réalisation de ces vérifications de bien-être par des non-vétérinaires?

Comments/Commentaires :

Name/Nom :

Address/Adresse :

Responses to the case presented are welcome. Please limit your reply to approximately 50 words and forward along with your name and address to: Ethical Choices, c/o Dr. Tim Blackwell, 6486 E. Garafraxa, Townline, Belwood, Ontario N0B 1J0; telephone: (519) 846-3413; fax: (519) 846-8178; e-mail: tim.e.blackwell@gmail.com.

Suggested ethical questions of the month are also welcome! All ethical questions or scenarios in the ethics column are based on actual events, which are changed, including names, locations, species, etc., to protect the confidentiality of the parties involved.

Les réponses au cas présenté sont les bienvenues. Veuillez limiter votre réponse à environ 50 mots et nous la faire parvenir par la poste avec vos nom et adresse à l’adresse suivante : Choix déontologiques, a/s du Dr Tim Blackwell, 6486, E. Garafraxa, Townline, Belwood (Ontario) N0B 1J0; téléphone : (519) 846-3413; télécopieur : (519) 846-8178; courriel : tim.e.blackwell@gmail.com.

Les propositions de questions déontologiques sont toujours bienvenues! Toutes les questions et situations présentées dans cette chronique s’inspirent d’événements réels dont nous modifions certains éléments, comme les noms, les endroits ou les espèces, pour protéger l’anonymat des personnes en cause.
Ethical question of the month — October 2016

A couple living on a small rural property in a non-agricultural area purchase 2 Holstein bull calves at auction to teach their children basic principles of animal husbandry and food production. Two weeks after the calves arrive, the neighbor’s dog gets into the pen and attacks one of the calves. The owners hear the commotion and chase the dog away. One calf is bleeding badly around the face, an ear is torn, there are a couple of puncture wounds on a hind leg, and the calf is trembling constantly. The owners are very upset, as are their children. They call one veterinary clinic after another only to be told on each call that the veterinarian does not do food animal work. When the owners locate a food animal veterinarian 100 km away, they are told that that veterinarian is not accepting new clients. Are such responses in accordance with a veterinarian’s oath to prevent animal suffering?

Question de déontologie du mois — Octobre 2016

Un couple habitant une petite propriété rurale située dans un secteur non agricole fait l’achat de deux jeunes taureaux Holstein dans un encan afin d’enseigner à leurs enfants les principes de base de l’élevage animal et de la production alimentaire. Deux semaines après l’arrivée des veaux mâles, le chien du voisin pénètre dans l’enclos et attaque l’un des veaux. Les propriétaires entendent le tapage et chassent le chien. Un veau saigne abondamment autour de la face, une oreille est arrachée, il y a deux blessures punctiformes sur une jambe arrière et le veau tremble constamment. Les propriétaires et leurs enfants sont bouleversés. Ils appellent une clinique vétérinaire après l’autre seulement pour se faire dire que le vétérinaire ne traite pas les animaux destinés à l’alimentation. Lorsque les propriétaires trouvent finalement un vétérinaire traitant les animaux destinés à l’alimentation à une distance de 100 km, on leur dit qu’il n’accepte pas de nouveaux clients. De telles réponses sont-elles conformes au serment vétérinaire de prévenir la souffrance des animaux?

An ethicist’s commentary on a couple unable to find a veterinarian to treat injured bull calves

This case brings to mind an unforgettable story related to me by one of my most beloved friends — an internationally known psychiatrist, medical school faculty member, and Dean at a prominent Ivy League medical school. He told me of taking a drive on a Sunday on a very busy expressway alongside the Atlantic Ocean in New York City. Suddenly, he saw a dog hit by a car on the highway; it had managed to crawl onto the grassy central median. No one stopped to help. My friend drove onto the median, and began to comfort the animal. He informed me that he was totally frustrated by his lack of knowledge of how to manage this kind of trauma in an animal. He just sat there, weeping, and cuddling the dog until the animal died. He could not tell the story without re-experiencing the emotion that profoundly affected him. Years later, he still felt deep regret at his inability to treat the animal.

In the situation presented in this case, the animals have been savaged and torn, but there is no indication of any profound diagnosis being required. In terms of being able to anesthetize the animal, clean a wound, administer prophylactic antibiotics, and sew up the lacerations if necessary, I can see little difference between a farm animal veterinarian and one who specializes in companion animals. Therefore, there is no reason to believe that any of the veterinarians contacted would have been unable to provide the wounded, terrified animals with credible emergency care. The fact that none agreed to do so is a major discredit to all of those veterinarians who refused to even look at the animals. I frankly cannot imagine that they were able to do so without suffering any pangs of conscience.

In addition, it is almost impossible to believe that this story will not get around the community, and put the local veterinarians in an extremely negative light. Such a cavalier, callous, unfeeling, and ultimately unthinking attitude is impossible to ignore. Furthermore, it makes a mockery of the Veterinarian’s Oath. Some of the older veterinarians I have been privileged to know would not even dream of ignoring or turning their back on any animal in need of help, even during snowstorms or torrential rains. Indeed, I know numerous rural veterinarians who would never turn their back on any human in need of medical attention, particularly when the nearest physician may be six hours or more away.

I am well aware that the desire to help may be dampened and suppressed by fear of possible legal ramifications in which the veterinarian could possibly become embroiled. That is, unfortunately, the kind of society in which we live. As far as I am concerned, the veterinarian needs to view that possibility as an occupational hazard, not as a reason to withhold care! But that should no more deter doing the right thing than a raging fire should deter firefighters or physicians from ministering to victims of that fire. In both sets of cases, the people helping are bound by a sacred trust, and are thus obliged to do the right thing.

Bernard E. Rollin, PhD
Quiz Corner
Test éclair

1. A 6-year-old adult dog develops hyperglycemia, glucosuria, and ketonuria during treatment with immunosuppressive corticosteroid therapy for pemphigus foliaceus. Which of the following is the most appropriate therapeutic plan for management of this complication?
   A. Discontinue corticosteroid therapy.
   B. Discontinue corticosteroid therapy and begin insulin administration.
   C. Start a high-protein, low-carbohydrate diet.
   D. Start a high-carbohydrate, low-protein diet.
   E. This is a transient condition and therapy is not required.

2. A Jack Russell terrier presents with an acutely painful red eye, corneal edema, and IOP of 42 mmHg. Due to the signalment listed, which of the following conditions should be ruled out?
   A. Anterior lens luxation
   B. Hypermature cataract
   C. Retinal detachment
   D. Conjunctivitis

3. A 21-year-old pony is being evaluated for delayed shedding during the spring. Evaluation reveals a thick, shaggy, long haircoat that is especially prominent on the legs. The mane and tail appear normal. The pony also has a sway-backed and pot-bellied appearance. Which of the following is the most likely diagnosis?
   A. Functional lesion in the zona glomerulosa
   B. Functional lesion in the pars intermedia
   C. Functional lesion in the pars distalis
   D. Functional lesion in the pars nervosa
   E. Functional lesion in the zona reticularis

1. Un chien adulte âgé de 6 ans présente de l'hyperglycémie, de la glucosurie et de l'acétonémie durant le traitement aux corticostéroïdes immunosupresseurs pour contrer le pemphigus foliacé. Laquelle des thérapies suivantes est la plus appropriée pour prendre cette affection en charge?
   A. Arrêter le traitement de corticostéroïdes.
   B. Arrêter le traitement de corticostéroïdes et commencer l'administration d'insuline.
   C. Commencer une diète à forte teneur en protéines et à faible teneur en glucides.
   D. Commencer une diète à forte teneur en glucides et à faible teneur en protéines.
   E. C'est un problème passager et un traitement n'est pas nécessaire.

2. Un chien Terrier Jack Russell présente un œil rouge avec douleur aiguë, de l'œdème cornéen et une pression intraoculaire de 42 mmHg. À cause des signes manifestés, laquelle des conditions suivantes devrait être écartée?
   A. luxation du cristallin;
   B. cataracte hypermûre;
   C. décollement de la rétine;
   D. conjonctivite.

3. Un poney âgé de 21 ans est examiné parce qu'il y a un retard de la mue au printemps. L'examen révèle un pelage long, épais, ébouriffé, particulièrement visible sur les membres. La crinière et la queue sont normales. Le poney présente un dos creux et un ventre penduleux. Lequel des diagnostics suivants est le plus probable?
   A. lésion fonctionnelle de la zone glomérulaire;
   B. lésion fonctionnelle de la partie intermédiaire;
   C. lésion fonctionnelle de la partie distale;
   D. lésion fonctionnelle de la partie nerveuse;
   E. lésion fonctionnelle de la zone réticulaire.
4. A 6-year-old adult Simmental cross cow develops chronic diarrhea that does NOT respond to therapy. Which of the following organisms is the most likely cause?

A. Mannheimia haemolytica
B. Mycobacterium avium subsp. paratuberculosis
C. Haemophilus somnus
D. Bovine rotavirus
E. Mycoplasma bovis

5. An owner is trying to switch her/his budgerigar to a pellet diet. Which of the following is an appropriate recommendation to make?

A. Withhold all food but the pellets; when the bird gets hungry, it will eat the pellets.
B. Sprinkle the pellets on top of a small mirror.
C. Mix the pellets with the seeds in an increasing ratio until the bird is eating no seeds.
D. A and B
E. B and C

(See p. 94 for answers.)

Questions and answers were derived from Review Questions and Answers for Veterinary Boards 2nd ed., a 5-volume series including Basic Sciences, Clinical Sciences, Small Animal Medicine and Surgery, Large Animal Medicine and Surgery, and Ancillary Topics, by kind permission of the publisher, Mosby-Year Book, Inc., St. Louis, Missouri.
An Alliance That Benefits YOU

As you know, the CVMA is a proud associate member of Partners for Healthy Pets (PHP) and we are pleased to announce a collaborative program between PHP, Veterinary Medical Association Executives (VMAE) and our Association. We believe this initiative will have a significant impact on the health of your patients and your practice.

This collaborative program focuses on the importance of forward booking, which simply means scheduling all patients’ next appointments before they leave your practice, regardless of the reason for their current visit. This includes medical progress exams and preventive healthcare exams. Forward booking ensures your patients receive the highest quality of care at the right time.

You have probably been hearing about and maybe even considering implementing forward booking in your practice, but are not quite sure how to get started.

We can help you!

To get started, visit the forward booking section on the Partners for Healthy Pets website (www.partnersforhealthypets.org/forward_booking.aspx). Download the document titled, “The Key to Forward Booking Appointments: Unlock the Potential of a Best Practice for Your Practice.” This gives you a simple, step-by-step approach to how to use the handful of tools available to you to provide your practice team with the skills necessary to be successful. Ready. Set. Forward Book!

By using these tools, you will be able to easily implement forward booking in your practice. The result? Healthier patients and a healthier practice!

Un alliance à VOTRE avantage

Comme vous le savez, l’ACMV est fière d’être membre associé de Partners for Healthy Pets (PHP) et nous sommes heureux d’annoncer un programme de collaboration entre PHP, les Veterinary Medical Association Executives (VMAE) et notre association. Nous croyons que cette initiative aura un impact important sur la santé de vos patients et votre pratique.

Ce programme de collaboration porte sur l’importance de la prise de rendez-vous à l’avance, ce qui signifie simplement la prise de rendez-vous pour tous les patients avant qu’ils ne quittent votre pratique, sans égard à la raison de leur visite. Cela comprend des examens pour les progrès médicaux et des examens préventifs. La prise de rendez-vous à l’avance veille à garantir que vos patients recevront des soins de la plus haute qualité au bon moment.

Vous avez probablement entendu parler de la prise de rendez-vous à l’avance et vous avez peut-être même envisagé sa mise en œuvre dans votre pratique, mais vous ne savez pas tout à fait comment vous y prendre pour mettre cette pratique en place.

Nous pouvons vous aider!


En utilisant ces outils, vous pourrez facilement mettre en œuvre la prise de rendez-vous à l’avance dans votre pratique. Le résultat? Des patients et une pratique en meilleure santé!
CVMA Welcomes Two New Members to Council

Dr. Christiane Armstrong will join the Canadian Veterinary Medical Association (CVMA) Council on January 1, 2017 as representative of CVMA-SBCV Chapter members in British Columbia. The CVMA also welcomes Dr. Karen Machin to Council as the WCVM/UCVM/OVC rep.

Dr. Armstrong and Dr. Machin replace Drs. Rob Ashburner and Michele Guerin, respectively, whose terms end on December 31, 2016. We thank Dr. Ashburner and Dr. Guerin for their dedication and commitment to the CVMA.

Dr. Christiane Armstrong

Dr. Armstrong grew up in Burnaby, British Columbia, and attended Simon Fraser University before entering the Western College of Veterinary Medicine (WCVM), University of Saskatchewan. Upon graduating with distinction in 1987, she returned to her home province where she joined the Scottsdale Veterinary Hospital, an American Animal Hospital Association accredited small animal practice in Surrey. Dr. Armstrong became one of 3 practice owners in 1989 and became an associate at Scottsdale in 2016, after 29 years of practice.

In 2009, professional interests led Dr. Armstrong to become a councillor at the British Columbia Veterinary Medical Association, which transitioned into the College of Veterinarians of British Columbia (CVBC). She became vice president and then served as president of the CVBC.

Dr. Armstrong joined the Society of British Columbia Veterinarians Chapter Board as a director-at-large and was appointed CVMA liaison in 2016.

A long-time interest in downhill skiing led to a secondary career as a part-time ski instructor at Whistler/Blackcomb. Dr. Armstrong obtained a Canadian Ski Instructor Association Level 3 certification and Course Conductor 1, and continues to teach adult advanced level skiing at Blackcomb.

Dr. Karen Machin

Dr. Karen Machin is originally from Toronto, Ontario, and graduated from the Ontario Veterinary College, University of Guelph in 1993. She then went on to do an exotics, zoo, and wildlife residency combined MSc, and a PhD at the WCVM. Dr. Machin is currently an associate professor at the WCVM, teaching physiology, pain and analgesia, non-mammalian pain

La Dʳ Christiane Armstrong se joindra au Conseil de l’Association canadienne des médecins vétérinaires (ACMV) le 1ᵉʳ janvier 2017 à titre de représentante des membres de la Section locale de l’ACMV-SBCV en Colombie-Britannique. L’ACMV accueillera aussi la Dʳ Karen Machin au Conseil à titre de représentante des facultés WCVM/UCVM/OVC.

La Dʳ Armstrong et la Dʳ Machin remplacement les Dʳ Rob Ashburner et Michele Guerin, respectivement, dont les mandats ont pris fin le 31 décembre 2016. Nous remercions le Dr Ashburner et la Dʳ Guerin de leur dévouement et de leur engagement envers l’ACMV.

Dʳ Christiane Armstrong

La Dʳ Armstrong a grandi à Burnaby, en Colombie-Britannique, et a fréquenté l’Université Simon Fraser avant d’entrer au Western College of Veterinary Medicine (WCVM) de l’Université de la Saskatchewan. À l’obtention de son diplôme avec distinction en 1987, elle est retournée dans sa province natale où elle s’est joints à la clinique Scottsdale Veterinary Hospital, une pratique pour petits animaux agrée par l’American Animal Hospital Association située à Surrey. La Dʳ Armstrong est devenue l’une de trois propriétaires de pratique en 1989, puis associée à Scottsdale en 2016, après 29 années de pratique.

En 2009, ses intérêts professionnels ont poussé la Dʳ Armstrong à devenir conseillère de la British Columbia Veterinary Medical Association, qui est ultérieurement devenue le College of Veterinarians of British Columbia (CVBC). Elle est ensuite devenue vice-présidente et a occupé le poste de président du CVBC.

La Dʳ Armstrong a adhéré à la Section locale de la Society of British Columbia Veterinarians en tant que directrice par mandat spécial et a été nommée à titre d’agente de liaison auprès de l’ACMV en 2016.

Un intérêt de longue date pour le ski alpin a donné lieu à une carrière secondaire en tant qu’instructeur de ski à temps partiel à Whistler/Blackcomb. La Dʳ Armstrong a obtenu une certification de niveau 3 de l’Alliance des moniteurs de ski du Canada et de directeur de cours de niveau 1 et elle continue d’enseigner le ski de niveau avancé aux adultes à Blackcomb.

Dʳ Karen Machin

La Dʳ Karen Machin est originaire de Toronto, en Ontario, et elle a obtenu son diplôme de l’Ontario Veterinary College de l’Université de Guelph en 1993. Elle a ensuite suivi une maîtrise en sciences, combinée avec une résidence en médecine des animaux exotiques, de zoo et de la faune, et un doctorat au WCVM. La Dʳ Machin est
and analgesia, and communications, with research interests in pain and analgesia and stress in non-mammalian species and wildlife.

Dr. Machin serves on the University Animal Review Ethics Board and Animal Care Committee and is an advisory veterinarian for the Western and Northern Animal Care Committee for Environment Canada. She currently serves as a member of the Saskatchewan Veterinary Medical Association’s Animal Welfare Committee.

In her spare time, she is president of New Hope Dog Rescue in Saskatoon, and Diamonds in the Ruff Flyball Club, and the registrar for her children’s swim club. Dr. Machin’s husband Bob, a research scientist with Environment Canada, and sons, Max and Kade, share their home with 7 dogs, 3 ponies, and a “herd” of chickens. Dr. Machin is passionate about dogs, animal training and flyball, as well as quilting.

---

**Dr. Faizal Careem Joins the Journals Team**

The CVMA welcomes Dr. Faizal Careem to the Editorial Committee as an associate editor for the *Canadian Journal of Veterinary Research*. Dr. Careem is an associate professor (Virology) attached to the University of Calgary Faculty of Veterinary Medicine, Alberta. In addition to teaching veterinary virology for DVM students, he conducts research to understand innate host responses generated against poultry respiratory viral infections.

Dr. Careem completed his veterinary degree, BVSc (Hons) at the Peradeniya University, Sri Lanka in 1991 and his MVM degree from the University of Glasgow Veterinary School, United Kingdom in 1995. He obtained his PhD degree, in the field of host-viral interactions, at the Ontario Veterinary College, University of Guelph in 2008. Following the PhD degree, he was awarded a Canadian Institutes of Health Research Fellowship to conduct post-doctoral research on innate immune responses generated against mucosal viral infections at the Center for Gene Therapeutics of the McMaster University, Hamilton. Dr. Careem is a diplomate of the American College of Poultry Veterinarians and American College of Veterinary Microbiologists.

---

**Le D’ Faizal Careem se joint à l’équipe des revues**

L’ACVM accueille le D’ Faizal Careem au Comité de la rédaction à titre de rédacteur associé de la *Revue canadienne de recherche vétérinaire*. Le D’ Careem est professeur agrégé (virologie) à la Faculté de médecine vétérinaire de l’Université de Calgary, en Alberta. En plus d’enseigner la virologie vétérinaire aux étudiants du programme de D.M.V., il effectue de la recherche pour comprendre les réponses innées des hôtes qui se produisent pour lutter contre les infections respiratoires virales.

2017 CVMA Convention
Charlottetown, July 13–16
Unleash Your Potential!

The CVMA Convention returns to Charlottetown, Prince Edward Island after a 20-year hiatus! The 2017 CVMA Convention will be held July 13–16 at the Delta Prince Edward Hotel and PEI Convention Centre. Since the last CVMA Convention in 1996, Charlottetown’s skyline has been transformed with the opening of the Convention Centre in 2013. The Centre’s modern, bright space accommodates conventions with 700 to 1000 people and allows them to meet under one roof and that’s one of the reasons the CVMA chose this destination for the 2017 Convention.

The CVMA Convention is organized in collaboration with the Registered Veterinary Technicians and Technologists of Canada (RVTTC) and the Atlantic Veterinary College (AVC). Charlottetown is home to the AVC, the only institution in Atlantic Canada educating doctors of veterinary medicine. More than 1400 graduates now work in private practice, academia, research, government, and industry worldwide. During the Convention, the AVC will host the diverse wet labs including...
canine and feline dentistry, equine dentistry, small animal surgery, hematology, and dermatology. The AVC is also inviting all alumni to attend an all-years reunion on Friday, July 14.

Charlottetown has preserved the historic significance of its past as the birthplace of Confederation while attracting top-notch theatre productions, gourmet eateries, local breweries and a multitude of festivals and events. Victoria Row, a pedestrian street lined with restaurant patios and boutique shops, is frequented by locals and visitors alike. The charming seaside boardwalk (near the Delta Prince Edward Hotel) is perfect for a relaxing walk or stroll.

The Delta Prince Edward Hotel is directly connected to the Convention Centre. This waterfront hotel offers tastefully appointed hotel rooms equipped with flat-screen TVs, mini-fridges, and free Wi-Fi. Additional rooms have been booked at boutique hotels, The Great George and The Holman Grand Hotel, both within walking distance of the Convention Centre. The Holman Grand Hotel offers suites to accommodate family members.

Plan to attend the CVMA Convention, come early or stay late! PEI is home to world-class golf courses, cultural and historic venues, artists, craftspeople and musicians, exceptional cuisine featuring seafood (and much more than the humble potato), experiential and outdoor activities, Anne of Green Gables, exquisite beaches, and breathtaking scenery! While visiting the Island, you are never far from the ocean. In fact, no part of the island is more than 16 km away from the sea.

The Island has become a food haven known for its many food-oriented festivals. In 2016, celebrity chef Michael Smith and his wife Chazz Smith re-opened the first 5-star property on the Island, the Inn at Bay Fortune. The Inn offers a unique “Farm to Fork” experience sharing every single ingredient grown, produced, farmed or foraged locally.

No one knows the Island better than the people who live there and explore it every day. For ideas on what to see and do from a local’s perspective visit the website (www.welcompei.com). Visit the CVMA website (www.canadianveterinary.net) for updates on the 2017 CVMA Convention.

(by Ruta Klicius, CMP, Manager, CVMA Conventions)

organisera divers laboratoires de travaux pratiques, notamment dans les domaines suivants : dentisterie canine et feline, dentisterie équine, chirurgie des petits animaux, hémato et dermatologie. L’AVC invite aussi tous les anciens à assister à une réunion de toutes les promotions qui se déroulera le vendredi 14 juillet.

Charlottetown a préservé son cachet historique en tant que lieu de naissance de la Confédération tout en attirant d’excellentes productions théâtrales, des restaurants gastronomiques, des brasseries locales et une foule de festivals et d’événements. Victoria Row, une rue piétonnière où se dressent des terrasses et des boutiques, est fréquentée tant par la population que par les visiteurs. L’agréable promenade du littoral (près de l’hôtel Delta Prince Edward) est particulièrement propice à la marche et à la détente.

L’hôtel Delta Prince Edward est directement relié au centre des congrès. Cet hôtel au bord de l’eau offre des chambres décorées avec goût dotées de téléviseurs à écran plat, de mini-réfrigérateurs et du Wi-Fi gratuit. D’autres chambres ont été réservées à des hôtels boutique, les hôtels The Great George et The Holman Grand, qui se trouvent à distance de marche du centre des congrès. L’hôtel The Holman Grand offre des suites pouvant accueillir les membres de la famille.

Prévoyez votre participation au congrès de l’ACMV, venez tôt et attardez-vous après le congrès! L’Île-du-Prince-Édouard offre des terrains de golf de calibre mondial, des lieux culturels et historiques, des artistes, des artisans et des musiciens ainsi qu’une cuisine exceptionnelle offrant des fruits de mer (qui va bien au-delà l’humble pomme de terre), des expériences et de plein air, Anne aux pignons verts, des plages exquises et des panoramas à couper le souffle! Pendant votre visite dans l’Île, vous n’êtes jamais loin de l’océan. En fait, aucun secteur de l’île ne se trouve à plus de 16 km de la mer.

L’Île est devenue une destination réputée pour les foodies avec ses nombreux festivals gastronomiques. En 2016, le chef vedette Michael Smith et sa femme Chazz Smith ont rouvert le premier établissement cinq étoiles de l’Île, l’auberge Inn at Bay Fortune. L’auberge offre une expérience unique «de la ferme à l’assiette» offrant seulement des ingrédients qui ont été cultivés, produits, élevés ou cueillis localement.

Personne ne connaît mieux l’Île que les personnes qui habitent ici et l’expèrent tous les jours. Pour découvrir des idées sur les activités du point de vue d’un habitant de l’Île, visitez le site Web (www.welcompei.com). Visitez le site Web de l’ACMV (www.veterinairesaucanada.net) pour obtenir des mises à jour sur le congrès 2017 de l’ACMV.

(par Ruta Klicius, CMP, gestionnaire, Congrès de l’ACMV)
First Canadian Veterinarian Elected to WSAVA Presidency

A Canadian veterinarian is the new president of the World Small Animal Veterinary Association (WSAVA), Dr. Walt Ingwersen, a member of the Association’s Executive Board, was elected to the presidency during the WSAVA World Congress 2016, which took place in Cartagena, Colombia, from 27–30 September. He takes over from professor Colin Burrows and will serve a 2-year term.

Following qualification from the Ontario Veterinary College (OVC) and a year in general small animal practice, Dr. Ingwersen returned to the OVC for 4 years of postgraduate training. He followed this with 12 years in general and referral practice before going on to hold a range of non-clinical roles. Among his achievements, he helped to develop and popularize the Global ISO microchip (RFID) standard and bring it to North America — a project which brought him into contact with the WSAVA for the first time. He became involved in volunteer veterinary medicine while working with the Ontario Veterinary Medical Association, the Canadian Veterinary Medicine Association and the American Animal Hospital Association. He is currently a Technical Services Veterinarian with Boehringer Ingelheim Canada Ltd.

The WSAVA works to enhance the clinical care of companion animals globally, representing more than 160 000 veterinarians around the world through 94 member associations. Its core activities include the creation of Global Guidelines, which set standards for veterinary care and providing continuing education (CE) and other educational resources for its members, particularly those in which companion animal veterinary care is still emerging.

Dr. Ingwersen’s first role with the WSAVA was as a member of its Microchip Committee in 1996. He later worked as its news editor and webmaster and joined the Executive Board in 2008 as honorary secretary, a position he held for 4 years. In 2013, he led the creation of WSAVA Global Pain Council and he remains an active member of this WSAVA Committee. As president, he will lead the delivery of the WSAVA’s Strategic Plan, which is focused on engaging the Association’s growing membership into an active, connected and supportive global community of veterinary peers.

Commenting, he said: “We have come a long way in a short time — but there is much more to do and we have ambitious plans to continue to drive up standards of veterinary care globally, as well as to achieve the fundamental goal of the WSAVA Strategic Plan, which is to develop our members into an engaged and collaborative community. We also intend to make our voice heard on issues that affect our members and impact their ability to care for their patients to the highest standards. Our campaign against the proposed rescheduling of ketamine and our new initiative to secure the availability of medicinal products for companion animals to

Un Canadien élu pour la première fois à la présidence de la WSAVA

Un vétérinaire canadien est le nouveau président de la World Small Animal Veterinary Association. Le Dr Walt Ingwersen, qui est membre du comité exécutif de l’association, a été élu à la présidence durant le dernier congrès WSAVA, qui se déroulait à Cartagena, en Colombie, du 27 au 30 septembre 2016. Il remplace le professeur Colin Burrows et sera en poste pendant un mandat de deux ans.

Après ses études à l’Ontario Veterinary College (OVC) et une année consacrée à la pratique de la médecine vétérinaire des animaux de compagnie, le Dr Ingwersen est retourné à l’OVC pour des études spécialisées d’une durée de quatre ans. Il a ensuite exercé pendant douze ans en médecine générale et en pratique spécialisée avant de se consacrer à des rôles professionnels non cliniques. Parmi ses réalisations, citons son rôle dans le développement et la mise en marché des «puces électroniques» (norme ISO RFID) et leur diffusion dans toute l’Amérique du Nord et c’est ce projet qui lui a permis d’entrer en contact avec la WSAVA. Il a commencé à effectuer du travail bénévole auprès de l’Ontario Veterinary Medical Association, de l’Association canadienne des médecins vétérinaires et de l’American Animal Hospital Association (AAHA). Il travaille actuellement en tant que vétérinaire des services techniques chez Boehringer Ingelheim Canada Ltée.

La WSAVA a pour but de rehausser la qualité des soins des animaux de compagnie à l’échelle mondiale et elle représente plus de 160 000 vétérinaires dans le monde entier par l’entremise de 94 associations membres. Ses activités principales incluent la création de directives générales qui définissent les normes des soins vétérinaires et la prestation de formation continue et autres ressources éducatives pour ses membres, particulièrement ceux pour qui la médecine des animaux de compagnie est encore une discipline émergente.

Le premier rôle du Dr Ingwersen au sein de la WSAVA a été comme membre du Comité des puces électroniques en 1996. Il a ensuite œuvré comme administrateur de site Web et s’est joint au comité exécutif en 2008 en tant que secrétaire honoraire, un poste qu’il a occupé pendant quatre ans. En 2013, il a dirigé la création du «WSAVA Global Pain Council», un comité sur l’élaboration de directives pour la prise en charge de la douleur, dont il reste un membre actif. Dans son rôle de président, il assumera la direction de la mise en œuvre du Plan stratégique de la WSAVA qui porte sur l’engagement du nombre croissant de membres au sein d’une collectivité de pairs vétérinaires active, branchée et solidaire.

Le Dr Ingwersen a affirmé : «Nous avons accompli beaucoup en peu de temps — mais il y a encore fort à faire et nous avons des projets ambitieux pour continuer de rehausser les normes des soins vétérinaires à l’échelle mondiale ainsi que d’atteindre le but fondamental du Plan stratégique de la WSAVA, c’est-à-dire l’engagement actif de nos membres au sein d’une collectivité engagée et concertée.”

Dr. Walt Ingwersen
2017 CVMA Awards

Last Call! Nominations Close
January 31, 2017

Each year, through CVMA’s national veterinary awards program, veterinarians are honored for their exceptional contributions to veterinary medicine. We encourage you to nominate deserving colleagues for their hard work and dedication to the profession.

Award nominees (excluding those nominated for Honorary Membership) must be current CVMA members to be eligible for nomination; however, they can be nominated by non-CVMA members.

CVMA Awards will be presented during the CVMA Convention, which takes place in Charlottetown, Prince Edward Island from July 13 to 16, 2017. Nominations will be accepted until January 31, 2017 for the following awards:

- CVMA Humane Award (Sponsored by Merck Animal Health)
- Merck Veterinary Award (Sponsored by Merck Animal Health)
- Small Animal Practitioner Award (Sponsored by Petsecure Pet Health Insurance)
- CVMA Practice of the Year Award (Sponsored by Scotiabank)
- CVMA Industry Award
- CVMA Life Membership
- CVMA Honorary Membership

Nomination packages must be submitted by January 31, 2017 via email (communications@cvma-acmv.org), by fax to 613-236-9681, or by mail to the CVMA office at 339 Booth Street, Ottawa, ON K1R 7K1. Nomination packages must include a completed nomination form, an outline of the nominee’s key professional accomplishments, and letters of support.

For additional information, including updated award nomination guidelines, complete award descriptions, nomination forms, and a listing of past award recipients, please visit the CVMA Awards section of the CVMA’s website (www.canadianveterinarians.net) under About CVMA.

Prix 2017 de l’ACMV

Dernier appel! Clôture des mises en candidature le 31 janvier 2017

Chaque année, dans le cadre du programme des prix vétérinaires nationaux de l’ACMV, des vétérinaires sont honorés pour leurs contributions exceptionnelles à la médecine vétérinaire. Nous vous encourageons à mettre en candidature des collègues méritants pour leur travail ardu et leur dévouement envers la profession.

Les candidats (sauf ceux mis en candidature pour le titre de membre honoraire) doivent être des membres en règle de l’ACMV pour être admissibles à la mise en candidature. Cependant, ils peuvent être mis en candidature par des non-membres de l’ACMV.

Les prix de l’ACMV seront décernés durant le congrès de l’ACMV, qui se déroulera du 13 au 16 juillet 2017 à Charlottetown, à l’Île-du-Prince-Édouard. Des mises en candidature seront acceptées jusqu’au 31 janvier 2017 pour les prix suivants :

- Prix humanitaire de l’ACMV
  (Commandité par Merck Santé Animale)
- Prix vétérinaire Merck (Commandité par Merck Santé Animale)
- Prix du praticien des petits animaux
  (Commandité par Petsecure assurance maladie pour animaux)
- Prix de la pratique de l’année de l’ACMV
  (Commandité par la Banque Scotia)
- Prix de l’industrie de l’ACMV
- Membre à vie de l’ACMV
- Membre honoraire de l’ACMV

Les trousses de mise en candidature doivent être soumises d’ici le 31 janvier 2017 par courriel (communications@cvma-acmv.org), par télécopieur au 613-236-9681 ou par la poste au bureau de l’ACMV au 339, rue Booth, Ottawa (Ontario) K1R 7K1. Les trousses de mise en candidature doivent inclure un formulaire de mise en candidature complet, une description sommaire des principales réalisations professionnelles du candidat et des lettres d’appui.

Pour obtenir des renseignements additionnels, dont des lignes directrices révisées en lien avec la mise en candidature pour les prix, la description complète de chaque prix, des formulaires de mise en candidature et une liste des récipiendaires antérieurs, veuillez visiter la section des Prix de l’ACMV sur le site Web de l’ACMV (www.veterinairesaucanada.net) sous À propos de l’ACMV.
Estimated antimicrobial dispensing frequency and preferences for lactating cow therapy by Ontario dairy veterinarians

David F. Léger, Nathalie C. Newby, Richard Reid-Smith, Neil Anderson, David L. Pearl, Kerry D. Lissemore, David F. Kelton

Abstract — In this cross-sectional study, data were collected from responses to a questionnaire on dispensing frequencies of antimicrobials used by dairy practitioners in Ontario in dairy cattle in 2001. Data were validated through clinical case scenarios. Respondents reported using antimicrobials across all categories of importance to human medicine (medically important, Categories I to III) with a diversity of treatment combinations and routes of administration. Respondents anticipated that a request for direct veterinary supervision by producers was dependent on case severity, highlighting the importance of on-farm diagnostic and treatment protocols. Knowledge of the antimicrobials used in lactating cow therapy, and their frequency and reasons for use, will provide baseline information and contribute to antimicrobial stewardship in this food-animal production sector.

Introduction

The specter of human illness caused by bacterial infections that are resistant to antimicrobials commonly used in both livestock and human medicine has led to increased scrutiny regarding the use of these drugs in food-animal agriculture (1–3). Evidence for the dissemination of resistance determinants through clonal spread of bacterial strains or by the acquisition of transferable elements among bacteria, and the role of the food chain in bridging animal and human ecosystems has been described (4). The potential public health impact of resistant commensal bacteria and zoonotic pathogens of food-animal origin has resulted in calls for the containment of antimicrobial resistance in animals and prudent antimicrobial use in agriculture (5–7), which have in turn spawned the development of guidelines and policy recommendations regarding the use of antimicrobials by veterinarians and producers (8–13). Antimicrobial drugs are used commonly in the conventional management of dairy herds (14,15). Qualitative and quantitative information about the antimicrobials used by veterinarians for disease prevention and treatment in dairy cattle, including...
those that are of very high importance to human medicine, are fundamental to a better understanding of the associated potential public health hazards.

The first objective of this cross-sectional study was to describe antimicrobial use frequency by route of administration by dairy veterinarians in Ontario in 2001, which provided baseline data for any future studies. Future studies or surveillance programs will provide useful information that could describe any shifts in prescriber attitudes and antimicrobial use in the dairy sector since the time of this study. The second objective was to use clinical case scenarios to gain a contextual understanding of antimicrobial use practices at the time of the study.

Materials and methods

Data were collected using a self-administered questionnaire, which was mailed to food-animal veterinary practices in Ontario in 2001. This instrument was developed by the research group, pre-tested by 12 subjects to refine any ambiguous questions, and validated against expected demographic and antimicrobials use data at the time of this study. The College of Veterinarians of Ontario (CVO) sampling frame (n = 340), the target population of veterinarians accredited as “Food-Producing Animal Mobile” (n = 240) and the respondent (n = 124) demographics are described in a previous paper (16). The average question response rate was 99% (range: 95% to 100%). Antimicrobial use data were collected through a series of questions that listed antimicrobial agents/classes, grouped by routes of administration common to dairy medicine (injectable, intramammary, intrauterine, topical foot, and oral). Respondents (n = 117) were also asked to respond to 4 case-based clinical scenario questions and to specify any antimicrobial use in each case. Clinical case scenarios were drawn from diseases of bacterial etiology commonly seen in Ontario dairy practice. Respondents were also asked to rank their reasons for antimicrobial use in lactating dairy cows. The context of this survey was antimicrobial use in lactating cows; there were no questions pertaining to use in calves or replacement heifers.

Antimicrobial use findings from this study were categorized according to their importance in human medicine as described by the Veterinary Drugs Directorate, Health Canada: Category I — Very high importance, Category II — High importance, Category III — Medium importance, Category IV — Low importance (17). Categories I to III are considered to be medically important in human medicine.

Antimicrobial use frequencies by route of administration were captured as ordinal data along a 5-point scale: Daily, Weekly, Monthly, Yearly, or Never. To reflect the fact that the intervals between frequency levels were not equal in magnitude, the data were re-scaled to full-time equivalent (FTE) days (18), where Daily = 275 FTE days, Weekly = 48 FTE days, Monthly = 8 FTE days, Yearly = 1 FTE day, and Never = 0 FTE days. These estimates were calculated based on the available number of business days minus vacation time, statutory holidays, and continuing education days, assumed to be typical of a dairy practitioner year at the time of this study. Total and mean annual dispensing frequencies (tADF, mADF) were calculated as an expression of use frequency for each antimicrobial by route of administration and category of human health importance for each respondent veterinarian (total: n = 124).

To further assess antimicrobial use, the questionnaire presented 4 standardized clinical case scenarios: mild mastitis, acute metritis, digital dermatitis, and severe mastitis (19). For each of the 4 cases respondents were asked to indicate whether the majority of their dairy clients would request direct veterinary supervision of the case, what the typical initial treatment plan would include, and to specify any antimicrobials used. All cases were described as occurring in a standard cow producing 35 kg of milk in her second lactation. For the mild mastitis case, the cow was presented with cloths in milk, a moderately swollen quarter, not off-feed, and no fever. For the acute metritis case, the cow was presented with anorexia at 8 days in milk (DIM) and foul smelling uterine discharge containing tissue fragments and a body temperature of 39°C. For the digital dermatitis case, the cow was presented with “strawberry footrot” (i.e., digital dermatitis) with moderate swelling at the heel and between the claws. For the severe mastitis case, the cow was presented at 8 DIM with watery milk secretions with cloths, a swollen hard quarter, anorexia, and moderately dehydrated with a body temperature of 40.5°C.

Statistical analysis

Questionnaire data were stored in a relational database (Microsoft Access, 2000; Microsoft, Redmond, Washington, USA), and descriptive analysis, univariable and multivariable analyses were conducted using statistical software (SAS version 9.1.2; SAS Institute, Cary, North Carolina, USA). Test statistics were considered significant at P < 0.05.

Associations among antimicrobial use frequencies, practitioner and practice demographic factors, were investigated using mixed linear regression models with total annual dispensing frequencies (tADF) as the dependent variable. The following independent variables were controlled: gender, years in practice, Ontario region, percentage of time spent on dairy practice, percentage of time spent on individual cow medicine, practice size, the number of small/medium/large herds, and the number of free-stall/tie-stall milking cow facilities in a practice, percent gross revenue from drug sales, and veterinary-client-patient-relationship over-the-counter dispensing policy variables for penicillin and ceftiofur. The categorical variable (Ontario region) had 3 levels: North/South-Central, South-East, and South-West regions (19). Practice was included as a random effect in each model. Predictor variables were screened based on a causal diagram, descriptive statistics, correlation analysis, and unconditional associations among dependent and independent variables (20). Pairwise Spearman’s rank correlations were evaluated for all independent variables to identify potential sources of collinearity (r > 0.7). Variables were evaluated for evidence of confounding, by virtue of a substantive change (> 20%) in the coefficients of the predictors of interest in the model, and were retained in the model if they were identified as a confounder or if they were part of a significant interaction term.

Model assumptions were evaluated (homoscedasticity and normality of residuals) with a plot of standardized residuals against predicted values and a normal probability plot of
residuals. To meet the assumption of homoscedasticity, a log transformation of the dependent variables was performed. Continuous variables (years in practice, percent time spent on individual cow medicine, practice size, and percent gross revenue from drug sales) were assessed for linear relationships with tADF by plotting them against the residuals, and by assessing the significance of their quadratic terms. Significant quadratic terms were retained with their main effects. In all mixed models, best linear unbiased predictors (BLUPS) were examined for any outliers. Model fit was evaluated by identifying and assessing outlier, leverage, and influential observations.

**Results**

The overall response rate for the survey was 47% with 1/3 of respondents reporting < 50% of their time was spent on dairy practice. Beyond gender, practitioner and practice demographics were reflective of the distribution of the Ontario dairy industry [respondent demographics previously described (16)].

**Antimicrobials used and relative use frequencies**

Antimicrobial use in lactating dairy cattle was driven primarily by mastitis (Figure 1). The greatest mean annual dispensing frequencies (mADF) of antimicrobials by route of administration were as follows: injection, lactating and dry cow intramammary infusions, followed by intra-uterine administration, topical-foot application, and oral bolus/feed (Table 1; Figure 2). The antimicrobials in the 75th percentile [mADF greater than 104 full-time equivalent (FTE) days] included the following antimicrobials: cepapirin, tetracycline, ceftriaxone, penicillin, trimethoprim-sulfadiazine, combination preparation of penicillin-novobiocin-streptomycin-polyoxymyxin B for intramammary infusion product, monensin, and novobiocin-penicillin (Figure 2). The majority of antimicrobial use in dairy medicine fell under Category II (61%, 14/23 antimicrobials) (Figure 2). In assessing frequency of use by separate routes of administration the highest frequency was the injectable preparations of ceftriaxone (Category I), penicillin (Category II), tetracycline (Category III), and trimethoprim-sulfadiazine (Category II) (Figure 2). The next most frequent use was the lactating cow intramammary infusion product (penicillin-novobiocin-streptomycin-polyoxymyxin B; Category I), followed by the lactating and dry cow intramammary formulations of cefapirin (Category II) (Figure 2).

From the model findings [see thesis for model output tables (19)], the relevant information is as follows. Multivariable mixed linear regression models for antimicrobial use frequency indicated that practice location (Ontario region) had a significant association with tADF for Categories I-IV when controlling for practice size and the percentage of time spent on individual cow medicine. In the mixed linear model for tADF of drugs
Table 1. Mean annual dispensing frequencies (mADF, FTE days/year) by category of importance to human medicine and route of administration from the survey administered to Ontario dairy veterinarians in 2001

<table>
<thead>
<tr>
<th>VDD Category</th>
<th>Antimicrobial</th>
<th>IM-IV-SC</th>
<th>IMM LCT</th>
<th>IMM DCT</th>
<th>Intrauterine</th>
<th>Topical</th>
<th>Oral bolus</th>
<th>Oral bolus</th>
<th>Oral</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Cefotiofur</td>
<td>158.77</td>
<td>24.80</td>
<td>10.11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>193.69</td>
</tr>
<tr>
<td></td>
<td>PEN-NOV-STR-POL</td>
<td>122.35</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>122.35</td>
</tr>
<tr>
<td></td>
<td>Enrofloxacin</td>
<td>0.15</td>
<td>0.06</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.21</td>
</tr>
<tr>
<td>Total Category I</td>
<td></td>
<td>158.92</td>
<td>147.22</td>
<td>10.11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>316.25</td>
</tr>
<tr>
<td>II</td>
<td>Cephalosporin</td>
<td>111.17</td>
<td>104.03</td>
<td>80.50</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>295.70</td>
</tr>
<tr>
<td></td>
<td>Penicillin</td>
<td>157.76</td>
<td>9.60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>167.35</td>
</tr>
<tr>
<td></td>
<td>Trimethoprim-Sulfadoxine</td>
<td>130.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>130.00</td>
</tr>
<tr>
<td></td>
<td>Novobiocepin-Penicillin</td>
<td>26.16</td>
<td>78.69</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>104.85</td>
</tr>
<tr>
<td></td>
<td>Cloxacillin</td>
<td>23.30</td>
<td>80.43</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>103.73</td>
</tr>
<tr>
<td></td>
<td>Prilimycin</td>
<td>43.35</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>43.35</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>16.51</td>
<td>7.66</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>24.17</td>
</tr>
<tr>
<td></td>
<td>Lincomycin</td>
<td></td>
<td>18.45</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>18.45</td>
</tr>
<tr>
<td></td>
<td>Spectinomyacin (other)</td>
<td>14.47</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>14.47</td>
</tr>
<tr>
<td></td>
<td>Macrolides</td>
<td>13.44</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>13.44</td>
</tr>
<tr>
<td></td>
<td>Gentamicin</td>
<td>0.77</td>
<td>3.26</td>
<td>0.55</td>
<td>0.06</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.65</td>
</tr>
<tr>
<td></td>
<td>Timicosin (DCT)</td>
<td>1.50</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.50</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>0.06</td>
<td>0.39</td>
<td>0.19</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.65</td>
</tr>
<tr>
<td></td>
<td>Penicillin-Streptomycin</td>
<td>0.45</td>
<td>0.01</td>
<td>0.13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>Linco-Spectin (other)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Category II</td>
<td></td>
<td>303.99</td>
<td>224.15</td>
<td>271.65</td>
<td>105.24</td>
<td></td>
<td>18.52</td>
<td></td>
<td></td>
<td>923.54</td>
</tr>
<tr>
<td>III</td>
<td>Tetracycline</td>
<td>132.59</td>
<td>12.33</td>
<td>72.67</td>
<td>50.94</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>268.53</td>
</tr>
<tr>
<td></td>
<td>Florfenicol</td>
<td>13.06</td>
<td>0.77</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>13.82</td>
</tr>
<tr>
<td></td>
<td>Sulfonamides</td>
<td></td>
<td></td>
<td>2.76</td>
<td>0.16</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.92</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td></td>
<td></td>
<td></td>
<td>0.06</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td>Total Category III</td>
<td></td>
<td>145.65</td>
<td>13.10</td>
<td>75.43</td>
<td>51.17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>285.34</td>
</tr>
<tr>
<td>IV</td>
<td>Monensin</td>
<td></td>
<td></td>
<td>85.89</td>
<td>24.07</td>
<td>109.96</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Novobiocin</td>
<td></td>
<td></td>
<td>12.90</td>
<td></td>
<td>12.90</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nitrofurazone</td>
<td></td>
<td>0.55</td>
<td>3.58</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.13</td>
</tr>
<tr>
<td>Total Category IV</td>
<td></td>
<td>12.90</td>
<td>0.55</td>
<td>3.58</td>
<td>85.89</td>
<td>24.07</td>
<td>126.98</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NA</td>
<td>CuSu liquid</td>
<td></td>
<td></td>
<td></td>
<td>44.90</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>44.90</td>
</tr>
<tr>
<td></td>
<td>CuSu powder footbath</td>
<td></td>
<td></td>
<td>27.60</td>
<td></td>
<td>27.60</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Formaldehyde</td>
<td></td>
<td></td>
<td>9.69</td>
<td></td>
<td>9.69</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td></td>
<td>0.13</td>
<td>3.19</td>
<td>3.45</td>
<td>6.77</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Iodide</td>
<td>2.27</td>
<td></td>
<td></td>
<td></td>
<td>2.27</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MgSu paste</td>
<td></td>
<td></td>
<td>1.80</td>
<td></td>
<td>1.80</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total NA</td>
<td></td>
<td>2.27</td>
<td>0.13</td>
<td>3.19</td>
<td>87.44</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>93.03</td>
</tr>
</tbody>
</table>

Route of administration total 610.83 384.59 284.54 194.52 160.71 85.89 24.07 1745.15

* Full-time equivalent (FTE) days: Daily = 275 FTE days, Weekly = 48 FTE days, Monthly = 8 FTE days, Yearly = 1 FTE day, and Never = 0 FTE days.
* Categories I-IV: Categories of importance to human medicine (VDD 2006).
* PEN-NOV-STR-POL: Penicillin-Novobiocin-Streptomycin-Polymyxin B.
* IM-IV-SC — intramuscular, intravenous, or subcutaneous injection.
* IMM — intramammary; LCT — lactating cow treatment; DCT — dry cow therapy.

of Categories I-IV, a significant interaction was noted between practice size and individual cow medicine (P = 0.001). In general, the daily dispensing frequency was higher for veterinarians who spent less time on individual cow medicine (e.g., < 50%) in larger practices compared to smaller practices; in smaller practices the dispensing frequency was highest for veterinarians who spent most of their time (≈ 50%) on individual cow medicine. Dispensing frequencies were higher for veterinarians in large practices compared to those in small practices. Respondents in North/South-Central Ontario indicated a significantly lower dispensing frequency of antimicrobials across all Categories compared to those in South-Eastern Ontario [β = 0.50 FTE; 95% confidence interval (CI) = 0.29, 0.86; P = 0.01]. The models for Categories III and IV indicated significantly greater variation in dispensing frequency by veterinarians in South-Eastern Ontario (SEOnt) compared to those in South-Western Ontario (SWOnt) (SEOnt Category III β = 1.8 FTE; 95% CI = 1.1, 2.9; P = 0.02; SEOnt Category IV β = 2.5 FTE; 95% CI = 1.3, 4.6; P = 0.01).

The tADF of antimicrobials increased with practice size (β = 1.0 FTE; 95% CI = 1.0, 1.1; P < 0.001) and the percentage of time spent on individual cow medicine first increased and then declined following a quadratic association [β (% time) = 1.1 FTE; 95% CI = 1.0, 1.0; P < 0.001; β (%time²) = 1.0 FTE; 95% CI = 1.0, 1.0; P < 0.001].

Clinical case scenarios
The use of specified antimicrobials by clinical case scenario and route of administration is described in Table 2. In the first clinical case, mild mastitis, only 2 of the 117 respondents
indicated producers would request a veterinary consultation prior to treatment initiation; 24% (28/117) indicated producers would not use an antimicrobial in the treatment of this case. Of all of the individual treatment options, intramammary (IMM) antimicrobial infusion was the most frequently selected followed by stripping of the quarter with or without the use of injectable oxytocin. The primary treatment approach included: IMM antimicrobial infusion with/without a non-antimicrobial treatment (e.g., stripping the quarter), or non-antimicrobial treatments only. Sixteen respondents specified other treatments which included various topical udder preparations, injectable steroidal and non-steroidal anti-inflammatory drugs (NSAIDs), and diuretics. Of the IMM antimicrobial products specified, 85%, (99/117) cited the use of penicillin G-streptomycin-novobiocin-polymyxin B, followed by 45% (53/117) for cephalixin. The use of IMM pirlimycin for this case was low.

In the second clinical case, acute metritis, antimicrobial therapy by IM injection was the most frequently selected (58%, 68/117) individual treatment option followed by intrauterine (IU) administration. Seventy-one percent (83/117) of respondents thought that producers would request veterinary supervision for a case of metritis of this nature. There was considerable diversity in the treatment combinations for this case, but the majority included an injectable antimicrobial, IM and/or IV, along with an IU infusion and/or a non-antimicrobial treatment. Three respondents indicated they would not use antimicrobials for this case scenario. Twenty-one percent (24/117) of the treatment combinations included injectable and IU antimicrobial administration along with other supportive therapies (IV and oral fluid therapy, NSAIDs, and hormone therapies). A number of antimicrobial combinations were also noted for this case, involving mainly 4 injectable antimicrobials: oxytetracycline, procaine penicillin G, ceftiofur, and trimethoprim-sulfadixine. Oxytetracycline and trimethoprim-sulfadixine were the most frequently used for IV administration, and penicillin and ceftiofur for IM administration. Oxytetracycline was the dominant antimicrobial specified for intrauterine infusion, followed by cephalixin, with the remainder indicating the use of iodine infusions or intrauterine boluses containing tetracycline or sulfonamide drugs.

In the third clinical case, digital dermatitis, only 10% (12/117) of respondents felt they would be consulted in managing this case in an individual cow. The most common treatment options selected were to apply an antimicrobial as a topical spray

---

**Figure 2.** Dispensing frequencies of antimicrobials by category of importance to human medicine and route of administration that were identified by respondents in the survey administered to Ontario dairy practitioners in July 2001. Categories I–IV: Categories of importance to human medicine (Veterinary Drugs Directorate, 2006); NA — Not applicable; PEN-NOV-STR-POL — Penicillin-Novobiocin-Streptomycin-Polymyxin B; Injection – includes intramuscular, intravenous, or subcutaneous injection; LCT — lactating cow treatment; DCT — dry cow therapy.
Table 2. Case counts\(^{a}\) of specified antimicrobials by clinical case and route of administration (respondents: \(n = 117\))

<table>
<thead>
<tr>
<th>VDD Cat(^{b})</th>
<th>Antimicrobial(^{c})</th>
<th>CASE 1: Mild mastitis(^{d})</th>
<th>CASE 2: Postpartum metritis</th>
<th>CASE 3: Digital dermatitis</th>
<th>CASE 4: Severe mastitis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>IM</td>
<td>IMM</td>
<td>IV</td>
<td>Total</td>
</tr>
<tr>
<td>I</td>
<td>Enrofloxacin</td>
<td></td>
<td>59.3</td>
<td></td>
<td>59.3</td>
</tr>
<tr>
<td></td>
<td>PEN-STR-NOV-POL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftiofur</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category I Total</td>
<td></td>
<td>59.3</td>
<td>59.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Ampicillin</td>
<td>25.8</td>
<td></td>
<td>25.8</td>
<td>11.0</td>
</tr>
<tr>
<td></td>
<td>Cephaiprin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lincomycin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>LIN-SPT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Penicillin</td>
<td>2.5</td>
<td></td>
<td>1.8</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>Pitrimycin</td>
<td>2.0</td>
<td></td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SXT + PEN</td>
<td>2.0</td>
<td></td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>Category II Total</td>
<td></td>
<td>7.0</td>
<td>27.7</td>
<td>1.0</td>
<td>35.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Chlorotetraycline</td>
<td>2.0</td>
<td></td>
<td>2.0</td>
<td>12.3</td>
</tr>
<tr>
<td></td>
<td>Florfenicol</td>
<td>2.0</td>
<td></td>
<td>2.0</td>
<td>4.0</td>
</tr>
<tr>
<td></td>
<td>Neomycin</td>
<td>2.0</td>
<td></td>
<td>2.0</td>
<td>12.3</td>
</tr>
<tr>
<td></td>
<td>Oxytetracycline</td>
<td>2.0</td>
<td></td>
<td>2.0</td>
<td>12.3</td>
</tr>
<tr>
<td></td>
<td>Sulphonamides</td>
<td>2.0</td>
<td></td>
<td>2.0</td>
<td>12.3</td>
</tr>
<tr>
<td></td>
<td>Tetracycline</td>
<td>2.0</td>
<td></td>
<td>2.0</td>
<td>12.3</td>
</tr>
<tr>
<td></td>
<td>Tylosin</td>
<td>2.0</td>
<td></td>
<td>2.0</td>
<td>12.3</td>
</tr>
<tr>
<td>Category III Total</td>
<td></td>
<td>2.0</td>
<td>20.0</td>
<td>1.0</td>
<td>22.0</td>
</tr>
<tr>
<td>Route of administration and case totals</td>
<td></td>
<td>9.0</td>
<td>87.0</td>
<td>1.0</td>
<td>97.0</td>
</tr>
</tbody>
</table>

\(^{a}\) When multiple antimicrobials were specified the count for that observation was divided equally by the number specified.

\(^{b}\) VDD Cat — Categorization of antimicrobial drugs based on their importance in human medicine (Veterinary Drugs Directorate, 2006).

\(^{c}\) LIN-SPT — lincomycin-spectinomycin; NOV — novobiocin; PEN — penicillin; POL — polymyxin B; STR — streptomycin; SXT — trimethoprim-sulfadoxine (World Health Organization, 1999).

\(^{d}\) IM — intramuscular injection; IMM — intramammary infusion; IU — intrauterine infusion or oblets; IV — intravenous injection; Tp — topical (spray, footbath, dressing).
or as a dressing with a foot bandage. These approaches were reflected in most of the 22 treatment combinations for this case, with the remainder including various combinations of other topical and systemic therapies. Most of the topical antimicrobial exposure (94%, 110/117) was in the form of tetracycline spray or dressing followed by lincomycin alone or in combination with spectinomycin. Ceftiofur was the main injectable antimicrobial used with 16% (19/117) of respondents citing this drug for IM administration in treating a case of digital dermatitis.

In the final case scenario, severe mastitis, the full range of available treatment options was selected. Ninety-three percent (109/117) of respondents expected that they would be called by the producer to attend this case. Of the many treatment combinations for this case, most respondent veterinarians (78.6%, 92/117) indicated they would treat this case with an IV antimicrobial and some form of supportive therapy (IV and oral fluid therapy and injectable NSAIDs), with or without IMM and IM antimicrobials. Trimethoprim-sulfadiazine was generally the antimicrobial of choice for IV and IM administrations followed by oxytetracycline; cephaoripin and the penicillin-streptomycin-novobiocin-polymyxin B combination were selected at similar frequencies for IMM use in this case.

Responses to the clinical scenarios revealed extra-label drug uses (ELDU) in the form of unregistered disease and species indication, and route of administration for ceftiofur, enrofloxac cin, trimethoprim-sulfadiazine, lincomycin, spectinomycin, and oxytetracycline at varying frequencies across the 4 cases.

**Discussion**

Antimicrobials frequently dispensed by Ontario dairy veterinarians included antimicrobials that are highly important to human medicine (Categories I and II). Drug use spanned several antimicrobial classes, mainly beta-lactam antibiotics including cephalosporins, tetracyclines, and potentiated sulfonamides, with less frequent use of lincosamides, aminoglycosides, and macrolides. Unlike other food animals for which administration is commonly at the herd/flock level through feed or water, antimicrobial use in Ontario dairy cattle is primarily at the individual cow-level via parenteral (IM/IV/SC, IMM/II infusion) or topical (foot) routes of administration. The tADF for antimicrobials across all categories differed by region, with respondents from South-Eastern Ontario reporting higher dispensing frequencies, driven largely by more frequent dispensing of tetracyclines and monensins.

Bacterial infections that may cause reproductive tract infections, respiratory disease, lameness, and mastitis, are prevalent in dairy herds (21–25) and have been associated with much of the antimicrobial use in milking and dry cows (14,15,26–29).

Prior to the mid-1980s, antimicrobials commonly used to treat dairy cattle were injectable penicillin-streptomycin, chloramphenicol, tetracycline, and cloxacillin, with lesser use of neomycin, sulphonamides, trimethoprim-sulfadiazine, erythromycin, gentamicin, and ampicillin (14,26). In a 1981 study of 110 South-Western Ontario dairy herds, the rate of prophylactic and therapeutic use of antimicrobials was estimated to be 3.85 doses per animal-year, with mean rates for the 2 most commonly used antimicrobials, penicillin-streptomycin and chloramphenicol, being 1.45 and 1.03 doses per animal-year, respectively (14). Over the ensuing years chloramphenicol was banned from use in food-producing animals (30), the use of injectable penicillin/streptomycin diminished, and cephalosporin products became more prevalent, while procaine penicillin G, trimethoprim-sulfadiazine, and tetracycline persisted as mainstay antimicrobial agents in dairy medicine in Ontario herds (28,29,31). The findings of the current study reflect this industry shift in use profile.

In the decades preceding this study, agri-food uses of antimicrobials were being scrutinized for their “profitability” and the public health risks associated with antibiotic residues in dairy and meat products (15,32). While residue avoidance continues to be a major food safety concern, the potential microbial hazard, antimicrobial resistance and dissemination, should also be considered in decision-making on antimicrobial therapy and drug selection. Acknowledging that several antimicrobial classes are common to human and veterinary medicine, it is important that the results herein are presented in this context. Findings from our questionnaire on antimicrobial use were reported by category of importance to human medicine (17), reflecting the relative importance of certain antimicrobial drugs and/or drug classes by virtue of their indication in the treatment of serious human infection and the lack of alternative drug choices. For example, respondent veterinarians in this study reported frequent use of the Category I injectable antimicrobial ceftiofur, and a previous study suggested that milk withdrawal was a primary consideration in drug selection (16). The use of this third generation cephalosporin, as opposed to an equally efficacious alternative of a lower category, may be driven largely by economics due to its zero milk withdrawal time. However, this may be a public health concern given the potential for the emergence of antimicrobial resistance. With additional research on antimicrobial resistance in this sector (33) and an increased emphasis on the judicious use of antimicrobials, it would be interesting to see how trends in ceftiofur use and resistance may have shifted in the industry over time.

This study identified significant interactions between veterinary demographic variables related to dispensing frequencies. For example, the association of practice size and the amount of time spent on individual cow medicine by a veterinarian suggests that veterinarians in larger practices and/or those that do more individual cow medicine have refined their list of frequently used drugs to include fewer antimicrobials or they dispense antimicrobials at lower frequencies. A survey-based study of US dairy practitioners developed regression models that found the interaction between the number of herds served and the percent time spent in dairy medicine was significantly associated with average use scores of FDA-approved antimicrobials (31). Models for antimicrobials not approved by the FDA indicated that these 2 variables remained as significant main effects along with region, but their interaction was not significant. Compared to anti-inflammatory, tranquilizer, or analgesic drugs, respondents to the USA study used antibiotics most frequently, with penicillin G, ceftiofur, oxytetracycline, cloxacillin, cephaoripin, and ampicillin the 5 most often prescribed. All but oxytetracycline were β-lactam antibiotics with FDA-approval
for use in lactating cows. In a study of Michigan dairy herds, the proportional use of penicillins, tetracyclines, cephalospo-
rins, aminoglycosides, and sulphonamides in cows was similar
across lower herd size strata, but in herds milking 200 cows or
more, cephalosporin and aminoglycoside use declined in favor
of greater tetracycline use (27). Findings from our study, and
other similar research, suggest that dispensing frequencies and
antimicrobial selection are associated with herd demographics
and veterinary practice profiles.

Clinical case scenarios validated the antimicrobial use fre-
quency data from the questionnaire by reflecting a similar list
of antimicrobials. Data from clinical cases provide additional
contextual information, including relative case frequency of
use by route of administration and reasons for use, and level
of veterinary supervision of specified antimicrobials. The per-
ception that veterinary consultation or supervision would be
requested was highest for those cases with signs of systemic
illness, namely, metritis and severe mastitis. These cases also
resulted in more aggressive treatment with higher levels of inject-
able antimicrobial use, whereas the mild mastitis and digital
dermatitis cases tended to be managed using local antimicrobial
therapies. Similar to the clinical case findings of this study, other
researchers described how veterinary supervision influenced anti-
microbial use by dairy producers (27,28,33). From our results,
the severe mastitis case resulted in the highest antimicrobial
use counts per case and the mild mastitis case was associated
with the lowest use, while the metritis and digital dermatitis
cases resulted in similar use levels. Most of the antimicrobials
used to treat the severe mastitis case were Category II. Of the
3 drugs in Category I, the IMM infusion product containing
penicillin-streptomycin-novobiocin-polymyxin B had the highest
frequency of use followed by ceftiofur, one of the primary inject-
able treatments used for the metritis and digital dermatitis cases.
The metritis case saw mainly Category II and III drug use at
similar levels and antimicrobial treatments for digital dermatitis
were primarily from Category III.

The number and variety of treatment combinations that
emerged from the clinical cases implied that both theoretical
and empirical knowledge are brought to bear in determining a
therapeutic approach. Understanding the diversity in treatment
approaches can direct veterinary and producer education, and
is fundamental to the development of clinical guidelines and
farm protocols. Furthermore, the recent increase in awareness
of antimicrobial stewardship may direct alternative management
approaches aimed at reducing antimicrobial use on dairy farms,
thereby influencing dispensing practices by veterinarians.

Extra-label drug use (ELDU), identified as the use of a
drug not approved for use in lactating dairy cattle (species and
production class) and/or a use for an unapproved indication
and/or route of administration, was noted in responses to clinical
case scenarios. In undertaking an ELDU in a food-animal,
a veterinarian should be aware of the potential consequences to
human health and the legislative authority pertaining to this “right” (34). The criteria for ELDU include: a veterinarian has
made a diagnosis under a valid VCPR, there is no approved drug
labeled to treat the diagnosed condition or the drug therapy as
per label has been ineffective, treated animals are identified,
and an extended withdrawal period has been applied to any
food product after treatment. A policy statement released by
Health Canada provides a definition for ELDU and a list of
recommendations (35). Regulations and recommendations
notwithstanding, different types of ELDU may not elicit an
increase in antimicrobial resistance and will need to be evaluated
through clinical trials.

Limitations of this cross-sectional study are related to the
potential for selection (e.g., non-response bias) and misclassifi-
cation bias (e.g., recall bias), which are common concerns with
questionnaires-based research (36,37). The target population
was practitioners who provided veterinary services to Ontario
dairy producers. To maintain the internal validity of the study,
the number of responses from practices categorized as dairy-
intensive was monitored to ensure an adequate level of response
from this group. To limit design-based selection bias, in the form
of non-response bias, all non-respondent practices and veterin-
arians were contacted with equal rigor through multiple follow-up
telephone reminders. As with most questionnaire-based research,
the impact of non-response/response bias on study findings is
difficult to assess. Recognizing that the data were collected in
2001, these data will provide a baseline for future survey studies
of this nature.

In conclusion, antimicrobial use was identified across all
4 categories of importance to human medicine and several
frequently used antimicrobials were of very high or high impor-
tance (Categories I and II). Ceftiofur was the most frequently
dispensed Category I antimicrobial, administered primarily by
injection, and its economic appeal (zero milk withdrawal) may
be displacing the selection of similarly efficacious antimicrobials
from lower categories. Extra-label drug use was evident among
the drugs specified in responses to case-based questions. The
producer approach to managing clinical cases, as anticipated
by veterinary respondents, underscores the importance of
on-farm diagnostic and antimicrobial use protocols for those
cases in which direct veterinary supervision was not sought.
Regular collection of antimicrobial use data along with targeted
research can identify the animal and public health benefits and
hazards associated with antimicrobial use in this sector. This
paper along with a previously published paper (16) provides a
comprehensive baseline description of antimicrobial use in the
Ontario dairy industry at the time. This baseline information
will facilitate comparisons with future research in this area to
describe changes in antimicrobial use by dairy practitioners,
given anticipated legislative change and evolving awareness of
antimicrobial stewardship. O

References
1. O’Brien TF. Emergence, spread, and environmental effect of anti-
microbial resistance: How use of an antimicrobial anywhere can
increase resistance to any antimicrobial anywhere else. Clin Infect Dis
2002;34:S78–84.
2. Singer RS, Finch R, Wegener HC, Bywater R, Walters J, Lipsitch M.
Antibiotic resistance — The interplay between antibiotic use in animals
3. Molbak K. Human health consequences of antimicrobial drug-resistant


A comparison between maropitant and metoclopramide for the prevention of morphine-induced nausea and vomiting in dogs

Augusto M. Lorenzutti, Manuel Martín-Flores, Nicolás J. Litterio, Martin A. Himelfarb, Sergio H. Invaldi, María P. Zarazaga

Abstract — Morphine is widely used as a preanesthetic agent in dogs, but it often produces signs of nausea and vomiting. Maropitant (MRP) and metoclopramide (MCP) prevent emesis attributable to the opioid agent apomorphine in dogs. We evaluated the antiemetic efficacy and the discomfort in response to SQ injection of MRP [1 mg/kg body weight (BW)], MCP (0.5 mg/kg BW), and normal saline (SAL; 0.1 mL/kg BW) administered to 63 dogs, 45 minutes prior to morphine (0.5 mg/kg BW) and acepromazine (0.05 mg/kg BW). Dogs were observed for signs of nausea (ptyalism, lip licking, and increased swallowing) and vomiting for 30 minutes after morphine/acepromazine. The incidence of emesis was 0% for MRP, 38% for MCP, and 71% for SAL ($P < 0.001$). The incidence of signs of nausea was not different between groups. Discomfort due to injection was higher after MRP (48%), than after MCP (9.8%) and SAL (4.8%) ($P < 0.001$).

Résumé — Comparaison entre le maropitant et la métoclopramide pour la prévention de nausée et des vomissements induits par la morphine chez les chiens. La morphine est largement utilisée comme agent préanesthésique chez les chiens, mais elle produit souvent des symptômes de nausée et de vomissements. Le maropitant (MRP) et la métoclopramide (MCP) préviennent le vomissement causé par l’agent opioïde apomorphine chez les chiens. Nous avons évalué l’efficacité antiémétique et l’inconfort en réponse à une injection SC de MRP [1 mg/kg de poids corporel (PC)], de MCP (0,5 mg/kg PC) et d’une solution saline normale (SAL; 0,1 mL/kg PC) administrée à 63 chiens, 45 minutes avant la morphine (0,5 mg/kg PC) et l’acépromazine (0,05 mg/kg PC). Les chiens ont été observés pour détecter des signes de nausée (ptyalisme, léchement des lèvres et déglutition accrue) et le vomissement pendant 30 minutes après l’administration de morphine/acépromazine. L’incidence du vomissement était de 0% pour MRP, de 38% pour MCP et de 71% pour SAL ($P < 0.001$). L’incidence des signes de nausée n’était pas différente entre les groupes. L’inconfort attribuable à l’injection était supérieur après MRP (48%) par rapport à celui après MCP (9,8%) et SAL (4,8%) ($P < 0.001$).

Can Vet J 2017;58:35–38

Introduction

Morphine and acepromazine are widely used as preanesthetic agents in dogs. However, morphine produces gastrointestinal disturbances including constipation, salivation, signs of nausea, and vomiting (1), the latter two being particularly important as they not only produce discomfort, but may also increase the risk for aspiration of the vomitus (2,3). Morphine is a potent emetogenic agent; the incidence of emesis ranges between 50% and 75% after IM administration of 0.5 mg/kg body weight (BW) (4,5). Acepromazine is commonly administered with morphine, and while it has antiemetic effects via dopamine D2 receptor antagonism, its use reduces, but does not eliminate the incidence of morphine-induced emesis when administered simultaneously with morphine (4).

Additional antiemetic agents might be used to prevent signs of nausea and vomiting and improve the overall quality and comfort of the peri-anesthetic period. Maropitant (MRP) is a neurokinin-1 receptor antagonist that inhibits substance P and has potent anti-emetic effects (6). Maropitant completely prevented morphine-induced vomiting when administered SQ 30 to 45 min prior to an opioid (7,8). Administration of MRP, however, does not consistently reduce signs of nausea (7,9) or the incidence of gastroesophageal reflux (10), and causes pain at the injection site (5,8,11).
Metoclopramide (MCP) exerts its antiemetic effects via dopamine D2 and serotonin 5-HT3 antagonism. Additionally, it has a prokinetic effect in the upper segment of the gastrointestinal tract via serotonin 5-HT4 agonism; it increases the tone of the lower esophageal sphincter, and increases gastric and duodenal motility (12). The antiemetic efficacy of subcutaneous MCP for apomorphine-induced emesis in dogs is similar to that of MCP (13). Moreover, MCP reduces the incidence of gastroesophageal reflux in anesthetized dogs (14). To our knowledge, it has not been reported that MCP injection results in pain. Providing apomorphine-induced emesis in dogs is similar to that of MCP (13). Moreover, MCP reduces the incidence of gastroesophageal reflux in anesthetized dogs (14). To our knowledge, it has not been reported that MCP injection results in pain. Providing similar efficacies in preventing opioid-induced emesis, there might be advantages to the use of MCP in the perianesthetic period in dogs.

In this investigation we evaluated the anti-nausea and antiemetic effects of MRP and MCP, administered 45 min prior to morphine/acepromazine to healthy dogs. Our null hypothesis was that the incidences of signs of nausea and vomiting would be equal for both agents. In addition, we evaluated signs of discomfort after subcutaneous administration of either antiemetic agent.

### Materials and methods

This study was approved by the Committee on Bioethics and Animal Welfare of Universidad Católica de Córdoba. We enrolled 63 adult mixed-breed dogs, American Society of Anesthesiology (ASA) classification I (based on physical examination, complete blood cell count and basic serum biochemistry consisting of total serum protein, blood urea nitrogen, and blood glucose), and scheduled for orchietomy or ovariohysterectomy as part of a canine population control program. Owner’s consent was requested prior to the inclusion of the animals in the study. Solid food was withheld overnight but dogs had access to water until 1 h prior to the beginning of the study. Dogs with a history of vomiting, inappetence, diarrhea, abdominal pain, or concurrent treatment with drugs that affect gastrointestinal motility or produce signs of nausea and vomiting in the last month were excluded. This study was designed as a randomized, blinded, prospective controlled trial, and was completed within a period of 1 mo. The experiments were carried out 3 days a week, in groups of 4 to 6 animals. Dogs were weighed prior to the beginning of the experiment, as part of the pre-surgical physical examination. All dogs received morphine 1% (Amiadiz; Laboratorios Richmond, Buenos Aires, Argentina), 0.5 mg/kg BW, IM, and acepromazine 1% (Acedan; Laboratorios Hollyday, Buenos Aires, Argentina), 0.05 mg/kg BW, IM, in the middle gluteal muscle at time zero, as part of their preanesthetic medication. Dogs were randomly assigned to 1 of 3 treatment groups of 21 animals each by extracting labels from an opaque envelope: MRP 1% (Cerenia; Pfizer PGM, Péocé sur Cisse, France), 1 mg/kg BW; MCP 0.5% (Pileran; Laboratorios Hollyday), 0.5 mg/kg BW; and a control group receiving normal saline (SAL; 0.1 mL/kg BW). MRP, MCP or SAL was administered SQ between the shoulders 45 min before morphine and acepromazine by 1 investigator (MAH) who was unaware of treatment allocation. The dogs were observed for signs of discomfort after injection of the treatment solutions. Discomfort to injection was considered to occur when the dogs vocalized and/or attempted to bite the skin at the site of injection, immediately after administration of either solution. After the administration of morphine/acepromazine, each dog was observed continuously for 30 min for signs of nausea (ptalism, lip licking, and increased swallowing), retching, or vomiting. Vomiting was recorded when there was expulsion of gastric contents through forceful contractions of the abdominal muscles, and retching was considered as a nonproductive act of vomiting. In dogs that vomited, the time to the first emesis and number of emetic events per dog [median (minimum – maximum)] and the incidence of pain after injection are also reported. Different superscript letters indicate significant differences between groups.
veterinary medicine students who registered each event. All students were supervised by 3 of the authors (NJL, MPZ, SHI); the students and supervisors were unaware of treatment allocation.

**Statistical analysis**

Data were analyzed using commercial software (InfoStat 2008; Grupo InfoStat, FCA, Argentina). Nonparametric distribution of all continuous variables was confirmed with the Shapiro-Wilk test. Age, body weight, and distribution of gender were compared between groups with the Kruskal-Wallis test. The incidence of signs of nausea, retching, and vomiting, and the incidence of discomfort to treatment administration were compared between groups with the Kruskal-Wallis test by ranks. Time to first emesis and the number of emetic events per dog were also compared between groups with the Kruskal-Wallis test by ranks. Results are reported as median (minimum-maximum). Significance was set at 5% throughout.

**Results**

All animals completed the study. No differences were observed between groups for age, body weight, and gender (Table 1). The incidence of signs of nausea was not different between the 3 groups (Table 2). Retching occurred less frequently with MRP than in the 2 other groups, and was not different between MCP and SAL. Maropitant prevented emesis, and MCP reduced its incidence compared with SAL (Table 2). When emesis occurred, the number of emetic events per dog and the time to first emetic event were not different between MCP and SAL.

Discomfort following injection was observed more frequently with MRP than in the 2 other groups (Table 2).

**Discussion**

The main findings of this study are that MRP (1 mg/kg BW) administered SQ 45 min prior to morphine and acepromazine prevented vomiting and substantially reduced the incidence of retching, but did not reduce the incidence of signs of nausea in dogs. The efficacy of MCP as an antiemetic was less than that of MRP; it reduced the incidence of vomiting by ~50% compared with saline, and it did not produce a noticeable reduction of signs of nausea.

The high efficacy of MRP to prevent opioid-induced emesis is in accord with previous findings. MRP (1 mg/kg BW, SQ) abolished emesis induced by hydromorphone when administered 30 to 45 min prior to the opioid (7,8). MRP (1 mg/kg BW, SQ) was also evaluated in dogs receiving morphine; in that study, it reduced morphine-induced emesis by 70% when administered 30 min in advance (9). The apparent lower efficacy between both studies might be the result of insufficient time for MRP to peak, or differences in the emetogenic potencies of the 2 opioids: the incidence of emesis after IM administration of morphine (0.5 mg/kg BW) was 75% while that of hydromorphone (0.1 mg/kg BW) was 44% (4). In our study, we increased the interval between MRP and morphine administration to 45 min, and this resulted in 100% reduction of emesis in that group. Taken together, these data suggest that when used to prevent emesis from morphine, > 30 min are necessary for MRP to exert its maximal effect.

In the present study, MCP (0.5 mg/kg BW, SQ) reduced the incidence of emesis by 53%, which was significantly lower than that produced by MRP. This observation is at odds with previous findings showing that MCP (0.5 mg/kg BW) prevented apomorphine-induced emesis in dogs. Apomorphine is typically considered a potent emetogenic agent, and it shares with morphine the mechanisms for producing vomiting. This discrepancy between the results of that study and ours highlights the limitations of extrapolating data when different emetogenic agents are used. In closer agreement with our current results, the antiemetic efficacy of MCP was less than that of MRP when emesis was the result of various disease processes, including gastroenteritis, pancreatitis, uremia, and poisoning (11).

Signs associated with nausea were not reduced by the administration of either MRP or MCP. These findings are in agreement with previous reports showing a limited effect of MCP (1 mg/kg BW, SQ) (7,8,15) and MCP (0.55 mg/kg BW, IM) (15) as anti-nausea medication against other emetogenic agents, such as lycorine (2 mg/kg BW, SQ) and hydromorphone (0.1 to 0.2 mg/kg BW, IM). Only MRP (1 mg/kg BW) prevented signs of nausea when administered SQ 60 min before administration of hydromorphone (0.1 mg/kg BW, IM) (8).

The number of emetic events and time to first emesis in those dogs that vomited was not different between groups MCP and SAL. Most dogs vomited before 10 min in both groups, with only 1 dog in group MCP and 2 dogs in group SAL vomiting after 10 min. We saw no evidence that MCP (0.5 mg/kg BW, SQ) either reduced the number of emetic events per dog, or delayed the onset of emesis; it appears that emesis is either prevented or not in each individual dog, as an all-or-none phenomenon.

In the present study, 48% of the dogs receiving MRP (1 mg/kg BW) showed signs of discomfort after SQ injection, and this was significantly higher than the 9.5% in those receiving MCP (0.5 mg/kg) or the 4.8% receiving SAL (0.1 mL/kg BW). Behavioral signs of discomfort were transient, and resolved quickly. The incidence of this adverse reaction in our study was higher than that reported by the manufacturer (4%) or other authors (4 to 11%) (8,5,11). The discrepancy between our results and those from other authors is likely due to different criteria for evaluating the dogs’ responses to injections. A study in cats reported a high incidence of adverse reactions to SQ administration of MRP (1 mg/kg BW) (16). Moreover, those authors suggested that the responses were often severe.

In summary, our results show that MRP prevents vomiting, and that MCP has a moderate antiemetic efficacy, when either antiemetic agent was administered 45 min prior to morphine and acepromazine. Neither agent was effective in preventing signs of nausea. Injection of MRP was associated with signs of discomfort more frequently than occurred with MCP or saline.

**Acknowledgments**

This study was funded by Universidad Católica de Córdoba. The authors thank Drs. M. Priotto, C. Ghersевич, and X. Rodríguez-Bertola of the Canine Population Control Program of the Universidad Católica de Córdoba for their assistance in making this study possible.
References


Comparison of complication rates of unilateral, staged bilateral, and single-session bilateral surgery for the treatment of bilateral medial patellar luxation in dogs

Bronwyn A. Fullagar, Päivi Rajala-Schultz, Bianca F. Hettlich

Abstract — This retrospective study compared complication rates in 93 client-owned dogs (119 stifles) undergoing single-session bilateral, staged bilateral, or unilateral surgery for bilateral medial patellar luxation. Clinical characteristics and complication rates were compared and risk factors for major complications were explored. Sixty-five dogs had unilateral, 16 staged bilateral and 11 single-session bilateral surgery. Complications occurred in 28/119 stifles (24%), 11 (9%) of which required revision surgery. Patellar reluxation occurred in 7/119 (6%) stifles, with no revision required. There was no significant association between timing of surgery and incidence of complications. In dogs < 10 kg with bilateral medial patellar luxation, single-session bilateral surgery is a feasible treatment option with a complication rate comparable to staged bilateral or unilateral medial patellar luxation surgery.

Résumé — Comparaison des taux de complication de la chirurgie unilatérale, bilatérale à étage, et bilatérale à session unique pour le traitement de la luxation patellaire chez le chien. Cette étude rétrospective a comparé les taux de complications observés chez 93 chiens de propriétaires (119 genoux) subissant une chirurgie bilatérale simultanée, une chirurgie bilatérale en deux temps ou une chirurgie unilatérale pour luxation médiale de la rotule bilatérale. Les données cliniques et les taux de complications ont été comparés et les facteurs à risque de complications majeures ont été étudiés. 65 chiens ont subi un traitement unilatéral, 16 un traitement bilatéral en deux temps et 11 un traitement bilatéral simultané. Des complications sont survenues dans 28/119 grassets (24 %), dont 11 (9 %) ont nécessité une chirurgie de révision. Une relaxation de la rotule s’est produite dans 7/119 grassets (6 %), sans qu’une révision n’ait été nécessaire. Aucune association significative entre le planning chirurgical et l’apparition de complications n’a pu être mise en évidence. Chez les chiens < 10 kg souffrant de luxation médiale de la rotule bilatérale, une chirurgie bilatérale simultanée est une option thérapeutique valable, possédant un taux de complications comparable à celui de la chirurgie en deux temps ou seulement unilatérale.

(Traduit par les auteurs)

Introduction

Patellar luxation (PL), due to malalignment of the quadriceps mechanism, is one of the most common orthopedic conditions of the canine stifle and results in progressive pain, cartilage wear, and osteoarthritis (1–4). The etiopathogenesis of patellar luxation has been extensively reviewed elsewhere (4–7). Medial patellar luxation (MPL) occurs more commonly than lateral patellar luxation in both small breed (95% to 98% of PL cases) and large breed (67% to 83%) dogs (1–8), and approximately 50% of dogs with MPL are bilaterally affected (5,8–12). In clinically affected individuals with MPL, surgical realignment of the quadriceps-patellar mechanism is indicated and various surgical procedures, including bony and soft tissue reconstruction, have been described (4,5,7–10,12–16). Clinical outcome is improved in > 90% of dogs treated surgically (8–10,14), although lack of standardization of surgical
procedure and grade of luxation makes comparison of reported outcomes challenging. Reported surgical and postoperative complications include patellar relaxation, delayed healing or nonunion of the osteotomy, implant infection, implant failure or loosening, fracture/avulsion of the tibial tuberosity, fracture of the lateral trochlear ridge, septic arthritis, wound dehiscence and seroma formation (3,11,17,18). Complication rates range from 18% to 43%, with 7% to 18% of cases experiencing major complications that require surgical revision (8,10–12,19–21). Increasing grade of luxation, body weight > 20 kg and concurrent cranial cruciate ligament (CCL) rupture have been identified as risk factors for postoperative complications (7,10,11,19).

In patients with bilateral patellar luxation, most reports advocate staged surgical procedures 4 to 12 wk apart (8,10,12,14,22). Recently, single-session bilateral surgery for correction of MPL was described in 27 dogs (20). That study included only dogs weighing < 12 kg, and found no significant difference in complication rates or overall outcome between dogs that underwent unilateral or single-session bilateral MPL surgery. A small number of dogs (n = 3) in that study underwent staged bilateral surgery, but these were not analyzed as a separate group. Two other studies (19,21) have supported the finding of similar complication rates in dogs which underwent single-session bilateral surgery compared to unilateral surgery for MPL. However, those studies included dogs with both unilateral and bilateral MPL, as well as concurrent orthopedic abnormalities such as CCL rupture. Conversely, another recent study (18) investigated lateral patellar luxation in dogs and found single-session bilateral surgery to be significantly associated with patellar relaxation. Single-session bilateral tibial plateau leveling osteotomy (TPLO) and tibial tuberosity advancement have been reported for the treatment of dogs with bilateral CCL rupture (23–29). Advantages over staged bilateral procedures include reduced total anesthetic time, more rapid overall recovery, reduced owner expense, and prevention of disease progression of the non-operated limb during recovery (24,25). Some authors report no difference in complication rates compared to unilateral or staged bilateral procedures (23–25), while others found a significantly increased incidence of major complications, such as tibial tuberosity fracture, following single-session bilateral procedures (27,28,29).

The purpose of this retrospective study was to compare complication rates in dogs with bilateral MPL undergoing single-session bilateral surgery to those that had unilateral or staged bilateral surgery. By including dogs that underwent staged bilateral surgery as a separate group, we aimed to more accurately assess the effect of surgical timing on complication rates in dogs with bilateral clinical signs. We hypothesized that there would be no significant differences in complication rates or outcome among the 3 groups, supporting the recent evidence that single-session bilateral surgery for MPL is a feasible treatment option for selected dogs.

**Materials and methods**

**Case selection**

Medical records of dogs with bilateral medial patellar luxation that underwent surgery at The Ohio State University Veterinary Medical Center between 1999 and 2012 were identified through the hospital’s surgical database. Data extracted from the medical records included breed, age, gender, body weight at surgery, MPL grade (1 to 4), duration of lameness before surgery, concurrent orthopedic disease and surgical procedure. Details regarding the timing of surgery were obtained. The procedure was classified and dogs were categorized into 3 groups as follows: i) unilateral if 1 stifle was operated and the other stifle had not had MPL surgery; ii) staged bilateral if both stifles had been operated on separate occasions; or iii) single-session bilateral if both stifles had MPL surgery during the same anesthetic session. Intra- and postoperative complications were identified from the medical record, evaluation of postoperative radiographs (if available) and by telephone follow-up with owners and referring veterinarians (> 6 wk after surgery). If less than 6 mo of follow-up was available in hospital medical records, owners were contacted via telephone and a series of standardized questions were asked, to determine whether further medical or surgical treatment was required for MPL in the operated limb(s) since the last discharge from our hospital. In addition, owners were asked to grade the function of each operated limb on a scale of 0 to 10, where 0 indicated consistent, non-weight bearing lameness on the operated limb, and 10 indicated normal limb use with no lameness or stiffness. Owners were also asked whether their dog was currently being given pain relief medications to treat stifle pain and stiffness, and how they thought function on the operated limb was compared to normal, pre-injury function. If owners were unavailable for questioning, referring veterinarians were contacted and asked to review their medical records to determine whether any complications associated with MPL surgery had been noted, or whether any additional medical or surgical treatments had been prescribed. They were also asked to grade the dog’s function on its operated limb(s) on a scale of 0 to 10 in the same fashion as owners were asked. However, if the veterinarian who had evaluated the patient was not available for questioning, functional assessment was extrapolated from description of limb use available in the rDVM medical records. Limb function was then graded according to the scheme proposed by Cook et al (30), with full function defined as restoration to full intended level and duration of activities and performance from predisease status without medication; acceptable function defined as restoration to intended activities and performance from predisease status that is limited in level or duration and/or requires medication to achieve; and unacceptable function defined as all other outcomes. Complications were classified as major if further surgery was required (e.g., implant removal, repeat stabilization), or minor if the complication resolved without surgical intervention (e.g., minor wound dehiscence, seroma, or mild relaxation not resulting in lameness).

**Inclusion criteria**

Dogs were included if they had documentation of bilateral medial patellar luxation, had intact cranial cruciate ligaments, and did not undergo concurrent orthopedic procedures at the time of MPL surgery (e.g., distal femoral osteotomy, femoral head ostectomy, total hip replacement, or TPLO). Only dogs with primary MPL (not secondary to trauma, fracture, infection, or...
other developmental orthopedic disease) that had not undergone previous stifle surgery on the operated limb(s) were included.

**Statistical analyses**

Descriptive statistics on the signalment of dogs (body weight, age, gender) as well as grade of MPL, the surgical techniques used (sulcoplasty and tibial tuberosity transposition (TTT)) and proportion of stifles experiencing major or any complications were calculated and compared between groups using Kruskal-Wallis non-parametric analysis of variance (ANOVA) (continuous variables; body weight, and age) or Chi-square test (or Fisher’s exact test, as needed due to small sample size). To evaluate potential predictors both for any or major complications after MPL surgery, GLIMMIX procedure in SAS (Statistical Analysis System, v.9.3; SAS Institute, Cary, North Carolina, USA), with binomial distribution and logit link was used. With the occurrence (yes/no) of complications as the outcome, the impact of body weight, age, and gender of the dogs, timing of the surgery (unilateral, staged, and single-session bilateral), grade of MPL (1 to 4), and whether sulcoplasty (none, wedge recession, block recession, or abrasion) and TTT (yes/no) were performed on the likelihood of complications was assessed. Occurrence of any complications (major and minor combined) and only major complications were used as the outcome in separate analyses. To adjust for the correlated data structure (some dogs having both stifles operated), dog was included in the models as a random effect. Additional models were run to evaluate the effect of surgical timing on incidence of complications after excluding dogs that did not undergo TTT from the analyses. Significance was set at \( P \leq 0.05 \).

**Results**

Ninety-seven dogs (127 stifles) met the inclusion criteria. Four dogs (8 stifles) were lost to follow-up and were excluded from the study. Of the 93 remaining dogs (119 stifles), 65 had unilateral surgery, 16 dogs (32 stifles) had staged bilateral surgery and 11 dogs (22 stifles) had single-session bilateral surgery. For dogs that had bilateral MPL but underwent unilateral surgery (group 1), 40/65 dogs had a lower grade (grade 1 or 2) MPL on the contralateral, non-operated limb, that was deemed at the time of initial examination to be either non-clinical or causing only minor, intermittent lameness. In 25/65 dogs, the grade of patellar luxation at initial examination was reported to be the same bilaterally (grade 2 or 3). At our institution, the recommendation to proceed with surgery on the contralateral limb was made at the 6- to 8-week follow-up visit, based on clinical signs of lameness or unacceptable function in the non-operated limb. The final decision of whether to proceed with a second surgery was determined by owners. The median duration of follow-up was 25 mo (range: 6 wk to 8.4 y). Median follow-up times for the unilateral, staged bilateral, and single-session bilateral groups were 20 mo, 35 mo and 22 mo, respectively. Thirty-seven dogs (40%) were male and 56 (60%) were female. Thirty-one breeds were represented. The most common were mixed breed (n = 23), Yorkshire terrier (n = 11), Chihuahua (n = 7), Labrador retriever (n = 6), and Cavalier King Charles spaniel (n = 6). The median age was 1.75 y (range: 7 mo to 11 y). There was no significant difference in median age between dogs that underwent unilateral surgery (median: 1.5 y), staged bilateral surgery (2 y) and single-session bilateral surgery (1.5 y) (\( P = 0.458 \)). The median body weight was 6.6 kg (range: 1.5 to 54 kg). Dogs which underwent single-session bilateral surgery (median: 4.0 kg) were lighter than dogs that underwent staged bilateral (median: 5.3 kg) or unilateral (median: 7.7 kg) surgery, but this difference did not reach statistical significance (\( P = 0.062 \)). Of 119 included stifles, 1 (0.8%) had grade 1, 51 (42.9%) had grade 2, 53 (44.5%) had grade 3, and 14 (11.8%) had grade 4 MPL. The median grade of luxation was 3 for all groups.

Femoral trochlear sulcoplasty was performed in 112 (94%) stifles. Of these, 48 (43%) stifles had block recession, 34 (30%) stifles had abrasion sulcoplasty, and 30 (27%) stifles had wedge recession. Tibial tuberosity transposition (TTT) was performed in 100 (84%) stifles. In 24 of these stifles, the osteotomy was stabilized with 2 or 3 k-wires and a figure-of-eight tension band wire, in 66 stifles the TTT was stabilized with k-wires (minimum 2) alone, and in 10 stifles, a cerclage wire was used in a mattress pattern to stabilize the osteotomy, without the use of pins. An anti-rotational lateral suture was performed in 2 stifles. Soft tissue augmentation was performed in all stifles in the study population, and consisted of lateral capsular or fascial imbrication and/or medial release. Lateral imbrication alone was performed in 38/119 (32%) stifles, medial release alone was performed in 1119 (0.8%) stifle, and both procedures were performed in 80 (67%) stifles. The decision to proceed with various surgical augmentations was at the discretion of the surgeon.

Follow-up was available in the form of rechecks at the surgical institution for 38/65 stifles (group 1), 12/32 stifles (group 2), and 8/22 stifles (group 3). For 15/65 (group 1), 13/32 (group 2), and 8/22 stifles (group 3) stifles, telephone follow-up with owners and medical records at our institution were available. For 3/65 (group 1), 7/32 (group 2), and 2/22 (group 3) stifles, telephone follow-up with owners was the sole means of follow-up and for 9/65 (group 1), 0/32 (group 2), and 4/22 (group 3) stifles rDVM medical records were the only available follow-up. Repeat radiographs at > 6 wk after surgery were available for review in 46/65 (70.7%) stifles in group 1, 21/32 (65.5%) stifles in group 2, and 14/22 (63.6%) stifles in group 3. Postoperative complications occurred in 28 of 119 (24%) stifles and were reported a median of 8 wk after surgery. Minor complications occurred in 17 (14%) stifles and included low-grade patellar relaxation (n = 7), intermittent mild lameness (n = 3), soft tissue irritation associated with pins (n = 6), and delayed wound healing (n = 1). Of 7 stifles (5 dogs) that experienced patellar relaxation, 1/7 was grade 1, 4/7 were grade 2, and in 1 dog hospital medical records state both patellae were reduced at 8 wk after surgery, but follow-up telephone correspondence with the referring veterinarian identified bilateral relaxation of unknown grade. Pre-operative grade was 3 or 4 in all stifles that experienced relaxation. In 5/7 stifles with patellar relaxation, owner-assessed function was graded full or acceptable at telephone follow-up.

Major complications that necessitated further surgery occurred in 11 (9%) stifles and included pin-related complications.
For the 8 dogs (11 stifles) that experienced a complication in group 2 (staged bilateral surgery), the complication occurred in the second stifle operated in 3 dogs, the first stifle operated in 2 dogs and in both stifles in 3 dogs. Major complications occurred in 6 (9%) stifles in the unilateral surgery group, 3 (9%) stifles in the staged bilateral group, and 2 (9%) stifles for which single-session bilateral surgery was performed (Figure 1). No significant association was identified between timing of surgery and incidence of overall complications ($\chi^2 = 3.03; P = 0.220$) or major complications (Fisher’s exact $P = 0.999$).

For dogs undergoing unilateral surgery, function was graded as full in 52.3% (34/65), acceptable in 43% (28/65) and unacceptable in 4.6% (3/65) of stifles. In the staged bilateral group, 53.1% (17/32) of stifles returned to full function, 43.8% (14/32) of stifles had acceptable function and 3.1% (1/32) had unacceptable function. Function for dogs in the single-session bilateral surgery was considered full in 77.3% (17/22) of stifles, acceptable in 18.2% (4/22) of stifles and unacceptable in 4.5% (1/22) of stifles.

After controlling for the effect of dogs undergoing surgery on both limbs, mixed-effect logistic binomial regression revealed no significant association between gender, body weight, MPL grade, age, surgical timing, sulcoplasty type or TTT and incidence of complications. When dogs that did not undergo a TTT were excluded, no significant association was identified between major complication ($P = 0.9937$) or any complication ($P = 0.513$) and surgical timing. Stifles that had staged bilateral surgery were 1.96 times more likely to experience a complication (major or minor) than stifles undergoing unilateral surgery, and 1.92 times more likely to experience a complication than stifles in the single-session bilateral group. However, these differences were not statistically significant ($P = 0.269$ and $P = 0.429$, respectively).

### Discussion

In this study population, single-session bilateral surgery was not associated with an increase in overall or major complication rate, which supports our hypothesis, as well as the findings of other recent studies (19–21). The complications reported here are similar to those of previous studies (8,10–12,19,21), and our overall (24%) and major (9%) complication rates compare favorably. However, many previous studies included dogs with both medial and lateral patellar luxation, as well as those which had concurrent CCL rupture or which had undergone previous stifle surgery. One study (12) of MPL surgery excluded dogs with CCL rupture and reported a major complication rate of 6.6%. However, in that study, additional surgery for TTT implant removal was not classified as a major complication since all implants were removed as standard at the 8-week postoperative recheck.

One recent study (20) compared complication rates and outcomes in small breed dogs with bilateral MPL which underwent either unilateral or single-session bilateral surgery. They found no significant difference in complication rate or outcome between groups. However, most dogs which underwent unilateral surgery in that study did not have clinical signs on the opposite side. Through inclusion of dogs that underwent staged bilateral surgery as a separate group, we were able to more effectively assess the effect of surgical timing on complication rate and outcome, since all dogs in groups 2 and 3 had bilateral clinical signs of MPL. In addition, to adjust for the correlated data structure (repeated measurements performed in the same dog), ‘dog’ was included in the statistical model as a random effect. This served to account for the effect of individual patient characteristics on incidence of complications, so that other factors (including timing of surgery) could be evaluated more accurately.

In order to maintain consistency across groups and allow for analysis of the effect of surgical timing on complication rate, dogs that underwent additional orthopedic procedures at the time of MPL correction were excluded from the study. In doing so, many large breed dogs were excluded, which may have influenced the complication rates of groups 1 and 2. Distal femoral osteotomy (DFO) has been reported to reduce the incidence of patellar luxation in large breed dogs with MPL and excessive distal femoral varus angle $\geq 12^\circ$ (15). Craniocaudal femoral radiographs were not available for all large breed dogs in our study population which underwent MPL correction without DFO, so it is not possible to determine whether their post operative complications were a result of failure to address excessive distal femoral varus.

Similarly, dogs with concurrent CCL rupture were excluded from this study to more accurately evaluate surgical timing as a risk factor for complications. Incidence of CCL rupture in dogs with patellar luxation has been reported as 12% to 41% in small breed dogs (8,31) and 5% to 20% in large breed dogs.
Earlier reports suggested that patellar luxation increases stress on the CCL, predisposing it to rupture (7,9). However, Hayes et al (1) found the incidence of CCL rupture in dogs with patellar luxation to be no higher than in dogs with other orthopedic conditions. Historically, dogs without concurrent stifle pathology had better outcomes (96% good outcome) compared to dogs with concurrent CCL rupture, meniscal injury, or existing osteoarthritis (79% good outcome) (7). More recently, CCL status was found to have no effect on complication rates following MPL correction (10,11).

Body weight > 20 kg has been identified as a risk factor for major complications and patellar relaxation following MPL surgery (10,11,19). In our study, increasing body weight did not increase the risk of major complications, which supports the findings of another recent study (21). However, case selection in this study was biased toward smaller dogs, due to exclusion of dogs that had corrective osteotomies. All dogs that underwent single-session bilateral surgery weighed < 10 kg and their median body weight was lower than dogs in the other 2 groups, which may have contributed to their low complication rate. The lack of uniformity of patient body weight among surgical groups was a limitation of this retrospective study. In addition, our low sample sizes may have meant that lack of association between patient weight and complications was due to lack of power and a result of type II statistical error. However, since dogs with other conformational or orthopedic abnormalities were excluded, some of the risk of complications associated with increasing body weight may have been mitigated.

Increasing grade of relaxation has also been associated with increased risk of complications in some studies (9,11,21), but not in others (8,10,20,22). In our study, there was no significant association between MPL grade and complication rate, although all dogs that experienced patellar relaxation had preoperative grades of 3 or 4. Concurrent CCL rupture is reportedly more likely to be present in dogs with grade 4 MPL (31). By excluding dogs with CCL rupture, dogs with lower grade MPL may have been selected for the study, which may have confounded the results.

Patellar relaxation was reported in 7 of 119 (6%) stifles in this study, which compares favorably to previous studies. Relaxation rates of 6% to 48% have been reported, but inconsistent follow-up is likely to have resulted in under-reporting of low-grade relaxation in most studies (8,11,12,14). In this retrospective study, grade 1 relaxation is likely to have been under-reported, since incidence of complications was determined largely by review of medical records and telephone follow-up with owners. However, no dogs in this study required revision surgery for patellar relaxation, which is in contrast to previous studies. This may be because most (84%) dogs received a TTT as part of their surgical correction, which reportedly reduces the incidence of patellar relaxation (10–12,21). Trochleoplasty procedure was not associated with incidence of complications in this study. Some previous studies describe lack of a trochleoplasty to predispose dogs to patellar relaxation (10,18,21), whereas others have reported a comparable rate of relaxation (19.8%) in dogs of all MPL grades that did not have a groove deepening procedure (12). A cadaver study found that block recession trochleoplasty was superior to wedge recession in preservation of articular cartilage, proportion of trochlear surface area recessed, and resistance to patellar luxation proximally (32). However, these results have yet to be validated by clinical studies.

Implant-associated morbidity following TTT was the most common major complication in our study, which supports the findings of 2 recent studies (19,21). Only dogs that underwent TTT experienced a major complication. However, pin migration and subsequent removal was not necessarily associated with poor outcome, raising the question of whether the definition of a major complication should be reconsidered to reflect outcome. In our study population, the rates of tibial tuberosity avulsion (0.8%) and implant failure were lower than in previous reports (2.9% to 13.8%) (19,21). However, those studies found an increased risk of implant failure or tuberosity avulsion when a screw (19) or a single Kirschner wire (21) was used to stabilize the osteotomy. All of the TTTs in this study were stabilized with at least 2 Kirschner wires and screw fixation was not used.

When dogs that did not have a TTT were excluded from the model and complications were again compared between surgical groups, there was a trend towards increased risk of complications in stifles that had staged bilateral surgery. Previous studies have reported unilateral or staged bilateral surgery in dogs with bilateral MPL and did not find that the non-operated limb was adversely affected by the delay (10,13,21). The significance of this trend in our results is unclear and it is probably the result of low sample sizes.

This study has several important limitations. Due to its retrospective nature, the selection of cases for each of the 3 groups was not randomized and there was bias towards selecting for smaller patients for single-session bilateral surgery. Multiple board-certified surgeons, as well as surgery residents under direct diplomate supervision operated on patients, and surgical procedures were not standardized, rather, they were at the discretion of the surgeon. However, due to the variable stifle conformation and degrees of bony and soft tissue pathology present in dogs with MPL, standardization of surgical procedures would be challenging and may result in increased morbidity for the patient. Finally, our small sample size, especially in the staged and single-session bilateral groups, may have led to type II error when comparing complication rates.

Another study limitation is lack of consistent, objective follow-up. Many patients were taken to their referring veterinarian for postoperative rechecks, meaning that orthopedic examination findings and recheck radiographs were not available for review in all cases. However, the overall median follow-up time in our study was longer than that of previous studies (19–21), providing more definitive evidence of favorable long-term outcomes in patients following MPL surgery. Our assessment of complications in many cases relied on telephone conversations with owners, which may have resulted in under-reporting of minor complications, especially patellar relaxation. However, the major complication rate was likely accurate, since most owners remember whether their dog had revision surgery.

The results of this study support the findings of others that single-session bilateral surgery for MPL is a feasible treatment.
option in selected cases, specifically in dogs < 10 kg, with a complication rate comparable to staged bilateral or unilateral MPL surgery. Further investigation, in the form of prospective, randomized, clinical studies involving a greater number of patients (including large-breed dogs) and objective, long-term follow-up is warranted.

Acknowledgment

The authors thank Dr. John Bonagura for his assistance with the statistical analyses on this project.

References

Analysis of canine urolith submissions to the Canadian Veterinary Urolith Centre, 1998–2014

Doreen M. Houston, Heather E. Weese, Nick P. Vanstone, Andrew E.P. Moore, J. Scott Weese

Abstract — Understanding urolith trends and risk factors is important for understanding urolithiasis, which is a common problem in dogs. This study evaluated 75 674 canine cystolith submissions to the Canadian Veterinary Urolith Centre between 1998 and 2014. Struvite and calcium oxalate uroliths comprised 80.8% of all uroliths, with calcium oxalate outnumbering struvite. There were significant increases in the proportions of calcium oxalate, mixed and cystine uroliths, and significant decreases in struvite, urate, silica, and calcium phosphate carbonate over the study period. Breeds associated with increased risk of calcium oxalate urolithiasis tended to be small breeds, while those that were at increased risk of struvite urolith formation were larger breeds. Dalmatians were at increased risk of forming both urate and xanthine uroliths while Scottish deerhounds had a remarkably high association with cystine urolithiasis. Males were more likely to form calcium oxalate and metabolic uroliths and females were more likely to develop struvite and mixed uroliths.

Résumé — Analyse des soumissions d’urolithes canins au Canadian Veterinary Urolith Centre, 1998–2014. Il est important de comprendre les tendances et les facteurs de risque des urolithes pour comprendre l’urolithiase, qui est un problème fréquent chez les chiens. Cette étude a évalué 75 674 soumissions d’urolithes canins au Canadian Veterinary Urolith Centre entre 1998 et 2014. Les urolithes de struvite et d’oxalate de calcium représentaient 80,8 % de tous les urolithes, et le nombre de soumissions d’oxalate de calcium dépassait celui des soumissions de struvite. Il y avait des hausses importantes dans les proportions d’oxalate de calcium, des urolithes mixtes et de cystine et des baisses importantes de la struvite, de l’urate, de la silice et du carbonate de phosphate de calcium pendant la période à l’étude. Les races associées à un risque accru d’urolithiase d’oxalate de calcium étaient surtout des petites races tandis que celles qui présentaient un risque accru de formation d’urolithes de struvite étaient les grandes races. Les Dalmatiens présentaient un risque accru de formation d’urolithes d’urate et de xanthine tandis que les Deerhounds avaient une association remarquablement élevée avec l’urolithiase de cystine. Il était plus probable que les mâles forment des urolithes d’oxalate de calcium et des urolithes métaboliques et il était plus probable que les femelles développent des urolithes de struvite et mixtes.

Introduction

Urolithiasis is an important problem in dogs and cystoliths of various compositions can be encountered. While relative proportions of urolith types vary, struvite (magnesium ammonium phosphate hexahydrate) and calcium oxalate are the pre-dominant types, followed by ammonium urate/uric acid (1–8). Various other urolith types, such as calcium phosphate, silica, xanthine, cystine, and sodium pyrophosphate are uncommon.

Understanding factors associated with urolith formation is important for client counseling and implementation of control measures. Breed predilections worldwide for canine struvite and calcium oxalate urolithiasis have been reported to include a number of small breed dogs (2,3,5,9). The Dalmatian breed is over represented with urate uroliths (3,7). Gender predispositions have also been reported, with calcium oxalate and urate uroliths tending to occur in male dogs and struvite in females (3,10).

The incidence of urolithiasis and ability of veterinarians to submit uroliths for analysis results in accumulation of large amounts of data regarding canine urolithiasis. Analysis of large datasets can provide additional insight into risk factors and trends in canine urolithiasis. The objectives of this study were to describe the composition of uroliths submitted to the Canadian Veterinary Urolith Centre (CVUC) from 1998 to 2014, to evaluate changes in urolith types in Canadian dogs over time, and to evaluate associations of breed and gender with urolith types in Canadian submissions.
Materials and methods

A computer-assisted search of data from questionnaires submitted to the CVUC was used to compile information about all urinary bladder calculi from dogs analyzed between February 1, 1998 and November 30, 2014. Uroliths could have been surgically removed, naturally voided, voided with assistance, or fragmented with lithotripsy and removed. Urinary plugs and uroliths from the upper urinary tract were excluded.

Urolith composition was assessed using various assays. After sectioning, each layer was analyzed by optical crystallography, using polarized light microscopy. If additional clarification was needed, another technique such as X-ray microanalysis coupled with scanning electron microscopy or Fourier transformation infrared spectroscopy was used. Uroliths consisting of at least 70% of a single mineral were classified as that mineral type. If 2 mineral types were present in separate, distinct layers within the same urolith, the urolith was classified as compound. Uroliths containing < 70% of a single mineral component and without an obvious nidus or surface layers were classified as mixed. Uroliths comprised of calcium oxalate monohydrate or calcium oxalate dihydrate or both were classified as calcium oxalate. Uroliths comprised of any of the salts of uric acid (ammonium, potassium, and sodium acid urate) were classified as urate. Calcium phosphates represented calcium phosphate apatite, calcium phosphate carbonate, and brushite.

Changes in proportions of urolith types over time were assessed using linear regression. Associations between breed and urolith type were evaluated using logistic regression analyses, with mixed breed dogs as the referent for breed and urolith comparisons involving the targeted urolith compared to other urolith types combined. Odds ratios and 95% confidence intervals (CI) were calculated for breeds for which a significant association was identified. The association between gender and urolith type was also evaluated using logistic regression. A P-value of < 0.05 was considered significant for all comparisons. Statistical analyses were performed using JMP 11 (SAS Institute, Toronto, Ontario).

Results

A total of 101,391 uroliths were submitted to the CVUC from February 1, 1998 to November 30, 2014. Of these, 79,965 (78.9%) were from dogs, with 75,674 (94.6%) from Canada and 4,291 (5.4%) from other countries.

Of the 75,674 Canadian submissions, 42,581 (56%) were from females, 32,530 (43%) were from males, while gender was not reported for 563. Calcium oxalate was the most common submission (n = 34,270, 45%), followed by struvite (27,086, 36%), mixed (7,782, 10.3%), ammonium urate (2,445, 3.2%) and compound (1,632, 2.2%) (Table 1). Ammonium urate uroliths consisted of ammonium urate (2,270/2,445, 93%), sodium urate (95, 2,445, 3.9%), and uric acid (80/2,445, 3.3%).

During the study period, there was a significant increase in the prevalence of calcium oxalate (P = 0.016) and a significant decrease in struvite (P < 0.0001) submissions (Figure 1). There were also significant increases in the prevalence of mixed (P < 0.0001) and cystine (P < 0.0001) uroliths and decreases in urate (P < 0.001), silica (P < 0.0001), and calcium phosphate carbonate (P ≤ 0.0001) uroliths over the study period, but no change in the other urolith types.

Females were over-represented amongst struvite (P < 0.0001), mixed (P < 0.0001), calcium phosphate carbonate (P < 0.001), and compound (P = 0.0002) submissions, while males were significantly associated with calcium oxalate, urate, cystine, silica, and calcium phosphate apatite (all P < 0.0001).

Breed associations are presented in Tables 2 to 4. There were no breed associations for silica uroliths. Breed associations were not investigated for compound or mixed uroliths because of the non-homogenous nature of those urolith types.

Twenty-three breeds were associated with calcium oxalate stone urolith submissions. Of these, 17 (74%) were small breed dogs including the miniature schnauzer, bichon frise, Yorkshire terrier and Lhasa apso, while 3/17 (18%) breeds associated with struvite uroliths were classified as small breed dogs (Pekingese, pug, and shih tzu).

The Dalmatian was at highest risk for urate urolithiasis (926/988; 93.7%) with males accounting for 98% of the urate submissions. The Dalmatian was the only breed identified at risk for xanthine. Cystine uroliths were most common in the Scottish deerhound, mastiff, and Newfoundland dog. Calcium phosphate urolith associations mainly involved small breed dogs and in particular, the papillon, pomeranian, bichon frise, and lhaso apso breeds.

Discussion

Analysis of large databases such as this can allow for detailed study of factors associated with urolithiasis and identify novel associations, as was apparent here. The significant increase in calcium oxalate submissions from Canada is consistent with a change that has been noted in many countries since the early to mid 2000s, with predominance of calcium oxalate submissions in most countries (1,3,5,6,11). This is a change from earlier timepoints, during which struvite submissions tended to predominate internationally (2,6,8,10,12). Reasons for this change have not been specifically studied, but it could be, in part, a result of increasing medical management to dissolve struvite uroliths with continued surgical removal of (undissolvable) calcium oxalate uroliths. Another possible reason is more prompt
or effective diagnosis and treatment of urinary tract infections, as struvite urolithiasis is often associated with infection.

Alternatively, or additionally, the changing ratio of calcium oxalate: struvite urolith submissions could relate to a true increase in calcium oxalate urolithiasis. Theories on the cause of the increasing incidence of calcium oxalate over the last couple of decades include changes in dietary content of calcium, magnesium, phosphorus, or calcium oxalate, decreased water consumption, an increase in sedentary lifestyles of many dogs, and an aging population of small breed dogs that are more prone to calcium oxalate uroliths.

Previous publications have reported a predisposition for both struvite and calcium oxalate uroliths in toy and small breeds (1,7,10,11). In the present study, toy and small breed dogs accounted for most of the breeds that were significantly associated with calcium oxalate urolithiasis compared to mixed breed dogs, while struvite uroliths tended to be over-represented in medium and large breed dogs, most notably the Saint Bernard, Labrador retriever, and golden retriever.

The breed predispositions for calcium oxalate uroliths identified here are consistent with small breed predispositions reported in other regions of the world. The predisposition of small breed dogs is not fully understood but may include size or breed associated differences in mineral metabolism and urine composition. For example, miniature schnauzers urinate significantly less often and have a smaller urine volume than Labrador retrievers, leading to a more concentrated urine that is retained longer in the bladder and has higher urinary calcium and oxalate concentrations (13–15). Hypercalciuria is associated with calcium oxalate urolithiasis in the miniature schnauzer, bichon frise, and shih tzu. Genetic mapping in the miniature schnauzer identified Slc39a10 as a potential calcium oxalate susceptibility gene (16) and it is possible that similar genetic factors could account for calcium oxalate predispositions in other breeds.

The male predisposition to calcium oxalate was expected as it has been previously reported in dogs (17) and humans (18). In humans and rats, an association between testosterone and calcium urolithiasis has been identified (19). However, castration should reduce or negate this effect, and most of the male dogs were castrated. The predisposition may simply reflect a lower risk of infection-associated struvite uroliths in male dogs, leaving them over-represented in metabolic urolith groups. Obesity may also be a contributor to earlier onset of calcium oxalate urolithiasis in high risk breeds (20). Body condition data were not available to assess this.

The association of struvite uroliths with female dogs is consistent with the infection-associated nature of struvite uroliths. However, urinary tract infections can occur in any breed and reasons for breed associations with struvite urolithiasis have been minimally investigated. In a previous study, the odds of struvite urolithiasis were approximately 3.0 times as great in toy-breed dogs and 2.4 times as great in small-breed dogs, compared with medium-breed dogs, but were not significantly different between medium- and large-breed dogs (21). This is in contrast with the current study in which many medium and large breeds were identified as predisposed.

The reason that the proportion of urate submissions significantly decreased during the study period is unclear. This is in contrast to somewhat older data from the UK, in which the relative frequency of urate increased from 7% to 12% over a 10-year period.
period (1997 to 2006) (12). The most common breed for urate urolithiasis remains the Dalmatian and a hyperuricosuria genetic mutation responsible for that has been identified (22). While the focus of this mutation has been on Dalmatians, it has been identified in some other breeds, including giant schnauzers and Jack Russell terriers (22), 2 of the breeds identified as over-represented in this study.

Cystine uroliths continued to be uncommon. Breeds reported to be at risk include the Newfoundland, Scottish deerhound, English bulldog, Chihuahua, and Staffordshire bull terrier (12). All except the Staffordshire bull terrier were also identified as associated with cystine uroliths in this study, in addition to a number of other breeds. While the number of submissions was small, the odds ratios were remarkable for many breeds, including the Scottish deerhound (OR 2203), basenji (OR 275), mastiff (OR 346), Newfoundland (OR 394), and whippet (OR 252), strongly supportive of a genetic link. Recently, a classification scheme for dogs with cystinuria based on mode of inheritance, androgen dependence, and genetics has been published and it is hoped that screening and selective breeding will ultimately diminish cystine urolith submission numbers (23).

It is important to remember that these data do not indicate breed-level associations with urolithiasis, as that would require corresponding breed incidence data from dogs without uroliths. Rather, this study identified breeds at increased risk of certain urolith types, compared with a referent population, mixed breed dogs. As with any study, the study population must be considered. Since CVUC analysis is performed at no cost to

### Table 2. Significant associations between calcium oxalate and breed among 75,674 uroliths from dogs

<table>
<thead>
<tr>
<th>Urolith type</th>
<th>Breed</th>
<th>Prevalence</th>
<th>Odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium oxalate</td>
<td>Bichon frise</td>
<td>313/7215 (43.4%)</td>
<td>1.1 (1.05 to 1.18)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Boston terrier</td>
<td>55/102 (54%)</td>
<td>1.7 (1.1 to 2.5)</td>
<td>0.0078</td>
</tr>
<tr>
<td></td>
<td>Cairn terrier</td>
<td>251/356 (71%)</td>
<td>3.5 (2.8 to 4.4)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Cavalier King Charles spaniel</td>
<td>102/217 (47%)</td>
<td>1.3 (1.0 to 1.7)</td>
<td>0.049</td>
</tr>
<tr>
<td></td>
<td>Chihuahua</td>
<td>629/921 (68%)</td>
<td>3.5 (3.0 to 4.0)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Dobermann pinscher</td>
<td>69/108 (64%)</td>
<td>2.6 (1.7 to 3.8)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Fox terrier</td>
<td>125/158 (79%)</td>
<td>5.5 (3.8 to 8.2)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Havanese</td>
<td>118/238 (50%)</td>
<td>1.4 (1.1 to 1.8)</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>Jack Russell terrier</td>
<td>793/1322 (60%)</td>
<td>2.2 (1.9 to 2.4)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Keeshond</td>
<td>52/97 (54%)</td>
<td>1.7 (1.1 to 2.5)</td>
<td>0.0113</td>
</tr>
<tr>
<td></td>
<td>Kerry blue terrier</td>
<td>29/42 (69%)</td>
<td>3.2 (1.7 to 6.4)</td>
<td>0.0002</td>
</tr>
<tr>
<td></td>
<td>Lhasa apso</td>
<td>1609/2577 (62%)</td>
<td>2.4 (2.2 to 2.6)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Maltese</td>
<td>601/842 (71%)</td>
<td>3.6 (3.1 to 4.2)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Miniature pinscher</td>
<td>186/254 (73%)</td>
<td>4.0 (3.0 to 5.3)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Miniature poodle</td>
<td>620/1097 (57%)</td>
<td>1.9 (1.6 to 2.1)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Miniature schnauzer</td>
<td>6039/9309 (65%)</td>
<td>2.7 (2.5 to 2.8)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Papillon</td>
<td>255/370 (69%)</td>
<td>3.2 (2.6 to 4.0)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Pomeranian</td>
<td>1182/1640 (72%)</td>
<td>3.7 (3.4 to 4.2)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Standard poodle</td>
<td>152/257 (59%)</td>
<td>2.1 (1.6 to 2.7)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Portuguese water dog</td>
<td>75/108 (69%)</td>
<td>3.3 (2.2 to 5.0)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Schnauzer</td>
<td>117/164 (71%)</td>
<td>3.6 (2.6 to 5.1)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Wire fox terrier</td>
<td>47/58 (81%)</td>
<td>6.2 (3.3 to 13)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Yorkshire terrier</td>
<td>1677/2720 (62%)</td>
<td>2.3 (2.1 to 2.5)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Mixed breed</td>
<td>8789/21 468 (41%)</td>
<td>Ref</td>
<td></td>
</tr>
</tbody>
</table>

Ref — referent.

### Table 3. Significant associations between struvite and breed among 75,674 uroliths from dogs

<table>
<thead>
<tr>
<th>Urolith type</th>
<th>Breed</th>
<th>Prevalence</th>
<th>Odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Struvite</td>
<td>Australian shepherd</td>
<td>49/79 (62%)</td>
<td>2.3 (1.5 to 3.6)</td>
<td>0.0003</td>
</tr>
<tr>
<td></td>
<td>Beagle</td>
<td>244/425 (57%)</td>
<td>1.9 (1.6 to 2.3)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Bernese mountain dog</td>
<td>75/117 (64%)</td>
<td>2.5 (1.7 to 3.7)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Border collie</td>
<td>112/154 (64%)</td>
<td>3.7 (2.6 to 5.4)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Boxer</td>
<td>65/96 (68%)</td>
<td>2.9 (1.9 to 4.6)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Chow chow</td>
<td>86/124 (69%)</td>
<td>3.2 (2.2 to 4.7)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Cocker spaniel</td>
<td>464/690 (67%)</td>
<td>2.9 (2.5 to 3.4)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Corgi</td>
<td>141/206 (68%)</td>
<td>2.9 (2.0 to 4.1)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>German shepherd</td>
<td>109/163 (67%)</td>
<td>2.8 (2.0 to 3.9)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Golden retriever</td>
<td>281/365 (77%)</td>
<td>4.7 (3.7 to 6.0)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Labrador retriever</td>
<td>443/550 (81%)</td>
<td>5.8 (4.7 to 7.2)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Pekingese</td>
<td>262/485 (54%)</td>
<td>1.7 (1.4 to 2.0)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Pug</td>
<td>101/1842 (55%)</td>
<td>1.7 (1.6 to 1.9)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Rotweiler</td>
<td>109/151 (72%)</td>
<td>3.6 (2.6 to 5.2)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Saint Bernard</td>
<td>12/13 (92%)</td>
<td>17 (3.3 to 306)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Scottish terrier</td>
<td>87/127 (69%)</td>
<td>3.1 (2.1 to 4.6)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Shih tzu</td>
<td>513/212 (46%)</td>
<td>1.1 (1.05 to 1.2)</td>
<td>0.0003</td>
</tr>
<tr>
<td></td>
<td>Mixed breed</td>
<td>891/21 468 (42%)</td>
<td>Ref</td>
<td></td>
</tr>
</tbody>
</table>

Ref — referent.
Table 4. Significant associations between cystine, xanthine, urate, and calcium phosphate uroliths and breed among 75 674 uroliths from dogs

<table>
<thead>
<tr>
<th>Urolith type</th>
<th>Breed</th>
<th>Prevalence</th>
<th>Odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystine</td>
<td>Basenji</td>
<td>7/15 (47%)</td>
<td>275 (94 to 788)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Bull mastiff</td>
<td>5/21 (24%)</td>
<td>98 (31 to 259)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Bulldog</td>
<td>44/183 (24%)</td>
<td>100 (66 to 150)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Chihuahua</td>
<td>32/921 (3.5%)</td>
<td>11 (7.3 to 17)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Dachshund</td>
<td>39/985 (4%)</td>
<td>12 (8.3 to 18)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>English bulldog</td>
<td>53/247 (21%)</td>
<td>86 (58 to 126)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>French bulldog</td>
<td>24/74 (32%)</td>
<td>151 (87 to 258)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Great Dane</td>
<td>7/26 (27%)</td>
<td>116 (44 to 273)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Mastiff</td>
<td>11/21 (52%)</td>
<td>346 (141 to 857)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Miniature pinscher</td>
<td>16/252 (6.3%)</td>
<td>21 (12 to 36)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Newfoundland</td>
<td>20/36 (56%)</td>
<td>394 (156 to 802)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Pit bull</td>
<td>16/62 (26%)</td>
<td>109 (58 to 199)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Scottish deerhound</td>
<td>7/8 (88%)</td>
<td>2203 (385 to 41 463)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Whippet</td>
<td>4/9 (44%)</td>
<td>252 (61 to 972)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Mixed breed</td>
<td>68/21 468 (0.32%)</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>Xanthine</td>
<td>Dalmatian</td>
<td>8/991 (0.81%)</td>
<td>24 (8.9 to 71)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Mixed breed</td>
<td>7/21 468 (0.03%)</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>Urate</td>
<td>American bulldog</td>
<td>21/29 (72%)</td>
<td>226 (103 to 549)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Black Russian terrier</td>
<td>8/13 (62%)</td>
<td>138 (46 to 459)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Bulldog</td>
<td>6/178 (37%)</td>
<td>9.1 (1.4 to 31)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Chihuahua</td>
<td>29/921 (3.2%)</td>
<td>2.8 (1.8 to 4.1)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Dachshund</td>
<td>22/1024 (2.2%)</td>
<td>1.8 (1.1 to 2.8)</td>
<td>0.0132</td>
</tr>
<tr>
<td></td>
<td>Dalmatian</td>
<td>928/991 (94%)</td>
<td>1270 (962 to 1704)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>English bulldog</td>
<td>92/247 (37%)</td>
<td>51 (38 to 68)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Giant schnauzer</td>
<td>3/7 (43%)</td>
<td>65 (12.7 to 295)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Havanesse</td>
<td>10/239 (4.2%)</td>
<td>3.8 (1.8 to 7.8)</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Jack Russell terrier</td>
<td>42/1322 (3.2%)</td>
<td>2.8 (2.0 to 3.9)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Miniature schnauzer</td>
<td>166/9308 (1.8%)</td>
<td>1.6 (1.3 to 1.9)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Pekingese</td>
<td>15/485 (3.1%)</td>
<td>2.8 (1.6 to 4.5)</td>
<td>0.0011</td>
</tr>
<tr>
<td></td>
<td>Pit bull</td>
<td>21/62 (34%)</td>
<td>44 (25 to 75)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Shih tzu</td>
<td>281/11 212 (2.5%)</td>
<td>2.1 (1.8 to 2.3)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Yorkshire terrier</td>
<td>162/2720 (6.0%)</td>
<td>5.5 (4.4 to 6.7)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Mixed breed</td>
<td>255/21468 (1.2%)</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>Calcium phosphate</td>
<td>Bichon frise</td>
<td>196/7215 (2.7%)</td>
<td>1.5 (1.3 to 1.8)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Lhasa apso</td>
<td>71/2577 (2.8%)</td>
<td>1.5 (1.2 to 2.0)</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>Papillon</td>
<td>22/370 (6.0%)</td>
<td>3.4 (2.1 to 5.2)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Pomeranian</td>
<td>62/1640 (3.8%)</td>
<td>2.1 (1.6 to 2.8)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>Mixed breed</td>
<td>391/21 468 (1.8%)</td>
<td>Ref</td>
<td></td>
</tr>
</tbody>
</table>

Ref — referent.

the veterinary clinic or owner, potential submission biases are reduced. However, it is possible that there is still some submission bias if veterinarians select uroliths to submit. It is more likely, though, that such bias would decrease the ability to detect associations that have been previously reported, since it could lead to decreased submission of uroliths from known at risk breeds on the assumption that the urolith type can be readily predicted (e.g., urate uroliths in Dalmatians). Accordingly, this should not impact the numerous new associations that were identified.

Continued study of factors associated with urolithiasis is important to better understand and manage this common condition. In particular, identifying breed associations can be useful for client counseling and targeted study to identify genetic predispositions and potentially allow for eradication or reduction in some breed predispositions. Changes in urolith trends occur, as noted here, and determining reasons for those trends might also be useful for management and client education. This study has identified numerous associations that require further study to better manage urolithiasis in dogs.

Acknowledgments
The authors thank Mike Favrin, Carole White, Kayla Favaro, and Frankie Cooper for their assistance in performing quantitative analysis of the uroliths at the CVUC and Aaliyah Subang and Alannah Subang for data entry. The Canadian Veterinary Urolith Centre is supported financially by Royal Canin Canada.

References
Article

Evaluation of toxicity of a chronic alternate day metronomic cyclophosphamide chemotherapy protocol in dogs with naturally occurring cancer

Arata Matsuyama, J. Paul Woods, Anthony J. Mutsaers

Abstract — Sterile hemorrhagic cystitis (SHC) is an important complication of cyclophosphamide chemotherapy in dogs as it is reported in up to 23% of cases with various protocols. The current study reports toxicities of a protocol of metronomic cyclophosphamide, and identifies risk factors for development of adverse effects. A retrospective cohort study of dogs treated with metronomic cyclophosphamide at an intended dose of 25 mg/m² every other day was conducted. Fifty dogs were included with a median length of treatment of 90 days (range: 1 to 1305 days). Treatment was discontinued in 22 dogs (44%) due to adverse effects; 16 dogs (32%) developed SHC after a median time of 127.5 days (range: 54 to 1305 days). Higher cumulative dose was significantly associated with a higher risk of SHC development ($P = 0.048$). Therefore, close monitoring and/or prophylactic treatments should be considered for patients receiving chronic metronomic cyclophosphamide therapy.

Résumé — Évaluation de la toxicité du protocole de chimiothérapie prolongée à la cyclophosphamide métronomique tous les deux jours chez les chiens atteints d’un cancer acquis naturellement. La cystite hémorragique stérile (CHS) est une complication importante de la chimiothérapie à la cyclophosphamide chez les chiens car elle est signalée dans jusqu’à 23 % des cas avec divers protocoles. L’étude actuelle signale les toxicités d’un protocole de cyclophosphamide métronomique et identifie les facteurs de risque pour le développement d’effets indésirables. Une étude rétrospective auprès d’une cohorte de chiens traités à l’aide de la cyclophosphamide métronomique à une dose prévue de 25 mg/m² tous les deux jours a été réalisée. Cinquante chiens ont été inclus avec une durée moyenne de traitement de 90 jours (fourchette : de 1 à 1305 jours). Le traitement a été discontinué chez 22 chiens (44 %) en raison des effets indésirables; 16 chiens (32 %) ont développé la CHS après une durée moyenne de 127,5 jours (fourchette : de 54 à 1305 jours). Une dose cumulative supérieure était significativement associée à un risque supérieur de développer la CHS ($P = 0,048$). Par conséquent, une surveillance étroite et/ou des traitements prophylactiques devraient être considérés pour les patients recevant une thérapie prolongée à la cyclophosphamide métronomique.


Introduction

Low dose metronomic (LDM) chemotherapy is defined as the administration of lower doses of cytotoxic chemotherapeutic drugs without prolonged drug free intervals (1). Low dose metronomic chemotherapy targets tumor angiogenesis, especially vascular endothelial cells, whilst conventional cytotoxic chemotherapy drugs administered at the maximum tolerated dose (MTD) kill rapidly dividing cells with consequent toxic side effects to highly proliferative normal cell populations. The antiangiogenic properties of a LDM treatment regimen was originally demonstrated by a study using 3 cyclophosphamide (CYC) resistant tumors in mouse xenograft models (2). The more frequent administration at approximately 1/3 of the MTD induced apoptosis of both tumor and endothelial cells (2). Since this discovery, several preclinical studies and early phase clinical trials have evaluated various LDM protocols in both human and canine patients, with CYC being the most commonly utilized drug (3–8). One study also retrospectively investigated the tolerability of a LDM CYC protocol in cats (9).

Doses of CYC in LDM regimens can vary widely depending on the study. In a preliminary rodent study, tumor response and circulating endothelial precursor cell counts reached a plateau during dose escalation of CYC, while bone marrow toxicity and weight loss continuously progressed with further dose escalation (10). As a result, Shaked et al (10), based on their empirical definition of the optimal biologic dose as “the dose causing maximum reduction in the tumor volume with no or minimal
toxicity,” chose 20 mg/kg body weight (BW) of daily CYC as the optimal biologic dose in mice. In human oncology, where the impact of drug dose on degrees of antitumor and adverse effects has not been thoroughly investigated, approximately 5% to 10% of the MTD dose is often utilized for LDM protocols (3). In fact, most CYC LDM protocols in humans consist of a daily dose of a 50 mg tablet per patient, particularly in single agent protocols. However, the CYC dose can vary from 25 to 100 mg per patient with reported anti-tumor effects (3). Similar discord in dose optimization has been observed in veterinary studies. However, recently, Burton et al (11) demonstrated differences in efficacy for 2 distinctive LDM CYC protocols in dogs. In that study, there were significantly more potent effects on microvessel density and regulatory T-cell counts at a dose of daily 15 mg/m² compared to daily 12.5 mg/m² (11). Outside of this report, there is little scientific evidence for dogs that justifies an optimal dose within the range of 10 to 25 mg/m² every 24 to 48 h (5,7,8,11–14). In a study of daily 25 mg/m² CYC, no significant adverse events requiring discontinuation of treatment were reported. However, in another study of dogs receiving daily 10 mg/m² CYC, 40% experienced a side effect including gastrointestinal or urinary toxicity, although information is limited due to the small sample size of each study (5,13). These discordant results suggest that there could be other factors contributing to toxicity besides the dose and frequency of CYC administration, such as chronicity of treatment and/or concurrent drug use.

Reported complications of MTD CYC treatment in dogs include gastrointestinal and myelosuppressive toxicity, alopecia, and sterile hemorrhagic cystitis (SHC) (15). In LDM CYC protocols, the former 2 events are infrequent, with a reported incidence of 0% to 23% (7,8,11,13,14). Whether a chronic LDM CYC regimen is associated with a higher risk of SHC compared to conventional CYC dosing is currently unknown. In a recent case control study, cumulative dose was identified as a high risk factor for SHC development with MTD CYC chemotherapy in canine lymphoma patients (16). Although this information is limited to the population treated with MTD CYC, there has been a concern that chronic LDM administration could result in a higher risk of SHC development. Furthermore, 1 dog treated with a LDM CYC protocol was reportedly euthanized due to severe SHC (13). Given these results, and the increasing popularity of LDM CYC treatment in veterinary practice, a better understanding of the incidence and risk factors for toxicity associated with these protocols is necessary.

The objective of this study was to report toxicities of a specific protocol of LDM CYC at 25 mg/m² every other day, and identify possible risk factors for development of adverse effects in dogs.

Materials and methods

Study design and case selection

A retrospective cohort study of medical records was conducted. Inclusion criteria were dogs treated with LDM CYC at an intended dose of 25 mg/m² every other day at the Ontario Veterinary College Health Sciences Centre between January 2004 and December 2011. Sufficient follow-up information was necessary to assess toxicity profiles.

Data collection

The following data were retrieved from medical records: age, gender, neuter status, breed, body weight, diagnosis, presence of gross disease at the beginning of LDM CYC, previous treatment(s), baseline and follow-up complete blood (cell) count (CBC), serum biochemical profile, urinalysis, prescribed dose of CYC per body surface area, duration of treatment, number and severity of toxicity events, reason(s) for treatment discontinuation, and concurrent drug administration [chemotherapy, nonsteroidal anti-inflammatory drugs (NSAIDs), tyrosine kinase inhibitors, and radiation therapy]. Adverse events were not prospectively defined in the medical records based upon the Veterinary Cooperative Oncology Group — Common Terminology Criteria for Adverse Events since such a guideline was not available at the beginning of the study period (17). These criteria were retrospectively applied based on adverse event descriptions found in the medical record. Sterile hemorrhagic cystitis was defined as any urinary tract signs such as gross hematuria, stranguria, or urinary incontinence confirmed with microscopic hematuria on urinalysis without crystalluria or positive bacterial culture results.

Statistical analysis

Descriptive statistics were used for continuous data with median values and categorical data with frequencies. Risk factors for incidence of gastrointestinal and myelosuppressive events, SHC, and serum biochemistry abnormalities were analyzed. Analyzed factors included treatment duration (days); tumor type; age (y); body weight (kg); breed; presence of concurrent MTD chemotherapy, molecular target therapy, and NSAID administration; prescribed dose (mg/m²); and cumulative dose (day*mg/m²). Dichotomous and categorical data were analyzed by Chi-square test or Fisher’s exact test where appropriate. Continuous data were first analyzed for normality of distribution using the Shapiro-Wilk test. Independent sample t-test and Mann-Whitney test were used for parametric data and non-parametric data, respectively. A P-value < 0.05 was considered statistically significant for all comparisons. All statistical analyses were performed using a commercially available software program (SPSS Version 22.0; SPSS, Chicago, Illinois, USA).

Results

Patient characteristics

Fifty dogs met the inclusion criteria. The patient and tumor characteristics are presented in Tables 1 and 2. Previous treatment history included surgery (n = 45), radiation therapy (n = 8), MTD chemotherapy (n = 36), NSAIDs (n = 5), toceranib (n = 5), and melanoma vaccine (n = 1). The MTD chemotherapeutic agents included carboplatin (n = 19), doxorubicin (n = 18), gemcitabine (n = 2), epirubicin (n = 2), mitoxantrone (n = 2), vinorelbine (n = 2), and vincristine (n = 1). Twelve dogs failed multiple agents.

Low dose metronomic (LDM) chemotherapy

All dogs included in this study received oral CYC at a target dose of 25 mg/m² every other day. Drugs were not compounded but prescribed as available tablets in all patients, and as a result,
actual prescribed dosages varied from 17.5 to 46.7 mg/m² (median: 24.6 mg/m²; n = 50). The median length of treatment was 90 d (range: 1 to 1305 d; n = 50). Reasons for treatment discontinuation included adverse effects (n = 22), disease progression (n = 22), death for a reason unrelated to the primary tumor (n = 2), bacterial cystitis (n = 1), and unknown (n = 3). Forty-five dogs (90%) received multiple drugs concurrently with CYC as a part of the LDM protocol, including meloxicam (n = 30); meloxicam and doxycycline (n = 9); deracoxib (n = 4); piroxicam (n = 1); and meloxicam and methotrexate (n = 1).

Concurrent treatment. Sixteen dogs (32%) received concurrent treatments outside of the LDM protocol, including MTD chemotherapy (n = 5), molecular targeted therapy (n = 9: toceranib = 8, rapamycin = 1), hypofractionated radiation therapy (n = 2), and melanoma vaccine (n = 1). The MTD chemotherapeutic drugs included carboplatin (n = 2), doxorubicin (n = 2), and both epirubicin and vincristine (n = 1).

Toxicities
Gastrointestinal adverse events were recorded in 7 dogs (14%), consisting of grade II (n = 5) and grade III (n = 2). Three dogs with grade II side effects received concurrent carboplatin chemotherapy (n = 1) or toceranib (n = 2). Hematological toxicities were reported in 19 dogs (38%), all of which were anemia (15 grade I, 3 grade II, 1 grade III), while CBCs were not evaluated in 3 dogs. Nine of the 19 dogs with anemia (47%) were diagnosed with hemangiosarcoma. Sixteen dogs (32%) developed SHC. The median time to SHC development in the 16 dogs was 127.5 d (range: 54 to 1305 d). During the treatment period, the most common serum biochemical profile abnormalities included elevated urea (n = 14, 41%; 5 grade I, 5 grade II, 2 grade III, 2 grade IV), alanine aminotransferase (n = 12, 33%; 5 grade I, 6 grade II, 1 grade III), and creatinine (n = 7, 21%; 5 grade I, 1 grade III, 1 grade IV). All dogs with an elevated creatinine level also received meloxicam (n = 6) or deracoxib (n = 1), but no molecular target therapy or MTD chemotherapy. Various other biochemical abnormalities were mild and observed in 5 dogs. Among the 14 dogs with elevated urea or creatinine, urinalysis results were available in 6 dogs, of which 3 had appropriate urine concentration (urine specific gravity of > 1.030). Abdominal ultrasound examination was performed in 5 dogs, none of which had structural abnormalities of the kidneys.

Risk factors
Dogs that developed SHC had a significantly higher cumulative dose (P = 0.048) than dogs that did not develop SHC. The median cumulative dose for dogs with SHC was 3311 days*mg/m² (n = 16) compared to 1635 days*mg/m² (n = 34) for dogs without SHC. The difference was not statistically significant for prescribed dose or treatment duration (P = 0.074 and P = 0.256, respectively). Also, dogs that developed an elevated serum creatinine (n = 7) had significantly longer treatment durations than dogs with normal creatinine levels (n = 27) (P = 0.039; mean: 392 d versus 149 d). The difference was also not statistically significant for prescribed dose (P = 0.117) and cumulative dose (P = 0.097). No significant differences were seen for tumor type, age, body weight, breed, presence of concurrent MTD chemotherapy, molecular target therapy, NSAID administration, and prescribed dose (mg/m²).

Discussion
The toxicity profile and risk factors associated with a LDM CYC protocol were evaluated in this study. The CYC protocol was investigated at 25 mg/m² every other day; however, previously reported doses of LDM CYC have been highly variable, ranging from 10 mg/m² every other day to 25 mg/m² daily, with documented clinical efficacy and high tolerability for all doses within this range (5,7,8,11–14). The 25 mg/m² every other day regimen has historically been utilized at some institutions (Mutsaers AJ and Knapp DW, personal communication). Burton et al (11) investigated the potential effects of LDM CYC dose and demonstrated significantly more potent antiangiogenic and immunomodulatory effects of a daily 15 mg/m² compared to 12.5 mg/m² protocol in canine soft tissue sarcoma. Since then, the daily 15 mg/m² protocol has been prescribed at our

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>10</td>
</tr>
<tr>
<td>Median Range</td>
<td>4 to 15</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>32.1</td>
</tr>
<tr>
<td>Median Range</td>
<td>12.2 to 53</td>
</tr>
<tr>
<td>Gender</td>
<td>Female intact 1, Female spayed 18, Male intact 4, Male castrated 27</td>
</tr>
<tr>
<td>Breed</td>
<td>Labrador retriever 12, Golden retriever 7, Bulldog 2, Greyhound 2, German shepherd 2, Afghan hound (brindle), American Eskimo dog, Bichon frise, Bouvier des Flandres, Boxer (brindle), Flat-coated retriever, Irish setter, Scottish deerhound (grey), Shetland sheepdog, Siberian husky, Standard poodle 15</td>
</tr>
</tbody>
</table>

Table 2. Tumor characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor type</td>
<td>Hemangiosarcoma 12, Osteosarcoma 9, Anal sac adenocarcinoma 7, Pulmonary carcinoma 4, Malignant melanoma 2, Apocrine gland adenocarcinoma; Gastric fibrosarcoma; 1, Mammary carcinoma; Salivary adenocarcinoma; Thyroid carcinoma; Undifferentiated carcinoma; Mammary carcinoma and Adrenal carcinoma; and Osteosarcoma and Hemangiosarcoma 2</td>
</tr>
<tr>
<td>Tumor status</td>
<td>Microscopic disease 24, Macroscopic disease 26</td>
</tr>
<tr>
<td>Presence of metastasis</td>
<td>Primary 24, Metastasis 26</td>
</tr>
</tbody>
</table>
The aforementioned study did not escalate the dose above 15 mg/m² so it is uncertain whether a higher dose, such as 25 mg/m² administered in a metronomic fashion, would result in further reduction in angiogenesis or suppression of regulatory T-cells (5,11). In addition, only 2 studies have investigated the every other day dosing schedule, and toxicity or efficacy was not compared to that of a daily schedule regimen (8,13). The efficacy of the LDM CYC protocol herein is unknown; nonetheless, the risk factor analysis from our study may be informative for other LDM CYC protocols that are similarly administered on a chronic basis.

Gastrointestinal toxicities were seen in 7 dogs (14%). Of these 7 dogs, the adverse events were transient and mild in 3 dogs, while 4 dogs required discontinuation of the protocol. One dog with non-respondent pulmonary carcinoma needed to discontinue treatment due to acute onset of inappetence and a limb swelling 1 day after initiation. Another dog with metastatic melanoma developed anorexia, shivering, diarrhea, and lameness 8 d after the start of treatment. Both of these dogs had progressive macroscopic disease and therefore these events may be attributable to disease progression. None of the 7 dogs received toceranib concurrently as a part of LDM protocol. Nevertheless, the toxicities were mild, occasional, and consistent with those of other reported LDM CYC protocols with or without NSAIDs (7,8,11,13,14).

Neither neutropenia nor thrombocytopenia was documented in any dogs in the current study, which may be superior compared with reported LDM protocols for other alkylating agents (18,19). The result is consistent with other reported LDM CYC protocols (5,11–13), and might be explained by the platelet sparing effect of CYC (20). Almost all hematological toxicities were mild to moderate anemia, which may also have been related to disease progression, considering the fact that 9 of the 19 dogs with anemia (47%) had hemangiosarcoma, which is frequently associated with anemia, and 6 dogs had their treatment discontinued due to progression of hemangiosarcoma characterized by hemoabdomen. The lack of significant myelosuppressive toxicity with this LDM CYC protocol also suggests a possibility of combination therapy with other cytotoxic chemotherapy, and a recent report has investigated such a combination (6). The standard follow-up schedule for LDM CYC chemotherapy at our institution has been monthly recheck with physical examination, CBC, and urinalysis, which, appears to be adequate for monitoring hematological adverse effects in cancer-bearing dogs receiving LDM CYC protocols. However, careful monitoring of kidney function would be recommended especially for patients receiving NSAIDs concurrently, and the addition of monthly serum biochemistry panel assessment could also be considered.

The cause of SHC has been attributed to acrolein, a metabolite of CYC that irritates the urinary bladder mucosa. In the current study, 17 dogs (34%) developed SHC, which is higher than in previous reports that show an incidence of SHC of 0% to 22% of dogs treated with LDM CYC (8,11–14). A study that investigated a daily 25 mg/m² LDM CYC protocol did not report any SHC incidence (5), but it is possible that the treatment duration was shorter in that study, considering the reported median overall survival time of 3.4 mo, which is shorter than the median time to SHC development of 4 mo in the current study. In summary, the 25 mg/m² dosing schedule might carry too high a risk for SHC development, especially as a prolonged treatment. However, cautious interpretation of this result is required, since various other factors could impact SHC development, such as the time of the day CYC was given, whether and how owners encouraged urination after administration, and each dog’s access to water. Admittedly, consistent application of such management strategies is more challenging with chronic LDM CYC dosing compared to periodic MTD CYC administration. Nevertheless, these factors would be important considerations to help prevent SHC in LDM CYC protocols, considering its mechanism of development.

A recent case control study identified cumulative dose as a risk factor for development of SHC in dogs with lymphoma treated with MTD CYC (16). This result was consistent with the current study, showing a statistically significant difference in cumulative CYC dose between the 2 groups. Sterile hemorrhagic cystitis was not reported in a prospective study of 11 dogs treated with LDM CYC for 28 d, while, in another study, 1 of 2 dogs that developed SHC received more than a year of an alternating LDM CYC treatment regimen (11,12). Thus, clinicians may need to provide close monitoring and/or consider prophylactic treatments for patients receiving LDM CYC over a long period. There is no standard for prophylactic treatment or monitoring recommendations for SHC in veterinary patients receiving LDM CYC. At the authors’ institution, no prophylactic treatment is recommended. For MTD CYC protocols, prophylactic use of furosemide and/or the chemoprotective agent mesna prevented SHC in a few studies (21–23). Therefore, oral prophylactic diuretics such as furosemide could be considered for dogs receiving long-term LDM CYC treatment. Recommendations may be guided by the fact that 4 mo was the median time to SHC development in the current study.

Treatment duration was also identified as a risk factor for elevation in serum creatinine. Lack of significance of individual CYC dose and cumulative dose suggests that concurrent treatment rather than CYC itself could be a risk factor for creatinine elevation. Considering 90% of the dogs received an NSAID, predominantly meloxicam, as a component of the LDM protocol, it is possible that the observed creatinine elevations could be attributed to these drugs alone, or the CYC-NSAID combination. Although no significant association between the presence of concurrent NSAID and elevation in urea and creatinine was seen, the result could be a type II error since 90% of dogs received NSAID concurrently. Similarly, elevation in serum creatinine was reported in 2 of 30 dogs treated with LDM CYC and piroxicam, which resolved with reduction in the frequency of piroxicam administration (13). Meloxicam and other NSAIDs can inhibit prostaglandin synthesis, and subsequently may decrease renal blood flow. Although renal toxicity has not been reported during 4 to 6 wk of meloxicam administration in dogs with orthopedic pain, to the authors’ knowledge, no studies have assessed the potential long-term adverse effects of meloxicam in cancer-bearing dogs (24–26). It is possible that the affected dogs in our study had preexisting subclinical renal disease prior to starting therapy, or that progression of renal disease occurred concurrently with the LDM CYC protocol. The use of a chemoprotective agent mesna prevented SHC in a few studies (21–23). Therefore, oral prophylactic diuretics such as furosemide could be considered for dogs receiving long-term LDM CYC treatment. Recommendations may be guided by the fact that 4 mo was the median time to SHC development in the current study.

Treatment duration was also identified as a risk factor for elevation in serum creatinine. Lack of significance of individual CYC dose and cumulative dose suggests that concurrent treatment rather than CYC itself could be a risk factor for creatinine elevation. Considering 90% of the dogs received an NSAID, predominantly meloxicam, as a component of the LDM protocol, it is possible that the observed creatinine elevations could be attributed to these drugs alone, or the CYC-NSAID combination. Although no significant association between the presence of concurrent NSAID and elevation in urea and creatinine was seen, the result could be a type II error since 90% of dogs received NSAID concurrently. Similarly, elevation in serum creatinine was reported in 2 of 30 dogs treated with LDM CYC and piroxicam, which resolved with reduction in the frequency of piroxicam administration (13). Meloxicam and other NSAIDs can inhibit prostaglandin synthesis, and subsequently may decrease renal blood flow. Although renal toxicity has not been reported during 4 to 6 wk of meloxicam administration in dogs with orthopedic pain, to the authors’ knowledge, no studies have assessed the potential long-term adverse effects of meloxicam in cancer-bearing dogs (24–26). It is possible that the affected dogs in our study had preexisting subclinical renal disease prior to starting therapy, or that progression of renal
disease was disease-related and/or multifactorial. Nevertheless, based on these results, careful monitoring of renal function is advised when an NSAID is utilized in combination with LDM chemotherapy as a prolonged treatment strategy.

An important limitation of the current study is its retrospective design. Tumor response evaluation was not consistently applied to all patients, and the documentation of toxic events varied in the medical records. Presence of concurrent treatment could also veil the true prevalence of toxicity and efficacy of CYC specifically, although these results are clinically relevant, considering that LDM protocols consisting of multiple drugs, such as NSAIDs, have been commonly prescribed in clinical settings. Furthermore, the small sample size of the current study could lead to a type II error.

In conclusion, as has been reported in MTD CYC treatment, higher cumulative dose and longer treatment duration increased the risk of SHC development with this every other day LDM CYC protocol. Close monitoring and/or prophylactic treatments should be considered for patients receiving LDM CYC over a long period.

Acknowledgments

We are grateful to Patricia Sullivan and Judith Renaud from the Medical Records Service, and Elizabeth Reemeyer from the Information Technology Service at the Ontario Veterinary College, for their contributions to medical record collection.

References


**Reconnaitre la douleur est un élément crucial en pratique vétérinaire** (1). L'évaluation de la douleur est basée sur l'appréciation adéquate des changements de comportement en présence de douleur chez les chats (2). Des échelles de douleur ont été développées et validées en tant qu'instruments subjectifs pour évaluer la douleur clinique dans cette espèce (2–7). L'échelle de douleur composite UNESP-Botucatu (2–6) ainsi qu'un instrument de mesure composite basé uniquement sur le comportement (7), tiennent compte de différentes catégories telles que la posture, le confort, l'activité, et parfois des variables physiologiques (MCPS seulement). Ces systèmes fournissent un «point limite» pour l’analgésie interventionnelle (ou de secours) qui permet d’orienter la thérapie en contexte clinique. La MCPS a initialement été développée en portugais du Brésil (MCPS-Port), mais a également été validée en anglais (MCPS-Angl) et en espagnol (MCPS-Esp) (2–6).

Étant donné qu’un instrument doit être validé lorsqu’il est traduit dans une autre langue pour prendre en considération d’éventuelles différences culturelles (8–9), le but de cette étude était de procéder à la validation psychométrique de la MCPS en langue française (MCPS-Fr) à l’aide d’analyses de vidéos, tout...
en suivant les lignes directrices internationales pour la validation interculturelle (9–12). Les auteurs ont formulé l’hypothèse que la validité et la fiabilité de la version francophone de cet instrument seraient similaires aux caractéristiques de la MCPS en anglais et en espagnol.

**Matériels et méthodes**

**Traduction, traduction inverse et équivalence sémantique**

Tout d’abord, l’échelle de douleur a été traduite par deux traducteurs indépendants et francophones (MM et AML), à partir de la version anglophone de l’UNESP-Botucatu-MCPS (2). Ensuite, les deux versions ont été mises en commun par une tierce personne francophone (ET). Cette version a été traduite à nouveau en anglais par une traductrice indépendante (DF) parfaitement bilingue et sans accès à la version originale anglaise. La traduction anglophone a été comparée à l’échelle d’origine afin de déterminer si elles étaient comparables en termes de contenu (PS). Quelques ajustements mineurs ont été apportés par trois évaluateurs bilingues (PS, ET et BM) sur la MCPS-Fr basés sur la comparaison entre les deux échelles en anglais (Annexe 1) afin de maintenir une équivalence sémantique maximale.

**Analyse audiovisuelle**

Pour cette partie, les enregistrements («vidéos») utilisés ont été ceux obtenus lors de l’étude de la validation de l’échelle de douleur (5).

Trente chattes de race croisée ont subi une ovariohystérectomie (OVH) via une approche ventrale sur la ligne blanche (13). Les données détaillées de la population étudiée ont été rapportées lors de l’étude originale (13). Les comportements observés et interactifs ont été enregistrés à quatre moments spécifiques de la période péri-opératoire : T1 «préopératoire» (entre 18 et 24 heures précédant la chirurgie), T2 «entre 30 minutes et une heure après la fin de la chirurgie et avant l’administration d’analgésiques additionnels», T3 «environ quatre heures après l’analgésie postopératoire» et T4 «environ 24 heures après la fin de la chirurgie». Les vidéos ont été randomisées pour assurer l’évaluation à l’aveugle par les observateurs. Un total de 27 vidéos ont été regardées de façon indépendante par un groupe de trois francophones du même genre (une étudiante vétérinaire [AML], une candidate au doctorat [BM] et une vétérinaire comportementaliste certifiée [DF]) et l’évaluation de la douleur a été réalisée en utilisant la MCPS-Fr. Les évaluatrices étaient à l’aveugle, et ne savaient pas à quel moment de la période péri-opératoire, les enregistrements avaient été effectués.

**Validité de construit — Analyse factorielle**

L’analyse des principaux critères composant l’échelle en français a été effectuée sur la moyenne des appréciations données par les trois évaluatrices à l’aide de la rotation des axes factoriels (varimax). Cette information, ainsi que les critères de Kaiser, ont permis d’évaluer la structure interne de l’échelle; les facteurs de l’échelle ayant une valeur propre (eigenvalue) supérieure à 1 ont ainsi été sélectionnés (14).

**Validité de construit**

La validité de construit — La réactivité (un élément de sensibilité) a été évaluée en testant les hypothèses suivantes : 1) Si l’échelle mesure effectivement la douleur, le niveau de douleur obtenu en période post-opératoire avant l’administration d’analgésiques (T2) devrait être plus grand que celui obtenu en période préopératoire (T1); 2) la douleur post-opératoire avant l’administration d’analgésiques (T2) devrait être plus forte qu’après l’administration d’analgésiques (T3); 3) l’intensité de la douleur aiguë devrait diminuer dans le temps (entre T3 et T4). La médiane et l’étendue ont été calculées sur l’ensemble des résultats et une comparaison statistique a été réalisée à l’aide du test de Wilcoxon pour séries appariées (P < 0,05).

**Validité de critère — Analyse convergente par comparaison avec un observateur de référence**

La validité de critère — Convergence a été réalisée en évaluant la concordance entre les résultats obtenus par les observateurs précédents et ceux obtenus par l’observateur de référence JTB qui avait procédé à l’évaluation en direct du patient. Le degré de concordance a été déterminé par l’importance du coefficient Kappa avec un intervalle de confiance de 95 % (15). La classification d’Altman a été utilisée afin d’interpréter ce coefficient, soit : 0,81–1,00 pour un accord presque parfait (très bon); 0,61–0,80 pour un accord important (bon); 0,41–0,6 pour un accord modéré; 0,21–0,4 pour un accord passable et < 0,2 pour un accord faible (16).

**Fiabilité — Cohérence interne**

La cohérence interne de l’échelle francophone de douleur a été évaluée à l’aide du coefficient alpha de Cronbach (17). Le coefficient a été calculé pour l’ensemble de l’échelle et pour chacune des catégories identifiées par l’analyse factorielle. Les coefficients supérieurs à 0,7 ont été considérés comme étant acceptables.

**Fiabilité intra-observateur**

Pour évaluer la fiabilité intra-observateur, une deuxième analyse audiovisuelle a été faite par les mêmes trois observatrices que la première fois, mais deux mois plus tard. La séquence des vidéos pour chacun des chats avait été modifiée (randomisée) afin de ne pas influencer les résultats. Par la suite, les résultats ont été analysés tel que mentionné dans la section «fiabilité inter-observateur».

**Fiabilité inter-observateur**

La concordance des résultats entre les différents observateurs a été évaluée en utilisant le coefficient de concordance intra-classe avec un intervalle de confiance de 95 % (18). Les coefficients ont été calculés pour chaque élément contenu dans l’échelle à chaque temps donné. Les résultats ainsi obtenus ont été interprétés à l’aide de la classification d’Altman, qui a précédemment été présentée.

**Point limite pour l’analgésie de secours**

Pour identifier le score minimal auquel un animal devrait recevoir une thérapie analgésique, les observateurs devaient identifier les chats qui auraient nécessité des analgésiques additionnels.
à la fin de chaque vidéo. Les scores de douleur ont été résumés à la médiane et à la plage de variation. Le test signé des rangs de Wilcoxon a été utilisé pour fin de comparaisons statistiques ($P < 0.05$). Le point limite permettant de déterminer si l’administration d’un analgésique était nécessaire à la médiane et à la plage de variation. Le test signé des rangs à la fin de chaque vidéo. Les scores de douleur ont été résumés à la médiane et à la plage de variation. Le test signé des rangs de Wilcoxon a été utilisé pour fin de comparaisons statistiques ($P < 0.05$). Le point limite permettant de déterminer si l’administration d’un analgésique était nécessaire a été déterminé à l’aide d’une courbe «ROC» (receiver operating characteristic) (12). Pour chaque point limite, la sensibilité et la spécificité ont été calculées. Les différentes sensibilités ont ensuite été portées en ordonnée sur un graphique avec les pourcentages de faux positifs (1-spéficité) placés en abscisse. L’aire sous la courbe représente alors la capacité discriminatoire de l’échelle de la douleur. L’aire sous la courbe se situe théoriquement entre les valeurs de 0,5 (non discriminatoire) et 1,0 (parfaitement discriminatoire) avec des valeurs entre 0,50 et 0,70 (faiblement discriminatoire), 0,70 et 0,90 (modérément discriminatoire) et plus de 0,9 (fortement discriminatoire).

**Résultats**

**Validité de construit – Analyse factorielle**

Les analyses des principaux facteurs de la MCPS-Fr sont présentées au tableau 1. L’analyse factorielle de la version francophone a identifié 3 facteurs ayant des valeurs propres de

<table>
<thead>
<tr>
<th>Tableau 1. Résultats de l’analyse factorielle de la version française de l’échelle UNESP-Botucatu-MCPS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Facteur de charge</strong>*</td>
</tr>
<tr>
<td><strong>Item</strong></td>
</tr>
<tr>
<td>Posture</td>
</tr>
<tr>
<td>Confort</td>
</tr>
<tr>
<td>Activité</td>
</tr>
<tr>
<td>Comportements divers</td>
</tr>
<tr>
<td>Réaction à la palpation de la plaie chirurgicale</td>
</tr>
<tr>
<td>Appétit</td>
</tr>
<tr>
<td>Vocalisation</td>
</tr>
<tr>
<td>Pression artérielle</td>
</tr>
<tr>
<td>Événements</td>
</tr>
<tr>
<td>Variance (%)</td>
</tr>
<tr>
<td>Variance accumulée (%)</td>
</tr>
</tbody>
</table>

L’analyse a été faite par la méthode d’extraction de composante principale et la rotation des axes factoriels (varimax) avec le critère de Kaiser.

* Facteur de charge représente la corrélation entre les variables et facteurs.
* Communalité représente la proportion de la variance de chaque item qui peut être expliqué par le facteur.
† Item a été sensiblement chargé pour le facteur.
NA = Non applicable.

<table>
<thead>
<tr>
<th>Tableau 2. Scores totaux et partiels de douleur déterminée par des observateurs en aveugles et l’ observateur de référence – analyse de vidéos</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Période périopératoire</strong></td>
</tr>
<tr>
<td>T1 préopératoire</td>
</tr>
<tr>
<td>Sous-échelle 1 (0–18)</td>
</tr>
<tr>
<td>Sous-échelle 2 (0–6)</td>
</tr>
<tr>
<td>Sous-échelle 3 (0–6)</td>
</tr>
<tr>
<td>T2 post-opératoire : avant analgésie de seconds</td>
</tr>
<tr>
<td>Sous-échelle 1 (0–18)</td>
</tr>
<tr>
<td>Sous-échelle 2 (0–6)</td>
</tr>
<tr>
<td>Sous-échelle 3 (0–6)</td>
</tr>
<tr>
<td>T3 post-opératoire : après analgésie de seconds</td>
</tr>
<tr>
<td>Sous-échelle 1 (0–18)</td>
</tr>
<tr>
<td>Sous-échelle 2 (0–6)</td>
</tr>
<tr>
<td>Sous-échelle 3 (0–6)</td>
</tr>
<tr>
<td>T4 post-opératoire : 24 heures après la fin de la chirurgie</td>
</tr>
<tr>
<td>Sous-échelle 1 (0–18)</td>
</tr>
<tr>
<td>Sous-échelle 2 (0–6)</td>
</tr>
<tr>
<td>Sous-échelle 3 (0–6)</td>
</tr>
</tbody>
</table>

Médiane et la fourchette des scores totaux et partiels de douleur déterminée par observateurs en aveugles et l’observateur de référence et basée sur l’analyse de vidéo enregistrée à 4 points spécifiques durant la période périopératoire chez les chattes subissant une ovariohystérectomie.

* Scores de douleur à T2 était sensiblement plus élevé que T1 ($P < 0.001$).
† Scores de douleur à T3 et T4 étaient sensiblement plus bas que T2 ($P < 0.001$).

Sous-échelle 1 : posture, confort, activité, attitude, comportements divers et vocalisation.
Sous-échelle 2 : réaction à la palpation de la plaie chirurgicale et réaction à la palpation de l’abdomen/flanc.
Sous-échelle 3 : pression artérielle et appétit.
Tableau 3. Accord entre les observateurs en aveugle et l’observateur de référence pour chaque item — analyse des vidéos

<table>
<thead>
<tr>
<th>Item</th>
<th>Observateur 1 (BM)</th>
<th>Observateur 2 (DF)</th>
<th>Observateur 3 (AML)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posture</td>
<td>0,90 (0,86–0,95)</td>
<td>0,90 (0,86–0,94)</td>
<td>0,96 (0,93–0,99)</td>
</tr>
<tr>
<td>Confort</td>
<td>0,87 (0,80–0,94)</td>
<td>0,88 (0,81–0,95)</td>
<td>0,76 (0,67–0,86)</td>
</tr>
<tr>
<td>Activité</td>
<td>0,89 (0,80–0,95)</td>
<td>0,86 (0,80–0,94)</td>
<td>0,85 (0,78–0,93)</td>
</tr>
<tr>
<td>Attitude</td>
<td>0,90 (0,84–0,94)</td>
<td>0,94 (0,89–0,98)</td>
<td>0,73 (0,62–0,83)</td>
</tr>
<tr>
<td>Comportements divers</td>
<td>0,97 (0,95–0,99)</td>
<td>0,92 (0,88–0,96)</td>
<td>0,97 (0,96–0,99)</td>
</tr>
<tr>
<td>Réaction à la palpation de la plaie chirurgicale</td>
<td>0,97 (0,94–0,99)</td>
<td>0,90 (0,84–0,96)</td>
<td>0,91 (0,86–0,97)</td>
</tr>
<tr>
<td>Réaction à la palpation de l’abdomen/flanc</td>
<td>0,88 (0,83–0,92)</td>
<td>0,89 (0,82–0,95)</td>
<td>0,83 (0,75–0,91)</td>
</tr>
<tr>
<td>Appétit</td>
<td>0,84 (0,73–0,94)</td>
<td>0,92 (0,85–0,99)</td>
<td>0,75 (0,64–0,86)</td>
</tr>
<tr>
<td>Vocalisation</td>
<td>0,84 (0,72–0,96)</td>
<td>0,95 (0,87–0,98)</td>
<td>0,84 (0,74–0,93)</td>
</tr>
</tbody>
</table>

Accord entre les observateurs en aveugle et l’observateur de référence évalué par le coefficient poids de kappa (IC 95 %) pour chaque item contenu dans l’échelle à chaque temps donné (préopératoire, post-opératoire avant et après analgésie de secours, et 24 heures après la fin de la chirurgie). Interprétation : 0,81–1,0 très bon; 0,61–0,80 bon; 0,41–0,6 modéré; 0,21–0,4 passable; < 0,2 faible.

Tableau 4. Fiabilité intra-observateur pour chaque item — analyse des vidéos

<table>
<thead>
<tr>
<th>Item</th>
<th>Observateur 1 (BM)</th>
<th>Observateur 2 (DF)</th>
<th>Observateur 3 (AML)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posture</td>
<td>0,90 (0,86–0,95)</td>
<td>0,88 (0,83–0,92)</td>
<td>0,94 (0,90–0,96)</td>
</tr>
<tr>
<td>Confort</td>
<td>0,84 (0,78–0,89)</td>
<td>0,92 (0,88–0,95)</td>
<td>0,87 (0,78–0,89)</td>
</tr>
<tr>
<td>Activité</td>
<td>0,91 (0,87–0,94)</td>
<td>0,86 (0,80–0,91)</td>
<td>0,83 (0,75–0,88)</td>
</tr>
<tr>
<td>Attitude</td>
<td>0,85 (0,79–0,90)</td>
<td>0,93 (0,89–0,91)</td>
<td>0,87 (0,81–0,91)</td>
</tr>
<tr>
<td>Comportements divers</td>
<td>0,98 (0,98–0,99)</td>
<td>0,92 (0,88–0,94)</td>
<td>0,98 (0,97–0,99)</td>
</tr>
<tr>
<td>Réaction à la palpation de la plaie chirurgicale</td>
<td>0,91 (0,87–0,94)</td>
<td>0,93 (0,89–0,95)</td>
<td>0,90 (0,86–0,93)</td>
</tr>
<tr>
<td>Réaction à la palpation de l’abdomen/flanc</td>
<td>0,88 (0,83–0,92)</td>
<td>0,94 (0,92–0,96)</td>
<td>0,95 (0,93–0,97)</td>
</tr>
<tr>
<td>Appétit</td>
<td>0,73 (0,63–0,81)</td>
<td>0,97 (0,96–0,98)</td>
<td>0,77 (0,66–0,84)</td>
</tr>
<tr>
<td>Vocalisation</td>
<td>0,88 (0,83–0,92)</td>
<td>0,96 (0,94–0,97)</td>
<td>0,88 (0,83–0,92)</td>
</tr>
</tbody>
</table>

La fiabilité intra-évaluateur a été évaluée en utilisant le coefficient de concordance intra-classe (IC 95 %) pour chaque item contenu dans l’échelle à chaque temps donné (préopératoire, post-opératoire avant et après analgésie de secours, et 24 heures après la fin de la chirurgie). Interprétation : 0,81–1,0 très bon; 0,61–0,80 bon; 0,41–0,6 modéré; 0,21–0,4 passable; < 0,2 faible.

4,24; 2,32 et 1,50. Le facteur 1 a permis d’expliquer 42,4 % de la variance et a été dénommé « Changement psychomoteur ». Ce paramètre inclut la posture, le confort, l’activité, l’attitude, la vocalisation et divers comportements. Le facteur 2 comptait pour 23,2 % de la variance et représentait la dimension de « Protection de la région douloureuse », qui regroupait la réaction à la palpation de la plaie chirurgicale ainsi que la réaction à la palpation de l’abdomen/du flanc. Le facteur 3, composé des variables de pression sanguine et d’appétit, a été nommé « Variables physiologiques » et contribuait à 15,0 % de la variance totale.

Validité de construit — Réactivité
L’analyse des facteurs a confirmé la nature multidimensionnelle de l’échelle et, par conséquent, la validité de construit a été déterminée pour le score total ainsi que pour le score partiel, lesquels étaient significativement augmentés à T2 (après la chirurgie, mais avant l’analgésie postopératoire) lorsque comparés à T1 (période préopératoire). Les scores étaient significativement diminués après l’analgésie de secours (T2 vs. T3) et au fil du temps entre T2 et T4 (Tableau 2).

Validité de critère — Convergence par comparaison avec un observateur de référence
À toutes les périodes d’évaluation péri-opératoire, l’accord entre les observateurs et l’observateur de référence, évalué par le coefficient kappa, était bon à très bon, et ce pour le score total et tous les éléments de l’échelle (Tableau 3). Seule l’étudiante vétérinaire (AML) avait un accord légèrement plus faible avec l’observateur de référence.

Fiabilité — Cohérence interne
Le score total du coefficient alpha de Cronbach de l’échelle était de 0,918, ce qui indique une excellente cohérence interne. La cohérence interne des catégories 1 (Changements psychomoteurs) et 2 (Protection de la région douloureuse) était également excellente, soit 0,938 et 0,900, respectivement. La catégorie 3 (Variables physiologiques) démontrait une cohérence interne modérée, soit 0,608.

Fiabilités intra- et inter-observateur
Les résultats de la fiabilité intra-observateurs et inter-observateurs sont présentés aux tableaux 4 et 5, respectivement.
Point limite pour l’analgésie de secours

À partir de l’analyse de la courbe ROC, différents points limites ont été suggérés, mettant en évidence le point représenté simultanément par les plus grandes valeurs de sensibilité et de spécificité. Le point limite optimal identifié était > 7 points (échelle allant de 0 à 30 points), avec une sensibilité de 97,8 % (95 % IC : 92,2–99,7 %) et une spécificité de 99,1 % (95 % IC : 96,9–99,9 %). La grande aire sous la courbe (ASC ou AUC), soit 0,999 (95 % IC : 0,986–1,000 ; P < 0,0001) indique que l’instrument possède une excellente capacité discriminatoire (Figure 1 et 2). Ainsi, l’utilisation d’une analgésie supplémentaire est recommandée pour les scores ≥ 8 (0–30 points). Cela représente 26,6 % du score total maximal de l’échelle.

Discussion

Cette étude a confirmé la structure multidimensionnelle de la MCPS-Fr et en a atténué la validité et la fiabilité lorsqu’elle est utilisée par des individus ayant une expérience différente pour évaluer la douleur aiguë chez des chattes ayant subi une OVH. De plus, nous sommes parvenus à déterminer une valeur au-dessus de laquelle l’administration d’analgésie de secours est recommandée, de manière similaire aux MCPS en anglais et en espagnol. La validité et la fiabilité de la MCPS-Fr étaient excellentes, à l’instar de la version en anglais (2) et de la version originale en portugais brésilien (3–4). Ces résultats sont en faveur de l’hypothèse stipulant que la traduction et l’adaptation culturelle de la version francophone étaient adéquates.

La validité de construit se penche sur la capacité d’un instrument à détecter des changements dans la construction, ce qui fournit l’évidence la plus solide pour la validation (19). Dans cette étude, la validité de construit a été évaluée au moyen d’une analyse factorielle ainsi que par un test de réactivité de réponse de la grille. L’analyse factorielle est communément utilisée pour étudier la structure interne d’un indice de santé qui comprend des composantes séparées, chacune reflétant un aspect différent de la santé. L’analyse factorielle peut également être utilisée dans la validation de construit en indiquant une association entre les composantes des mesures d’une sous-échelle, où des échelles mesurant différents sujets se rapporteraient sur des sous-échelles ou sur des facteurs différents (11). La MCPS-Fr était semblable à la MCPS-Ang et à la MCPS-Esp en ce qui concerne la validité de construit — analyse factorielle puisque toutes ont donné lieu à l’identification de trois facteurs, à la différence de la MCPS-Port qui a montré une solution à quatre facteurs. Cependant, les valeurs propres (eigenvalue) de la version francophone différaient de celles de la version anglaise et anglophone. Pour cette dernière, les eigenvalues pour les facteurs 1, 2 et 3 étaient respectivement 4,24; 2,32 et 1,50; alors que pour cette dernière, ces valeurs étaient respectivement 3,07; 3,04 et 1,20. En raison de cela, les éléments de la version française ont été réorganisés en sous-échelles ou dimensions différentes. Chaque facteur ou sous-échelle pour chacune des versions de l’échelle était nommé différemment et contenait des points différents. Par exemple, le facteur 1 de la version française a été nommé «Changements...
psychomoteurs» et comprenait posture, confort, activité, attitude, vocalisation et comportements variés, alors que le facteur 1 de la version anglaise a été nommé «Expression de la douleur» et comprenait comportements variés, réaction à la palpation de la plaie de chirurgie, réaction à la palpation de l’abdomen/du flanc et vocalisation. Les critères «réaction à la palpation de la plaie de chirurgie» et «réaction à la palpation de l’abdomen/du flanc» ont été inclus au facteur 2 de la version française nommé «Protection de la région douloureuse», ce qui était similaire au facteur 2 identifié dans la MCPS-Port (3). Indépendamment des items compris dans chaque sous-échelle, il a été suggéré qu’une structure à trois facteurs serait plus appropriée que la structure à 4 facteurs de l’échelle originale en portugais (3).

La validité de construit — Réactivité a aussi été testée selon les hypothèses que le temps et l’intervention (chirurgie, administration d’analgésiques) modifieraient le score de douleur. Les changements dans les scores au fur et à mesure du temps ont déjà été utilisés en médecine vétérinaire pour valider des échelles de la douleur (20–21), tandis que les changements dans les scores de la douleur suite à une intervention sont décrits pour les patients pédiatriques (22–23). À l’instar des résultats de validation de la MCPS-Ang et de la MCPS-Esp, les scores de douleur totaux et pour chaque sous-échelle ont augmenté suite à la chirurgie et ont diminué après l’analgésie postopératoire ainsi qu’avec le temps, ce qui supporte la validité de construit.

La validité de critère — Convergence permet d’établir la validité d’un instrument de mesure en le comparant avec un critère externe et, dans la présente étude, elle a été déterminée en examinant l’accord entre les scores de douleur enregistrés par les observateurs et ceux de l’observateur de référence, tel que rapporté précédemment (2,24). L’observateur de référence considéré était le chercheur ayant développé l’échelle et qui possède une grande expertise en évaluation de la douleur feline. Tous les éléments ont démontré un accord allant de bon à très bon, confirmant la validité de convergence, même lorsqu’un individu avec moins d’expérience était inclus (étudiante vétérinaire). Cette dernière a suivi la formation sur l’évaluation de la douleur telle qu’offerte sur le site web www.animalpain.com.br. L’échelle peut donc être utilisée en toute confiance par des étudiants, par exemple, à condition qu’ils aient suivi une formation. Un tel accord s’est avéré supérieur à ce qui avait été observé pour la MCPS-Ang et pour la MCPS-Port, où chaque paramètre tel que le confort, l’attitude, l’activité et l’appétit avaient un accord moyen; et similaire à la MCPS-Esp. Ces différences pourraient être reliées au nombre d’observateurs dans chaque étude, qui contribuerait à augmenter la variabilité. Cinq observateurs distincts avec une expérience et une formation différentes ont été utilisés pour valider la MCPS-Ang et la MCPS-Esp. De plus, la validation en français ne comprenait pas de véritable étude clinique puisqu’elle reposait sur l’évaluation de vidéos. Ceci constitue une limite à l’application de l’échelle. Pour tenter de renforcer la validation de la MCPS-Fr, une application de cette échelle à la clinique est actuellement en développement à l’Université de Montréal. Une comparaison avec une autre échelle composite pour l’évaluation de la douleur aiguë chez le chat est aussi prévue (7). Cette dernière échelle est un outil basé sur le comportement avec un point limite pour le traitement de secours. Une discussion sur les différences entre la MCPS-Ang et l’échelle de Calvo et al. (2014) a été rapportée précédemment (7).

La fiabilité d’une échelle est évaluée en testant sa cohérence interne, ce qui vérifie les relations réciproques entre les différentes composantes de l’échelle. Il est également nécessaire d’évaluer la capacité de l’instrument à produire des résultats similaires lorsqu’il est utilisé par différents individus (fiabilité ou reproductibilité inter-observateur) ou lorsqu’il est utilisé à différents moments par le même individu (fiabilité ou stabilité intra-observateur) (25). De manière similaire à la MCPS-Ang, la cohérence interne du score total et des scores partiels des sous-échelles «changements psychomoteurs» et «protection de la région douloureuse», calculée par le coefficient alpha de Cronbach indiquait une excellente cohérence interne. La sous-échelle «variables physiologiques» indiquait qu’à elle une cohérence interne moyenne ou inacceptable pour la MCPS-Fr et pour la MCPS-Ang, respectivement. Ces résultats différaient de ceux observés pour la version originale de l’échelle, dont la cohérence interne pour cette sous-échelle était très bonne (3–4). Cependant, ces trois versions ne peuvent être comparées à ce sujet. En effet, dans la présente étude, le paramètre «pression sanguine artérielle» n’a pas été évalué puisque cette mesure n’était pas disponible lors de l’évaluation des vidéos. Ainsi, la cohérence interne de cette sous-échelle était basée uniquement sur l’évaluation de l’appétit. L’utilisation de variables physiologiques telles que la pression sanguine et l’appétit comme faisant partie de l’évaluation de la douleur est controversée (2), car elles sont réputées peu spécifiques à la condition douloureuse (influence importante du stress), et pourrait s’avérer peu pratique dans un contexte clinique. Considérant que ces paramètres comptent pour 15 % et 12 % de la variance totale dans les versions française et anglaise, ils pourraient être omis de l’échelle sans compromettre l’évaluation globale de la douleur. Toutefois, si cette sous-échelle était considérée, elle ne devrait être utilisée qu’en association avec les sous-échelles 1 et 2 (2).

Dans l’étude présentée ici, la fiabilité intra-observateur était bonne à très bonne pour tous les éléments de l’échelle, tel que cela a été observé dans toutes les versions précédentes de la MCPS. Ainsi, la MCPS-Fr a démontré une fiabilité adéquate. De manière similaire, la fiabilité inter-observateur variait de bonne à très bonne, ce qui est supérieur à la MCPS-Ang et semblable à la MCPS-Esp. La bonne performance de l’échelle en termes de reproductibilité et de stabilité lorsqu’utilisée par des évaluateurs ayant une expérience différente, résulte probablement de la description détaillée des comportements de douleur comprise dans la MCPS. Il est intéressant de noter que la validité de critère était bonne à très bonne, en comparant les résultats des analyses de vidéos avec ceux de l’observateur de référence qui avait évalué les chats dans un contexte clinique.

La définition d’un point limite au sein d’une échelle de douleur est un outil précieux pour recommander l’administration d’analgésie de secours lors de l’évaluation et de la reconnaissance de la douleur; de plus, cela fournit une mesure importante de l’efficacité de la thérapie analgésique, tant en recherche qu’en contexte clinique. Dans cette étude, l’analyse de la courbe ROC a été utilisée pour déterminer le point limite pour l’analgésie de secours (2–4). Cette technique permet de déterminer la capacité d’un test à faire la distinction entre deux groupes, à choisir le
point limite optimal et à comparer la performance de deux ou plusieurs tests (12). En utilisant le critère de sensibilité et spécificité balancées, le meilleur point limite identifié était > 7, ce qui signifie que l’utilisation d’analgésie additionnelle est recommandée pour les scores égalant 8 et plus (sur une échelle de 0–30 points). Cela représente 26,6 % du score maximal de l’échelle et est en accord avec la MCPS-Port, la MCPS-Ang et la MCPS-Esp (2–6). Sur la base de ce résultat, en présence de douleur postopératoire, on pourrait donc recommander d’appliquer une analgésie de secours dès que l’évaluation (quel qu’en soit l’outil) atteint 25 % du maximum. Par contre, une étude récente a démontré que l’administration de la kétamine peut produire un effet confondant sur le «Changement psychomoteur» (26). Une autre étude récente a démontré que l’administration de la kétamine peut produire un effet confondant sur le «Changement psychomoteur» (26). Cet effet pourrait surestimer les scores de la douleur (26).

L’analyse par vidéos a été faite par trois observatrices. Le genre a été rapporté comme un facteur de biais dans plusieurs études en médecine humaine (27–30). Récemment, il y a été rapporté que les femmes ont tendance à attribuer des scores de douleur plus forts que les hommes dans une variété de conditions douloureuses en médecine vétérinaire (31–32). Le genre de l’observateur doit donc influencer l’évaluation de la douleur. Cela pourrait avoir biaisé les résultats de notre étude.

La MCPS-Fr est une échelle valide, fiable et sensible, dans nos conditions expérimentales, pour l’évaluation de la douleur aiguë chez les chattes ayant subi une OVH, lorsqu’utilisée par des individus ayant chacun une expérience différente. Cette étude a également défini un point limite au-dessus duquel l’analgésie de secours est recommandée.

**Remerciements**

Maxim Moreau (MM) pour la traduction française de l’échelle à partir de la version anglphonique de l’UNESP-Botucatu-MCPS. D’Hélène Ruel pour la révision du français.
Annexe 1. Version française de l’échelle de douleur composite multidimensionnelle UNESP-Botucatu (suit)

Comportements divers
Observer et noter la présence de comportements définis ci-dessous :

- Le chat est couché et tranquille, mais il remue la queue
- Le chat contracte et étre ses membres pelviens et/ou contracte ses muscles abdominaux (flanc) et qu’une pression délicate est appliquée (appliquer la pression directement sur la région)
- Le chat a les yeux pratiquement fermés (yeux mi-clos)
- Le chat lèche et/ou mord la plaie chirurgicale

- Aucun des comportements ci-haut n’est présent
- Présence d’un de ces comportements
- Présence de deux de ces comportements
- Présence de trois ou de tous ces comportements

Vocalisation
- Le chat est tranquille, il ronronne lorsque stimulé ou miaule en interagissant avec l’observateur. Le chat ne grogne pas, ne gémit pas et ne crache pas
- Le chat ronronne spontanément (sans être stimulé ou manipulé par l’observateur)
- Le chat grogne, gémit ou crache lorsque manipulé par l’observateur (lorsque la position de l’animal est changée par l’observateur)
- Le chat grogne, gémit ou crache spontanément (sans être stimulé ou manipulé par l’observateur)

Sous échelle 2 : PROTECTION DE LA RÉGION DOULOUREUSE (0–12)

Réaction à la palpation de la plaie chirurgicale
- Le chat ne réagit pas lorsque la plaie chirurgicale est touchée ou pressée; ou il n’y a aucun changement par rapport à la réponse pré-chirurgicale (si une évaluation initiale a été effectuée)
- Le chat ne réagit pas lorsque la plaie chirurgicale est touchée, cependant il réagit lorsque la plaie est pressée. Il peut vocaliser et/ou tenter de mordre
- Le chat réagit lorsque la plaie chirurgicale est touchée et pressée. Il peut vocaliser et/ou tenter de mordre
- Le chat réagit lorsque l’observateur approche la plaie chirurgicale. Il peut vocaliser et/ou tenter de mordre. Le chat ne permet pas la palpation de la plaie chirurgicale

Réaction à la palpation de l’abdomen/flanc
- Le chat ne réagit pas lorsque l’abdomen/flanc est touché ou pressé; ou il n’y a aucun changement par rapport à la réponse pré-chirurgicale (si une évaluation initiale a été effectuée). L’abdomen/flanc n’est pas tendu
- Le chat ne réagit pas lorsque l’abdomen/flanc est touché, cependant il réagit lorsque l’abdomen/flanc est pressé. L’abdomen/flanc est tendu
- Le chat réagit lorsque l’abdomen/flanc est touché et pressé. L’abdomen/flanc est tendu
- Le chat réagit lorsque l’observateur approche de l’abdomen/flanc. Le chat peut vocaliser et/ou tenter de mordre. Il ne permet pas la palpation de son abdomen/flanc

Sous échelle 3 : VARIABLES PHYSIOLOGIQUES (0–6)

Pression artérielle
- 0 % à 15 % au-dessus de la valeur pré-chirurgicale
- 16 % à 29 % au-dessus de la valeur pré-chirurgicale
- 30 % à 45 % au-dessus de la valeur pré-chirurgicale
- > 45 % au-dessus de la valeur pré-chirurgicale

Appétit
- Le chat mange normalement
- Le chat mange plus que la normale
- Le chat mange moins que la normale
- Le chat n’est pas intéressé par la nourriture

Score totale (0–30)

Directives pour l’usage de l’échelle

Débute par observer le comportement du chat sans ouvrir la cage. Observer s’il est au repos ou actif, intéressé ou non par son environnement, calme ou vocalisant. Vérifier la présence de comportements spécifiques (voir «Comportements divers» ci-haut).

Ouvrir la cage et observer si le chat sort rapidement de la cage ou hésite à quitter la cage. Approcher le chat et évaluer sa réaction : amicale, agressive, effrayée, indifférente ou vocalisant. Toucher le chat et interagir avec lui, vérifier s’il est réceptif (il s’apprécie être caressé et/ou s’il est intéressé à jouer).

Si le chat hésite à quitter la cage, encourager le chat à bouger en le stimulant (appeler-le par son nom, caresser-le) et manipuler le chat en changeant sa position et/ou en le sortant de sa cage. Observer le chat hors de la cage, s’il bouge spontanément de manière réservée ou avec réticence. Offrez-lui de la nourriture appétissante et observer sa réponse.

Finalement, placer le chat en décubitus latéral ou sternal et mesurer sa pression artérielle. Évaluer la réaction du chat lorsque l’abdomen/flanc est touché (glisser vos doigts sur la région) et qu’une pression délicate est appliquée (appliquer la pression directement sur la région). Attendre un moment et répéter la même procédure pour apprécier la réaction du chat à la palpation de la plaie chirurgicale.

Pour évaluer l’appétit durant la période post-opératoire immédiate, débuter par offrir une petite quantité de nourriture appétissante immédiatement après le réveil anesthésique. À ce moment, la plupart des chats mangent normalement indépendamment de la présence ou non de douleur. Attendre un moment, puis offrir de nouveau de la nourriture et observer la réaction du chat.
Références

15. Cohen J. Weighted kappa: Nominal scale agreement with provision for scaled disagreement or partial credit. Psych Bull 1968;70:213–220.

Your Path to a Successful New Career
- Financial decisions when very little money is freely available
- Difficult client communications and challenging workplace relationships
- Reality of day-to-day practice and stressful decision-making

If any of these sound familiar, visit the CVMA Early Career DVM Resource Hub. You'll find information, tools and resources that we've gathered specifically to help support new veterinary graduates.

canadianveterinarians.net
Follicular dynamics and ovulation time in gilts and post-weaning sows
Sara I. Williams, R. Luzbel de la Sota

Abstract — Ultrasonography was used to study follicular dynamics from the beginning of estrus to ovulation in pubertal gilts and post-weaning sows. Ultrasound turned out to be a useful tool to determine patterns of growth of preovulatory follicles, to predict ovulation time, and to design protocols for fixed time insemination.

Introduction
During follicular development in the estrous cycle, 3 features appear in all species. These features are: i) sequence of events (recruitment, selection and dominance); ii) need for sequential gonadotropins, follicle-stimulating hormone (FSH) for recruitment and luteinizing hormone (LH for dominance); and iii) range of requirements (number of waves per cycle, follicles by wave number) as well as temporary requirements (time of selection and duration of dominance). When comparing the pattern of follicular development among animal species, follicular waves are described in bovine, ovine, and equine, while only observed during the prepubertal period in swine (1,2).

The process of follicular development in the sow involves 2 of the events mentioned above as the first feature: recruitment and selection. Both in prepubertal and pubertal gilts and in sows, there is a pool of approximately 50 follicles of 1 to 6 mm on the surface of the ovary (3).

In pigs, the ovaries are noteworthy for having a large number of follicles compared with other species (4). During the luteal phase, 30 to 90 small follicles of 1 to 2 mm, and 30 to 50 medium-sized follicles of 2 to 7 mm can be seen in each ovary (3,5,6). Conversely, during the follicular phase, the number of small and medium-sized follicles decreases dramatically in both ovaries, leaving a total of approximately 20 follicles, most of which are ovulatory follicles (5), which reach 7 to 10 mm in diameter prior to ovulation (7).

At the beginning of the luteal phase, immediately after ovulation, pig ovaries have only small antral follicles. However, following decreases in concentration of Inhibin and E2 after ovulation, negative feedback on FSH disappears, FSH concentrations increase, and a wave of synchronized follicle development is initiated. Afterwards, Inhibin production from this wave of follicles reduces FSH production and increasing concentrations of progesterone (P4) from developing corpora lutea suppress gonadotropin secretion (6,8). Hence, there is a continuous growth and atresia of ovarian follicles during the rest of the luteal phase (days 7 to 15 of the estrous cycle), without evidence of waves or follicular dominance (5,7,9). This lack of dominance is associated with no changes in plasma FSH and E2 concentrations for the remainder of the luteal phase (1,9). Ovulatory follicles start to grow between days 14 to 16 of the estrous cycle (10). Ovulatory follicles are recruited from the pool of antral follicles, which develop during the luteal phase of the cycle, and reach about 5 mm (11). Towards the end of the luteal phase, P4 levels fall and the increasing FSH and LH produce follicle recruitment. Small follicles that do not have enough FSH and LH receptors are not recruited and became atretic (12).

Ultrasonography has been available for the last 2 decades to study follicular development and time of ovulation in swine production (12). Initially, transabdominal ultrasonography was used to study follicular development and time of ovulation (13). More recently, it was demonstrated that transrectal ultrasonography is an appropriate method to study pig follicular dynamics because it allows for real-time studies of follicle development and time of ovulation without interfering with the processes (12).
The aim of the present work was to study the growth pattern of follicles from the beginning of estrus to ovulation in post-weaning sows using daily transrectal ultrasonography, and from day 15 of the estrus cycle until ovulation time in pubertal gilts, using trans-abdominal ultrasound. The information in this report warrants the study of size differences of ovulatory follicles between gilts and sows and the possibility of daily scans of the ovary by transrectal ultrasonography. Consequently, this information can be used to design protocols for fixed time insemination.

Figure 1. Mean [± standard error (SE)] number of follicles from 120 h before to 32 h after the onset of estrus [3 to 5 mm (A), 6 to 7 mm (B), 8 to 9 mm (C), and 3 to 9 mm (D)] in pubertal gilts. Values with different letters differ at \( P < 0.05 \).

Materials and methods
Pubertal gilts [crossbred Landrace (LD) × Large white (LW) 90 to 100 kg body weight (BW), aged 160 to 180 d] were used. Gilts (\( n = 7 \)) were housed in individual pens (Veterinary Teaching Hospital, Faculty of Veterinary Sciences, National University of La Plata, Argentina), fed a commercial gestation diet, and treated with gonadotropins (400 IU of eCG + 200 IU of hCG; Duogestal, Syntex SA, Buenos Aires, Argentina), 5 mL, IM, on the day of arrival. Estrus was observed for 96 h after...
treatment. All experimental procedures were in compliance with the EC guidelines for animal experimentation and were approved by the local animal care committee, the Graduate School and the Laboratory Animal Care and Use Committees of the Faculty of Veterinary Sciences at National University of La Plata.

Ultrasound examination started on day 15 of the estrous cycle. Animals were monitored once a day for ovarian mapping and to record the number, location, and size of follicles. From day 18 of the estrus cycle, estrus detection was performed twice a day, and from the time that gilts showed signs of estrus (0 h), ultrasound examinations were performed every 8 h. The time of ovulation was defined as the time of the first ultrasound images without suspected ovulated follicles, less 4 h. Ovulation was confirmed with a subsequent ultrasound examination. Follicular development was monitored by trans-abdominal ultrasonography using a Tringa S50 (Pie Medical, Maastricht, The Netherlands) ultrasound machine with a sectorial probe and a frequency of 5 to 7.5 MHz. The number of follicles according to size category (3, 4, 5, 6, 7, 8, and 9 mm) and the total number of follicles, from the first scan until ovulation time were recorded.

The study in post-weaning sows was conducted on a commercial farm and crossbred LD × LW multiparous sows were...
Transrectal ultrasonography allowed visualization of only 1 face of the ovary, and this could explain the total number of follicles reported in this study. Ovulation occurred at 29.1 ± 2.9 h from the onset of estrus and the size of the preovulatory follicles was 7.0 ± 1.0 mm, with a weaning-to-estrus interval close to 6 d [131.6 ± 11.3 h; 95% confidence interval (CI): 106.3 to 156.8].

**Discussion**

To our knowledge, this is the first study on follicular dynamics from the beginning of estrus to ovulation in pubertal gilts and in post-weaning sows. In pubertal gilts, follicles observed at the beginning of scans (towards the end of the luteal phase) were only 3 to 5 mm. After luteolysis, small and medium-sized follicles quickly disappeared, while the > 6.5 mm appeared and increased the number near the time of ovulation. Selection of follicles in pubertal gilts is a unique process that takes place in the presence of corpus luteum (CL). Previous data demonstrate that the presence of CL alters the blood supply and can indirectly influence the growth of follicles (14). In addition, the population of follicles differs dramatically before and after the formation of the CL, and before and after luteolysis.

The decrease in the number of ovarian follicles during the period studied was mainly due to a reduction in the number of follicles of 6 to 9 mm from the onset of estrus to the time of ovulation (Figure 2D). Follicles 6 to 7 mm in size grew to 8 and 9 mm, and thus the number of medium-sized follicles decreased and the number of large-sized follicles increased. The decrease in number of 6- to 7-mm follicles occurred between 0 and 24 h from the start of estrus and the increase in number of follicles of 8- and 9-mm took place from 24 to 32 h from the beginning of estrus. These 2 events made it possible to form a pool of preovulatory follicles. Some 6- to 7-mm follicles were atretic, became reduced in size and constituted the pool of follicles of 3 to 5 mm. The enlargement of the 3- to 5-mm follicle pool could be due to the atretic follicles, since the number of 6- to 7-mm follicles decreased.

For post-weaned sows, the onset of estrus-ovulation interval observed in this study is less than in previous reports, in which ovulation occurred at 35 ± 8 h after estrus (12) or at an interval of 39 ± 12.4 h from the onset of estrus until ovulation ended (7).

In the present work, the average size of the preovulatory follicles (7.0 ± 1.0 mm) observed in post-weaning sows was similar to that reported previously (12) (7.1 ± 0.9 mm); however, in post-weaning sows the diameter of the largest follicles during ovulation has been reported to be 9.3 mm (15).

In conclusion, the number of follicles changed throughout the period studied since only selected follicles subsequently reached ovulatory size. Ultrasound turned out to be a useful tool to describe the pattern of growth of preovulatory follicles and to predict the time of ovulation. The differences observed between pubertal gilts and post-weaning sows in size of ovulatory follicles and time of ovulation highlight the importance of using ultrasound to predict the onset of ovulation. Furthermore, ovulatory size and time of ovulation could be used to design protocols for fixed time insemination.
Acknowledgments

This study was supported in part by UNLP grants V11/162 and V11/200 to SI Williams and RL de la Sota.

References


Book Review

Compte rendu de livre

Clinical Veterinary Advisor: Dogs and Cats, 3rd edition


Many books sit on my shelf at work but one particular text sits at the ready: the “Clinical Veterinary Advisor.” I originally worked with the first edition, and I am very excited to now have the 3rd edition. It continues to be brief but complete, providing all the details required to manage a case in a busy practice. Not needing everything there is to know about a topic, nor having the time to research it thoroughly, this book provides a perfect synopsis including clinical presentation, epidemiology, diagnostic and treatment plans as well as “pearls and considerations” unique to the condition.

In addition to Dr. Côté, the editor-in-chief, 19 section editors and 400 authors have contributed their knowledge and expertise. Imagine! 400 veterinarians, all offering guidance! What a wonderful team behind you!

This 3rd edition continues to be conveniently divided into sections: “Diseases and Disorders, Differential Diagnosis, Procedures and Techniques, Laboratory Tests, Clinical Algorithms, and Drug Formulary.” New topics have been added to update the third edition, such as FAST ultrasound examinations, methicillin-resistant staphylococcal infections, and albuterol toxicosis. An assortment of videos have been added, while numerous photographs have been updated. The Drug Formulary now has an additional 30 new drugs listed.

The Differential Diagnosis section underwent a complete renewal. New tables have been added, listing the differentials on one side and typical clinical findings and helpful tests opposite. This improves navigation through long possible differential lists and how best to proceed.

This text includes a sister electronic version. There, one can find bonus material and extended versions of many subjects covered in the hardcopy version. Client Education Sheets, which contain 50 “how to” sheets, also continue to be included.

This textbook would certainly appeal to new or recent graduates, but I do think it is useful to even the well-seasoned veterinarian as Dr. Côté and team do a very good job at staying current and including cutting edge issues. Definitely a winner and certainly a text to purchase!

Feasibility of quantitative contrast ultrasound imaging of bladder tumors in dogs

Rachel E. Pollard, Katherine D. Watson, Xiaowen Hu, Elizabeth Ingham, Katherine W. Ferrara

Abstract – The purpose of this pilot study was to assess the feasibility of Cadence contrast pulse sequencing ultrasound to predict clinical and angiogenic tumor response in dogs undergoing chemotherapy. Contrast ultrasound facilitated visualization of bladder tumors but failed to identify a straightforward relationship between ultrasound measures and clinical outcome.

Introduction

Increasing evidence indicates that cancer growth and lethality are dependent on and related to angiogenesis (1). Angiogenesis is the process by which tumors recruit new blood vessels to deliver the nutrients and oxygen necessary for growth and metastasis. Microvascular density (MVD) is one of the most widely accepted markers of tumor angiogenesis (2). Elevated MVD is a negative prognostic indicator in a variety of tumor types including hepatocellular carcinoma (2), renal cell carcinoma (3), and bladder carcinoma (4) in humans. Moreover, MVD is known to decrease as angiogenesis is curtailed and vascular normality is restored with anti-angiogenic chemotherapy (5).

While tumor biopsy is routine for diagnosis, repeated biopsy is invasive and carries associated morbidity. Thus, surrogate markers to serially quantify angiogenic response are desirable. Diagnostic imaging is frequently used to evaluate the response of bladder transitional cell carcinoma to treatment. B-mode ultrasound is widely used to assess bladder tumor size because it is non-invasive and the equipment is readily accessible and inexpensive. With the addition of microbubble contrast agents, ultrasound becomes sensitive to capillary-sized vessels and very low flow rates while maintaining the ability to determine tumor size from traditional B-mode imaging. Ultrasound contrast agents are composed of high molecular weight gases encapsulated in an albumin, polymer, or lipid shell (6). A variety of contrast-specific pulse sequences designed to enhance non-linear echoes that are specifically produced by microbubble contrast agents have been developed and employed for the interrogation of regions of myocardial infarction, tumor microvasculature, and responses to therapy in both clinical and research settings (7–9). Cadence contrast pulse sequencing (CPS) is one such sequence which uses a multipulse transmit sequence with precise changes in interpulse amplitude and phase that when received and combined allow for the rejection of linear (tissue) echoes while non-linear contrast echoes are retained (10). Qualitative contrast ultrasound has been used to identify bladder tumors and to evaluate enhancement patterns in humans (11,12). Quantitative estimation of MVD with contrast ultrasound has been reported in a rodent model in which significant correlation was found between MVD and the enhanced area with vessels ranging from 6 to 30 μm (13).

The purpose of this preliminary study was to evaluate the feasibility of using contrast-enhanced CPS ultrasound estimates of MVD to predict clinical and angiogenic response to treatment in dogs with bladder tumors undergoing chemotherapy. We compared results to clinical outcome and urine vascular endothelial growth factor (VEGF) concentration. Angiogenic factors such as VEGF are upregulated by many tumors and evaluation of urine VEGF is thought to be representative of tumor angiogenesis in bladder transitional cell carcinoma (14).
We hypothesized that this ultrasound technique would predict which dogs would have clinical and/or angiogenic progression.

**Materials and methods**

To test this hypothesis, we recruited 6 dogs with 8 lower urinary tract transitional cell carcinomas (6 bladder, 2 prostate) into this pilot study. All procedures were approved by the institutional Clinical Trials Review Board and owner consent for the contrast ultrasound imaging studies was obtained before the procedures were carried out. 

Dogs were excluded if they had evidence of cardiac disease to eliminate the unlikely possibility of myocardial infarction by microbubbles. Dogs were also excluded if they had a history of anaphylactic reactions to vaccines, contrast agents, or other medications to minimize the likelihood of adverse response to the microbubble contrast agent. Additionally, dogs were not eligible if they had serum creatinine > 265 μmol/L, serum bilirubin > 17 μmol/L, serum ALT > 400 IU/L, hematocrit < 25%, platelet count < 50 000/μL or a urethral stent in place to ensure overall health and reduce risk of adverse response to the microbubble contrast agent. There were 3 spayed females and 3 castrated males. There was 1 each fox terrier, Scottish terrier, West Highland white terrier, pomeranian, Labrador retriever mix, and terrier mix. 

Mean [± SD (standard deviation)] age was 11.5 ± 2.1 y (range: 8 to 14 y). Mean body weight was 9.6 ± 3.7 kg (range: 4.8 to 16.0 kg). All dogs were receiving Piroxicam capsules (Teva Pharmaceuticals Sellersville, Pennsylvania, USA) (n = 5) or Meloxicam (Boehringer Ingelheim Vetmedica, St. Joseph, Missouri, USA) (n = 1) before and during the study period. 

Four dogs initially received Mitoxantrone (Teva Parenteral Medicines, Irvine, California, USA), 3 of which eventually developed progressive disease (n = 1), Vinblastine (APP Pharmaceuticals, Schaumburg, Illinois, USA) (n = 1) or Carboplatin, followed by Vinblastine (n = 1). Two dogs initially received Carboplatin, both of which developed progressive disease and were switched to Mitoxantrone. One of these dogs later received Vinblastine. 

Dogs were evaluated with B-mode ultrasound prior to chemotherapy induction (t = 0) and at every chemotherapy appointment thereafter (approximately once every 3 wk) until the owners opted to stop therapy or the animal died. B-mode ultrasound of the caudal abdomen was performed using a commercially available ultrasound unit (Acuson Sequoia 512; Siemens Medical Solutions USA, Ultrasound Division, Issaquah, Washington, USA) and a 15L8 MHz linear transducer. Mean tumor size before chemotherapeutic induction was 2.2 ± 2.6 cm$^3$ calculated as follows: ellipsoid volume = (length × width × height) × π/6. Considering all 8 tumors, a total of 59 imaging studies were performed, 8 of which were obtained before induction and 51 of which were follow-up evaluations. At follow-up, each tumor’s response was categorized as complete resolution of all evidence of tumor (CR) (0/51); partial response (PR), ≥ 50% decrease in tumor volume and no new tumor lesions (6/51); stable disease (SD), < 50% change in tumor volume and no new tumor lesions (28/51); and progressive disease (PD), ≥ 50% increase in tumor volume or development of new tumor lesions (17/51). Mean survival for 5 dogs was 373 ± 238 d (range: 120 to 755 d). One dog was lost to follow-up at 200 d after chemotherapy induction. 

After tumor response was determined, ultrasound contrast material (Definity; Bristol-Myers Squibb, N. Billerica, Massachusetts, USA) was injected intravenously (cephalic or saphenous) as a bolus with dosage based on body weight as previously described (0.1 mL for dogs ≤ 20 kg; 0.2 mL for dogs > 20 kg) (15). Cadence contrast pulse sequencing was engaged and longitudinal video clips were obtained for 20 s starting at the arrival of contrast agent into the imaging plane as previously reported (13). When 2 lesions were present, the primary lesion was imaged first and then the transducer was moved and a second video clip was obtained of the secondary lesion. After the imaging procedure, dogs received their assigned chemotherapy drug. Dogs were monitored for evidence of anaphylaxis (including but not limited to pruritis, head shaking, facial swelling, dermal redness, vomiting) for 1 h following contrast administration.

Image data were recorded digitally and were processed offline (MatLab; The MathWorks, Natick, Massachusetts, USA).

---

**Table 1.** The mean (± standard deviation) Cadence pulse sequencing (CPS) estimates of microvessel density (MVD) from 6 dogs with 8 bladder tumors undergoing chemotherapy. Dogs are separated into those with partial remission (PR), stable disease (SD), and progressive disease (PD). Also shown is the percent change in MVD and the number of dogs to have increased or decreased estimates of MVD in comparison to the previous examination.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean CPS estimate of MVD</th>
<th>% change MVD from previous</th>
<th>Number increased from previous</th>
<th>Number decreased from previous</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR (n = 6)</td>
<td>28.4 ± 13.8%</td>
<td>39.3 ± 67.7%</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>SD (n = 28)</td>
<td>19.9 ± 8.6%</td>
<td>9.8 ± 68.6%</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>PD (n = 17)</td>
<td>22.7 ± 9.9%</td>
<td>14.7 ± 81.8%</td>
<td>8</td>
<td>9</td>
</tr>
</tbody>
</table>

---

**Figure 1.** A region of interest (ROI) has been drawn around the tumor arising from the cranioventral bladder wall on this sagittal contrast-enhanced CPS ultrasound image obtained from a dog with transitional cell carcinoma.
Results

No evidence of acute toxicity was observed. All tumors were successfully detected with the contrast ultrasound technique and blood flow was visible at the microvessel level. The mean CPS estimate of MVD prior to chemotherapeutic induction was 24.6 ± 10.3% indicating that ~25% of the mm scale pixels within the image contained the vascular contrast agent. The data failed to identify a clear trend in CPS estimates of MVD which correlated to clinical assessment of PR, SD, or PD (Table 1) where the mean change in MVD was positive for each group; however, the standard deviation was large.

A total of 25 free catch urine samples were analyzed for VEGF concentration, 5 of which were obtained before induction and 20 were follow-up evaluations. Samples were centrifuged at 1000 × g for 20 min to remove particulate matter and the supernatants were aliquoted for VEGF concentration assessment using an ELISA kit (Canine VEGF DuoSet ELISA Kit, R&D Systems, Minneapolis, Minnesota, USA), following the manufacturer’s recommended protocol. Urine VEGF concentrations were normalized to the urine creatinine and expressed as nanograms VEGF/g creatinine. Mean urine VEGF concentration before chemotherapeutic induction was 1117.8 ± 413.3 ng/g creatinine. In dogs with 2 tumors, urine samples were considered to come from SD if both tumors had SD but were considered to come from PR or PD if either tumor was classified as PR or PD and the other was characterized as SD. Data failed to identify a correlation between urine VEGF concentration and CPS estimates of MVD. In addition, there was no clear trend for urine VEGF concentration or percent change urine VEGF concentration with PR, SD, or PD.

Discussion

Three dogs were diagnosed with bacterial cystitis during the study period. There was no clear trend identified between urine VEGF concentration, presence or resolution of cystitis, and percent change in CPS estimates of MVD.

In summary, data collected from this limited number of dogs indicated that contrast enhanced ultrasound of lower urinary tract tumors is feasible in dogs but failed to identify a connection between ultrasound data, urine VEGF concentration, and traditional criteria for tumor response to chemotherapy. Thus, our hypothesis that this ultrasound technique would predict which dogs would have clinical and/or angiogenic progression has been rejected. The disappointing early results have discouraged the continued enrollment of dogs in this study and a new study design with fewer confounding variables (only 1 chemotherapeutic protocol, cystitis as an exclusion criterion) is being considered. Interpretation of results should take into account the limited number of animals in this study.

Acknowledgments

The authors acknowledge the efforts of Dr. Katherine Skorupski, Dr. Carlos Rodriguez, and Ms. Teri Guerrero. This work was supported by NIH grant #NIHR01CA112356 and NIHR01CA113659.

References

Nasal carriage of methicillin-resistant Staphylococcus pseudintermedius in dogs treated with cephalexin monohydrate

Punpichaya Fungwithaya, Pattarapat Chanchaithong, Nathita Phumthanakorn, Nuvee Prapasarakul

Abstract — This study aimed to investigate the nasal carriage of methicillin-resistant Staphylococcus pseudintermedius (MRSP) in dogs treated with oral cephalexin monohydrate. Ten dogs with superficial pyoderma were monitored longitudinally for carriage of MRSP for up to 1 year after treatment; the strains were typed and antibiograms were determined. Methicillin-susceptible S. pseudintermedius (MSSP) was recovered prior to treatment in all dogs and could be isolated after 12 months in 1 dog. Methicillin-resistant Staphylococcus pseudintermedius was detected within 1 week of treatment in all dogs, and 3 clones represented by ST45, ST112, and ST181 were consistently present for up to 12 months after treatment. All MRSP isolates were resistant to at least 7 common antimicrobials. Oral cephalexin monohydrate treatment selected for strains of multi-resistant MRSP, which were still present after 1 year.

Résumé — Portage nasal de Staphylococcus pseudintermedius résistant à la méthicilline chez les chiens traités à l’aide de céphalexine monohydrate. Cette étude visait à étudier le portage nasal de Staphylococcus pseudintermedius résistant à la méthicilline (SPRM) chez les chiens traités à l’aide de céphalexine monohydrate par voie orale. Dix chiens ayant une pyodermie superficielle ont été surveillés dans une étude longitudinale pour le portage de SPRM pendant jusqu’à un an après le traitement; les souches ont été typées et des antibiogrammes ont été réalisés. Staphylococcus pseudintermedius susceptible à la méthicilline (SPSM) a été récupéré avant le traitement chez tous les chiens et pouvait être isolé jusqu’à 12 mois chez un chien. Staphylococcus pseudintermedius résistant à la méthicilline a été détecté une semaine après le traitement chez tous les chiens et 3 clones représentés par ST45, ST112 et ST181 étaient continuellement présents jusqu’à 12 mois après le traitement. Tous les isolats de SPRM étaient résistants à au moins sept antimicrobiens communs. Le traitement à la céphalexine monohydrate par voie orale a été choisi pour les souches multirésistantes de SPRM qui étaient toujours présentes après un an.

(Intégré par Isabelle Vallières)

Can Vet J 2017;58:73–77

Introduction

Staphylococcus pseudintermedius is a commensal bacterium on canine mucosa and skin that also can cause canine dermatitis. In rare cases it can opportunistically infect humans and contribute to detrimental outcomes such as septicemia, sinusitis, and dog bite wound infection (1–3). Systemic cephalexin administration is the primary choice of empirical therapy for canine superficial pyoderma (4); however, the use of antibiotics may encourage an increased frequency of resistant strains, resulting in recurrent infection or increased risk of bacterial zoonotic transmission to owners and veterinarians (5).

Antimicrobial resistant strains can be selected following exposure to antimicrobials. According to the selective pressure concept, antibiotic resistant strains may persist depending on the relative genetic fitness of resident susceptible and resistant strains (6). Methicillin-resistant S. pseudintermedius (MRSP), can be increasingly detected after routine antibiotic treatment for canine dermatitis, and these MRSP also express resistance to other beta-lactam drugs, namely, penicillins and cephalosporins (7). Previously, emergence of MRSP from dogs with a history of treatment for dermatitis was observed in a longitudinal study and was shown to be the source of contamination for in-contact animals and the environment within the same household (8). Methicillin-resistant S. pseudintermedius has been reported to persist on dog’s skin for more than 6 mo after antibiotic administration, and increased detection of MRSP during treatment seems to be common (9). However, changes in the S. pseudintermedius population and the duration of persistence of MRSP strains on dog skin following antimicrobial treatment still needs to be determined in index dogs. This study aimed to determine changes in the S. pseudintermedius population in dogs after treatment with cephalexin and to evaluate...
Table 1. Age, gender, breed, and treatment for the 10 dogs and the number of *Staphylococcus*-like colonies recovered at each collection time.

<table>
<thead>
<tr>
<th>Dog</th>
<th>Age</th>
<th>Gender</th>
<th>Breed</th>
<th>Other treatments</th>
<th>Log (CFU/swab)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pre-treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MSA&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>1</td>
<td>2 y</td>
<td>M</td>
<td>Beagle</td>
<td>2% Chlorhexidine</td>
<td>2.54</td>
</tr>
<tr>
<td>2</td>
<td>8 mo</td>
<td>F</td>
<td>Mixed</td>
<td>Herbal cream</td>
<td>2.84</td>
</tr>
<tr>
<td>3</td>
<td>9 mo</td>
<td>F</td>
<td>Mixed</td>
<td>Herbal cream</td>
<td>2.48</td>
</tr>
<tr>
<td>4</td>
<td>1 y</td>
<td>M</td>
<td>German shepherd</td>
<td>2% Chlorhexidine</td>
<td>2.75</td>
</tr>
<tr>
<td>5</td>
<td>1.5 y</td>
<td>F</td>
<td>Mixed</td>
<td>2% Chlorhexidine</td>
<td>2.35</td>
</tr>
<tr>
<td>6</td>
<td>10 mo</td>
<td>F</td>
<td>English cocker spaniel</td>
<td>None</td>
<td>2.56</td>
</tr>
<tr>
<td>7</td>
<td>1 y</td>
<td>M</td>
<td>Pug</td>
<td>None</td>
<td>2.25</td>
</tr>
<tr>
<td>8</td>
<td>1.5 y</td>
<td>M</td>
<td>Beagle</td>
<td>2.5% Benzyl peroxide</td>
<td>2.29</td>
</tr>
<tr>
<td>9</td>
<td>9 mo</td>
<td>M</td>
<td>Mixed</td>
<td>Herbal cream</td>
<td>2.36</td>
</tr>
<tr>
<td>10</td>
<td>1 y</td>
<td>M</td>
<td>Mixed</td>
<td>2.5% Benzyl peroxide</td>
<td>2.9</td>
</tr>
</tbody>
</table>

<sup>a</sup> Other treatments apart from oral cephalxin.

<sup>b</sup> Local herbal product containing custard apple seeds and other Thai herbal ingredients recommended for localized dermatitis.

<sup>c</sup> Mannitol salt agar containing oxacillin, 0.5 µg/mL.

<sup>d</sup> Mannitol salt agar containing oxacillin, 0.5 µg/mL.

<sup>e</sup> Numbers of *Staphylococcus*-like colonies between the 3 groups were significantly different (Kruskal-Wallis test; *P* = 0.007).

<sup>f</sup> Numbers of *Staphylococcus*-like colonies in the follow-up group were greater than in the pre-treatment and treatment groups (Wilcoxon Signed Ranks test; *P* = 0.005 and *P* = 0.013). ND — not detectable; M — male; F — female; CFU — colony-forming units. Chlorhexidine and benzyl peroxide were shampoos.

the persistence of the resistant population in a longitudinal study.

**Materials and methods**

**Animals and treatment**

This study was approved by the Chulalongkorn University Institutional Animal Care and Use Committee (permit number 113/56). Owner’s permission was obtained through a consent form. Between 2011 and 2013, 10 dogs from different households were recruited on a voluntary basis by the Dermatological Unit at the University’s Small Animal Teaching Hospital. Inclusion criteria for the dogs were generalized superficial pyoderma indicated by the presence of primary and secondary lesions including erythema, papules, pustules, or epidermal collarettes, and having no previous treatment with any drugs. All subjects were treated with cephalxin monohydrate (Sialexin; Siam Pharmaceutical, Bangkok, Thailand), 22 to 30 mg/kg body weight (BW), PO, q12h for 2 mo and with topical therapy in most cases (Table 1). The dose and duration of treatment were prescribed by the veterinary dermatologist.

**Bacterial collection**

Each dog was sampled at 3 times: i) prior to treatment with antibiotics (Pre-treatment group); ii) 1 wk after the start of treatment (Treatment group); and iii) 6 to 12 mo after the onset of treatment (follow-up group). Dog 9 was sampled at both 6 and 12 mo after treatment. Up to 4 samples from the same dog were collected over the duration of the study, depending on the cooperation of the animal owners.

**Isolation and identification of *S. pseudintermedius***

Samples were collected using sterile cotton swabs inserted at least 0.5 cm into the left rostral nares of the dogs. The tip of the cotton swab was added to 1 mL of 0.85% normal saline in a microcentrifuge tube, then vigorously mixed and kept at 4°C for no longer than 2 h before it was cultured for bacteria. Ten-fold serial dilutions were prepared as described in the ISO6888-1 guideline (10), and 100 µL of each dilution was plated onto mannitol salt agar (MSA) (Difco, Paris, France), and onto MSA containing 0.5 µg/mL oxacillin (Sigma-Aldrich, St. Louis, Missouri, USA) (MSA-O) (11). The plates were incubated at 37°C for 24 h and at 35°C for 48 h, respectively. Colonies of staphylococci that were pink, round, convex, smooth and 0.1 to 0.3 mm in diameter were counted on 2 plates per dilution series containing approximately 20 to 200 colonies and the average number was used to calculate the colony-forming units (CFU)/swab.

At the highest serial dilution plate with visible growth of bacterial colonies, 3 suspected staphylococcal colonies were selected from MSA-O plates for species identification. In the case of no bacterial growth on MSA-O, pink colonies were collected from MSA without oxacillin. *Staphylococcus pseudintermedius* from either MSA-O or MSA was identified by routine primary biochemical tests, the tube coagulase test and secondary biochemical properties, with confirmation by amplification of the *stu* gene by polymerase chain reaction (PCR) (12,13). After identification, non-staphylococci and coagulase negative staphylococci were excluded from the experiment. *Staphylococcus aureus* ATCC (American Type Culture Collection) 25923<sup>f</sup>, *S. pseudintermedius* CVMC [Chulalongkorn University Veterinary Microbiology (CUVM), canine strain] 0108, *S. intermedius* CVMP (CUVM pigeon strain) 0309, *Staphylococcus delphini* CVMP 0109 and *Staphylococcus schleiferi* subsp. *coagulans* CVMC 0208 were used as control strains. One *S. pseudintermedius* isolate per dog per time of collection, comprising 10 isolates from prior to treatment, 10 isolates from the first week, and 11 isolates from follow-up dogs, were used for susceptibility testing and molecular typing.

**Susceptibility testing and MRSP detection**

All *S. pseudintermedius* isolates were assessed for susceptibility against 8 antimicrobials by the disk diffusion method including 1 µg oxacillin (OXA), 200 µg mupirocin (MUP), 15 µg erythromycin (ERY), 2 µg clindamycin (CLI), 30 µg
Multilocus sequence typing (MLST) was performed to determine genetic diversity within the strains. A PFGE group was performed using CHEF-DRIII apparatus (Bio-Rad, Hercules, California, USA), with a voltage of 6 V/cm and a switch time of 0.5 to 15 s for 18 h. The DNA fingerprints were obtained for strain typing using the BandScan95/55 software (Syngene, Frederick, Maryland, USA) with normalization, and a dendrogram was constructed using Gene Dir® software (Syngene, Frederick, Maryland, USA) with UPGMA and setting at 1.0% position tolerance. A PFGE group was defined as clustering with an 80% similarity in pattern. Multilocus sequence typing (MLST) was performed to determine the sequence type (ST) of MRSP strains by amplification and sequencing of 7 housekeeping genes (gnd, rpsL, purA, sar, tuf, and tuf), and analysis with the PubMLST database (http://pubmlst.org/spseudintermedius/) (19).

### Table 2. Genotypic and antibiogram profiles of coagulase-positive staphylococci (CoPS) serially isolated from 10 dogs before treatment (0 month) until a maximum of 12 months after treatment.

<table>
<thead>
<tr>
<th>Dog</th>
<th>CoPS</th>
<th>PFGE type</th>
<th>ST</th>
<th>Antibiogram</th>
<th>SCCmec</th>
<th>Time of occurrence (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MSSP</td>
<td>A</td>
<td>45</td>
<td>OXA-ERY-CLI-GEN-DOX-SXT</td>
<td>Neg</td>
<td>0, 1*, 6, 8, 12</td>
</tr>
<tr>
<td>2</td>
<td>MRSP</td>
<td>A</td>
<td>45</td>
<td>OXA-ERY-CLI-GEN-DOX-SXT</td>
<td>NT</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>MRSP</td>
<td>F</td>
<td>45</td>
<td>OXA-ERY-CLI-GEN-DOX-SXT</td>
<td>NT</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>MSSP</td>
<td>B</td>
<td>45</td>
<td>OXA-ERY-CLI-GEN-DOX-SXT</td>
<td>NT</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>MSSP</td>
<td>C</td>
<td>112</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>A1</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>MSSP</td>
<td>C</td>
<td>112</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>A1</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>MSSP</td>
<td>E</td>
<td>181</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>V</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>MSSP</td>
<td>I</td>
<td>181</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>V</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>MRSP</td>
<td>C</td>
<td>112</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>A1</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>MSSP</td>
<td>C</td>
<td>112</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>A1</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>MSSP</td>
<td>A</td>
<td>45</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>NT</td>
<td></td>
</tr>
</tbody>
</table>

CoPS — coagulase-positive staphylococci; MSSP — methicillin-sensitive *S. pseudintermedius*; MRSP — methicillin-resistant *S. pseudintermedius*; PFGE — pulsed-field gel electrophoresis; ST — sequence type in multilocus sequence typing; NT — non-typable; Neg — negative.

1*: the samples were collected on the 7th day after onset of treatment. OXA — oxacillin; ERY — erythromycin; GEN — gentamicin; CLI — clindamycin; DOX — doxycycline; SXT — sulphamethoxazole; ENR — enrofloxacin.

A grey block indicates the presence of the clones at the time of sampling. All dogs had CoPS at each sampling time. Three samples were obtained from each dog, except for dog 9, which had 2 samples obtained.

<table>
<thead>
<tr>
<th>CoPS</th>
<th>Antibiogram</th>
<th>Time of occurrence (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSSP</td>
<td>OXA-ERY-CLI-GEN-DOX-SXT</td>
<td>0, 1*, 6, 8, 12</td>
</tr>
<tr>
<td>MRSP</td>
<td>OXA-ERY-CLI-GEN-DOX-SXT</td>
<td></td>
</tr>
<tr>
<td>MSSP</td>
<td>OXA-ERY-CLI-GEN-DOX-SXT</td>
<td></td>
</tr>
<tr>
<td>MRSP</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>A1</td>
</tr>
<tr>
<td>MSSP</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>A1</td>
</tr>
<tr>
<td>MRSP</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>V</td>
</tr>
<tr>
<td>MSSP</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>V</td>
</tr>
<tr>
<td>MRSP</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>A1</td>
</tr>
<tr>
<td>MSSP</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>A1</td>
</tr>
<tr>
<td>MSSP</td>
<td>OXA-ENR-ERY-CLI-GEN-DOX-SXT</td>
<td>NT</td>
</tr>
</tbody>
</table>

Molecular typing

SCCmec of MRSP isolates were classified by the presence of the *mec* complex class and the type *cfr* complex by PCR (17). The DNA fingerprints were obtained for strain typing using Cfr91-pulsed-field gel electrophoresis (PFGE) with the CHEF-DRIII apparatus (Bio-Rad, Hercules, California, USA), with a voltage of 6 V/cm and a switch time of 0.5 to 15 s for 18 h and 20 to 25 s for 5 h (18). A The *XbaI*-digested chromosome of *Salmonella* Braenderup H9812 was used as a standard marker for normalization, and a dendrogram was constructed using Gene Dir® software (Syngene, Frederick, Maryland, USA) with UPGMA and setting at 1.0% position tolerance. A PFGE group was defined as clustering with an 80% similarity in pattern. Multilocus sequence typing (MLST) was performed to determine the sequence type (ST) of MRSP strains by amplification and sequencing of 7 housekeeping genes (*ack, cpn60, fih, pta, purA, sar*, and *tuf*), and analysis with the PubMLST database (http://pubmlst.org/spseudintermedius/) (19).

**Statistical analysis**

Statistics 17 for Microsoft Windows (SPSS Inc.; Chicago, Illinois, USA) was used for all analyses. Category comparison for number of colonies cultured among groups (Pre-treatment, Treatment, and Follow-up) was done using the Kruskal-Wallis test. Differences between the numbers of colonies cultured at each observation were analysed using the Wilcoxon signed-ranks test. Values of *P* < 0.05 were statistically significant.

**Results**

All selected dogs were presumptively diagnosed with generalized superficial pyoderma. After 2 mo of administration of cephalaxin, all dogs had normal skin without the need for additional antibiotic or steroid therapies throughout the time of observation. All dogs had *S. pseudintermedius* isolated at each sampling time (Tables 1 and 2). On MSA, the numbers of CFU of staphylococcus-like colonies among the 3 groups
were significantly different ($P = 0.007$). Furthermore, the CFU for the dogs at follow-up were significantly greater than for the pre-treatment ($P = 0.005$) and treatment ($P = 0.013$) samples (Table 1). Only MSSP was isolated from all dogs before treatment, and dogs 9 and 10 also had MSSP isolated at 12 mo after treatment. Twelve MSSP isolates, including 10 from all dogs before treatment and 2 from Dog 9 and Dog 10 at 12 mo after treatment, were included for the PFGE fingerprint analysis. A total of 19 MRSP were selected from all dogs at the 1st week after treatment and the follow-up period (6 to 12 mo after treatment) (Table 2). All MRSP isolates were characterized by SCC\textit{mec} typing, MLST, and DNA fingerprint analysis. A dendrogram from DNA fingerprint analysis of 31 \textit{S. pseudintermedius} isolates illustrated with other characteristics and time of isolation is presented as a supplementary figure.

Isolates from the same dog having an identical PFGE pattern, sequence type (ST), SCC\textit{mec} type, and antibiogram are shown as 1 representative pattern.

By PFGE typing, 12 MSSP isolates clustered into 9 groups and 19 MRSP isolates clustered into 3 groups based on the 80% similarity cut-off. Typing by MLST identified 3 STs of MRSP including ST45, ST112, and ST181. MRSP ST181 contained SCC\textit{mec} V (MRSP ST181-V), and ST112 carried non-typable SCC\textit{mec} with a class A \textit{mec} complex and type 1 \textit{ccr} complex (MRSP ST112-A1). Multiplex PCR could not identify the SCC\textit{mec} type of MRSP ST45 (MRSP ST45-ND). Antibiograms of MRSP are presented in the supplementary figure (available from the author) and Table 2.

**Discussion**

In previous studies, risk factors associated with increased detection of MRSP included frequent visits to veterinary clinics, prolonged hospital stays, and having a breeding bitch in the same household — but the effects of administration of antimicrobials have not been consistent (20–22). Thus, this longitudinal study assessed the dynamic population change of \textit{S. pseudintermedius} between pre-treatment and drug-use, as well as the persistence of MRSP after treatment. Samples were taken from the nose, as this site is known to be an important source of staphylococcal carriage and contamination for other hosts (9). The careful selection of animals in the study may explain why untreated dogs had no resistant strains detected, which differed from previous reports (9, 21). In our study, \textit{S. pseudintermedius} could be a microbial marker for selection of antimicrobial resistant strains.

The use of MSA allowed growth of all staphylococci with pink colonies that could be used to differentiate them from other genera (12). The MSA-O agar was used to screen the staphylococci with the methicillin resistance trait, thus the bacterial number tentatively represented the MRSP number (15). The increased number of colonies of staphylococci on MSA found in the follow-up samples compared to pretreatment might have arisen from co-colonization with MRSP and pre-existing MSSP strains. Adaptation mechanisms of bacterial strains in their ecological niche in the canine nose following antibiotic treatment have not been investigated. In all treated dogs, MSSP appeared to be replaced by MRSP as the dominant coagulase-positive \textit{Staphylococcus} by the first week after treatment. Hence cephalexin treatment rapidly drove an increase in MRSP, consistent with the selective pressure theory for staphylococcal populations (23). This result confirms that selection of MRSP during treatment occurs frequently in the nasal environment (9). Moreover our follow-up demonstrated maintenance of a high level of persistence for 6 to 12 mo in this longitudinal study, which was concordant with the results of a previous cross-sectional study (9).

Pulsed-field electrophoresis typing is an approved genetic classification tool, and gave results consistent with the MLST results. The findings confirmed that clones of MSSP were genetically different from MRSP. The MLST and PFGE analysis confirmed that the persistent MRSP in follow-up dogs was the
same clone in all cases (8). The frequency of specific MRSP clones in an individual could be explained by a selective pressure phenomenon exerted by pre-existing resistant strains during antimicrobial exposure.

Isolates ST45-ND, ST112-A1, and ST181-V were shown to be multi-resistant to at least 5 additional antimicrobial classes. SCCmec of MRSP ST45 was not specifically identified in this study, but \( \Psi \text{SCCmec}_{57395} \) is commonly associated with this ST in Thailand and Israel (11,23,24). Additionally, ST45, ST112, and ST181 were previously reported as clones shared between dogs and owners (11). Our study showed that MRSP could be detected in healthy convalescent dogs, and that MLST and SCCmec typing were useful to study the molecular epidemiology of the infection.

In conclusion, we demonstrated that oral cephalaxin treatment of 10 dogs with pyoderma was associated with selection of MRSP clones with multidrug resistance. We observed a rapid onset of selective pressure and maintenance of MRSP for up to 12 mo after treatment.

Acknowledgments

This work was supported by the National Research Council of Thailand (2013–2014), the 90th Anniversary of Chulalongkorn University Fund (Ratchadapiseksomphot Endowment Fund) and a Conference Grant 2014 for PhD students, Graduate School, Chulalongkorn University and the Center of Excellence for Emerging and Re-emerging Infectious Diseases in Animals which supported a student research scholarship. We thank Professor David J. Hampson of Murdoch University, Australia and the Office of Research Affairs, Chulalongkorn University, for assistance during preparation of the manuscript and all staff of the Small Animal Hospital, Faculty of Veterinary Science, Chulalongkorn University for assistance in sample collection.

References

Dr. Ken Leslie named as the 2016 Metacam® 20 Bovine Welfare Award winner

The executive board of the Canadian Association of Bovine Veterinarians (CABV)/Association Canadienne des Vétérinaires Bovins (ACVB) and Boehringer Ingelheim (Canada) Ltd. have announced Dr. Ken Leslie as the recipient of the 2016 Metacam® 20 Bovine Welfare Award.

“It is our distinct pleasure to announce Dr. Ken Leslie as the recipient of the 2016 Metacam® 20 Bovine Welfare Award,” said Dr. John Campbell, Secretary-Treasurer of the CABV/ACVB.

Dr. Leslie spent 34 years as a faculty member at the University of Guelph in the Department of Population Medicine. He retired in 2011 and continues to teach at the Ontario Veterinary College as a sessional lecturer and advisor. Dr. Leslie is known internationally for his research and extension in mastitis control, calf health management and daily cattle well-being. Through his work, Dr. Leslie’s primary objective is to foster awareness and interest in the implementation of progressive health management programs for the dairy industry.

“It is an absolutely great honour to receive the Metacam 20 Bovine Welfare Award for 2016,” Dr. Leslie said following the award ceremony. “It is particularly gratifying to be recognized for contributions to the recognition and understanding of issues related to dairy cattle welfare, and to develop and promote solutions to some of these issues. I am sincerely grateful to the Canadian Association of Bovine Veterinarians for this recognition.”

Dr. Leslie was presented with the 2016 Metacam® 20 Bovine Welfare Award at the 49th Annual Conference of the American Association of Bovine Practitioners on September 15, 2016 in Charlotte, North Carolina.

“Throughout his career, Dr. Leslie has advanced knowledge of dairy cattle welfare and progressive health management programs in the dairy industry,” said Dr. Rob Tremblay, Bovine/Equine Specialist with Boehringer Ingelheim. “He is credited with helping shape new science and practice areas such as pain management in clinical disease and assistance to calves with compromised vitality. Dr. Leslie’s commitment to maintaining bovine health and welfare — and his desire to share his knowledge and insight through his teaching — is exemplary.”

Jeffrey Estabrooks, Business Unit Director (Bovine and Equine) with Boehringer Ingelheim Canada’s Animal Health division, explained the Metacam® 20 Bovine Welfare Award recognizes and encourages those who research and practice animal welfare and well-being. “We are pleased to see Dr. Leslie as the 2016 recipient of the award,” Estabrooks said. “His research work in pain management has greatly improved cattle welfare practices and he has also helped develop a generation of researchers who will continue to research and expand our understanding and practice of animal welfare.”
Case Report Rapport de cas

Primary frontal sinus squamous cell carcinoma in a dog treated with surgical excision

Janet A. Grimes, Candace J. Pagano, Bonnie B. Boudreaux

Abstract — An 8-year-old castrated male mixed breed dog was presented for a squamous cell carcinoma of the left frontal sinus. A partial craniectomy was performed and polytetrafluoroethylene mesh was placed over the craniectomy site. The dog recovered well with a good cosmetic outcome. Histopathology confirmed primary frontal sinus squamous cell carcinoma.

Résumé — Carcinome squameux primaire du sinus frontal chez un chien traité par excision chirurgicale.

Un chien castré de race croisée âgé de 8 ans a été présenté pour un carcinome squameux du sinus frontal gauche. Une craniectomie partielle a été réalisée et un tamis de polytétrafluoroéthylène a été placé sur le site de la craniectomie. Le chien s’est rétabli avec un bon résultat esthétique. L’histopathologie a confirmé un carcinome squameux primaire du sinus frontal.

Frontal sinus squamous cell carcinoma (FS-SCC) is extremely rare as a primary condition, with only 3 cases reported in the veterinary literature (1). Squamous cell carcinoma of the frontal sinus is more commonly seen as an extension of nasal SCC (2). In humans, primary FS-SCC is also rare, comprising 0.009% to 0.03% of head/neck cancers and 0.3% of all paranasal sinus cancers with case reports predominating (3,4). Principal treatments for humans with primary FS-SCC include surgery, radiation therapy, chemotherapy, or combinations thereof, with surgery being the mainstay option in most cases (5–7). Three cases reported in the veterinary literature were treated with chemotherapy alone with survival times ranging from 6 mo to 3 y (1). There are no reports of surgery as a component of treatment for primary FS-SCC in the veterinary literature.

Case description

An 8-year-old castrated male mixed breed dog was presented for SCC of the left frontal sinus. The dog was taken to the primary care veterinarian for sensitivity over the left frontal sinus. A mass was detected and skull radiographs revealed a bony defect over the frontal sinus. Biopsy was performed and it was noted that a soft tissue mass was attached to the rim of bone overlying the left frontal sinus and a portion of the external table of the frontal sinus had presumably been eroded by the tumor. After removal of this soft tissue mass, the tumor was noted to extend caudolaterally within the sinus. No bone was taken during this incisional biopsy. The mass was diagnosed by histopathology as SCC. The patient was referred to the Louisiana State University Veterinary Teaching Hospital for further evaluation.

A computed tomography (CT) scan revealed a defect within the left frontal bone overlying the left frontal sinus with extension of disease, seen as sclerosis and thickening of the bone, into the left frontal and parietal bones that crossed the midline caudally, extending into the right parietal bone (Figure 1). A complete blood (cell) count (CBC) and serum chemistry performed at this visit were unremarkable. Treatment options discussed with the owner included surgical excision with partial craniectomy, radiation therapy, or chemotherapy. The owners elected surgical excision, which was performed 1 wk later. The extent of the tumor was measured on CT images and a 1-cm margin was obtained around the biopsy scar and the visible extent of the tumor on the CT images. There are no reports of surgery as a component of treatment for primary FS-SCC in the veterinary literature.

Department of Veterinary Clinical Sciences, School of Veterinary Medicine, Louisiana State University, Skip Bertman Drive, Baton Rouge, Louisiana 70803, USA.

Address all correspondence to Dr. Janet Grimes; e-mail: jgrimes@uga.edu

Dr. Grimes’ current address is the Department of Small Animal Medicine and Surgery, College of Veterinary Medicine, University of Georgia, 501 D.W. Brooks Drive, Athens, Georgia 30602, USA.

Use of this article is limited to a single copy for personal study. Anyone interested in obtaining reprints should contact the CVMA office (hbroughton@cvma-acvm.org) for additional copies or permission to use this material elsewhere.
allowed removal of the external table of the frontal sinus and the septum. The caudolateral portion of the left frontal sinus was noted to have a plaque of abnormal tissue. Rongeurs were used to break through the internal table of the frontal sinus to connect the previously drilled lines in the cranium. Elevation of this bone from rostral to caudal proceeded with ease and the dorsal calvarium was removed without incident. The bone at the edges of the excision appeared grossly and palpably normal. The left temporal muscle was elevated and released caudally to allow for rotation rostrally to cover the defect. At the rostral most aspect, a temporalis muscle fascia flap from the left side was used to separate the frontal sinus from the brain. The dog recovered well from surgery.

The morning following surgery, the dog was bright, alert, and responsive and ambulating normally. Two hours later, the dog became comatose with normal vital signs and serum chemistry values. A CT scan was performed and revealed left-sided cerebral compression and displacement to the right from the swollen left temporalis muscle (Figure 2). The dog was returned to surgery where the compression was immediately relieved by releasing the left temporalis muscle. Polytetrafluoroethylene mesh was cut to size to cover the defect. A 1.1-mm drill bit was used to drill holes into the cranium surrounding the defect. The mesh was sutured to the calvarium using 2-0 polypropylene, resulting in a domed shape over the defect. A second temporalis muscle fascia flap was elevated from the left temporalis muscle and used to close the defect overlying the mesh. Post-operative radiographs confirmed appropriate placement of the mesh (Figure 3). The patient was administered 1 mg/kg body weight (BW) maropitant citrate (Cerenia; Zoetis, Kalamazoo, Michigan, USA) subcutaneously 30 min prior to treatment with 5-fluorouracil (Adrucil; Teva Pharmaceuticals, Haarlem, Netherlands), 150 mg/m², administered over 10 min. Thirty minutes later, carboplatin (Carboplatin; Teva Pharmaceuticals Industries, Haarlem, The Netherlands), 200 mg/m² was administered over 20 min. Complete blood cell counts were evaluated before treatment and every week after therapy until the next dose. Treatment was delayed if the neutrophil count was $< 3000/µL$ and/or the platelet count was $< 150,000/µL$. A renal panel and urinalysis/urine specific gravity were used to assess renal function.

After the initial dose of chemotherapy, the patient had a double nadir with a grade I neutropenia at week 1 (2700 neutrophils) and week 3 (2400 neutrophils). No adverse events occurred due to the neutropenia. Treatment was delayed 1 wk and the interval of subsequent treatments extended to every

Figure 1. Sagittal reconstruction of CT images. The defect in the frontal sinus is indicated by the asterisk. The sclerosis of the parietal bone is indicated by the arrow. H — rostral; F — caudal.

Figure 2. Transverse CT image showing left-sided cerebral compression and displacement to the right from the swollen left temporalis muscle. P — dorsal; R — right side; A — ventral; L — side.
28 d. No gastrointestinal side-effects were reported. The patient received 6 total cycles of chemotherapy and a CT scan was performed 6 mo after surgery. Significant findings on the CT scan included a healing left dorsal craniectomy with a metal mesh implant and no evidence of recurrence of disease. The dog continues to do well 16 mo after surgery with no signs of recurrence.

Discussion

This is the first report in veterinary medicine of treatment of a primary FS-SCC with surgery. The only previous report of primary FS-SCC described 3 dogs that were treated with chemotherapy consisting of piroxicam and carboplatin and piroxicam and toceranib (1). Survival times were 6.5 mo, 11.5 mo, and 1 dog was still alive 3 y after diagnosis. Surgery was not used as a component of treatment in these cases due to extension of the tumor. Radiation therapy was not pursued due to risk of side-effects to adjacent structures (eye, brain). Surgery is often the chief treatment for primary FS-SCC in humans, with chemotherapy and radiation therapy used as adjuvant treatments (6,7). Chemotherapy for human paranasal sinus carcinomas using combination therapy including cisplatin has been shown to have an 82% response rate in previously untreated patients (10). Radiation therapy alone or combined with surgery for paranasal sinus carcinomas has not proven to significantly improve local control, with only 37% of patients remaining disease-free and 54% overall survival at 2 y (11). Use of chemotherapy induction followed with chemoradiation in patients with paranasal sinus undifferentiated carcinomas resulted in slight improvement with 43% progression-free survival and 64% overall survival at 2 y (12).

Squamous cell carcinoma is locally invasive but typically slow to metastasize. When located in the nasal cavity, SCC is typically treated with radiation therapy, as surgical treatment is unlikely to result in a cure due to early bone invasion (5,8). When confined to the nasal planum, surgery can result in a cure if adequate margins are obtained, although cosmesis is significantly affected (13). Based on pre-surgical imaging, it was believed that margins could be obtained with an aggressive surgical approach and acceptable cosmesis. The owners elected surgical treatment because of the chance of complete removal, and a concern that the cost and risks of radiation therapy were undesirable. More advanced imaging, such as positron emission tomography-computed tomography (PET-CT), may have been able to provide a more definitive margin assessment before surgery, but is not available in our practice.

After the initial surgery, the dog became comatose. On CT scan, the left temporal muscle was swollen, causing left-sided compression and rightward deviation of the brain. Neurological abnormalities were not seen initially and this delayed onset was most likely due to progressive swelling of the left temporal muscle until the brain could no longer compensate. It is likely that this compression and deviation affected the brainstem and cerebellum, resulting in coma and central vestibular signs in this patient. The dog’s condition immediately improved after a second surgery to relieve the compression. With time, the vestibular signs completely resolved, further supporting the theory that the temporary compression was the cause of the vestibular signs. Magnetic resonance imaging (MRI) was not performed, thus detail of the cerebral and cerebellar parenchyma were not available.
Primary FS-SCC is extremely rare in dogs. Chemotherapy has been shown to provide reasonable survival (1). Radiation therapy has not been evaluated for use in treatment of this condition. This report documents, for the first time, that surgery can be used as a primary treatment in some cases. In cases in which surgical margins cannot be achieved, surgical debulking may allow for better control by adjuvant therapies.

References
Suspected immune-mediated neutropenia and corticosteroid responsive pancytopenia in a Portuguese water dog

Ellen B. Denstedt

Abstract — An 8-year-old spayed Portuguese water dog was presented with dysuria, lethargy, and anorexia. A profound neutropenia and pancytopenia were identified. Bone marrow aspirates revealed neutrophilic hyperplasia, a significant left shift, and toxic changes, suggesting immune-mediated destruction as a likely underlying mechanism. Immunosuppressive therapy was instituted and clinical signs improved.

Résumé — Neutropénie à médiation immunitaire suspectée et pancytopénie répondant aux corticostéroïdes chez un Chien d’eau portugais. Un Chien d’eau portugais femelle stérilisée âgée de 8 ans a été présentée avec de la dysurie, de la léthargie et de l’anorexie. Une neutropénie profonde et de la pancytopénie ont été identifiées. Des aspirations de la moelle osseuse ont révélé une hyperplasie neutrophilique, un virage important vers la gauche et des changements toxiques suggérant une destruction à médiation immunitaire comme mécanisme sous-jacent probable. Une thérapie immunsuppresseive a été instituée et les signes cliniques se sont améliorés.

Can Vet J 2017;58:83–86

In May 2016, an 8.7-year-old spayed female Portuguese water dog was presented to the Central Island Veterinary Emergency Hospital on Vancouver Island with clinical signs of lethargy, dysuria, stranguria, and possible hematuria. A urine dipstick identified proteinuria, hematuria, and a urine specific gravity (USG) of 1.033. The patient was treated with amoxicillin/clavulanic acid (Clavaseptin; Vétoquinol, Lavaltrie, Quebec), 12.5 mg/kg body weight (BW), PO, q12h for 10 d, resulting in marked improvement. In early June 2016, the dog ate a piece of clothing, vomited 2 to 3 times, and remained anorexic for several days. Her owners reported that she spontaneously urinated 2 to 3 times, and remained anorectic when in the clinic and urinalysis revealed a USG of 1.044, pH of 8.0, bilirubinuria, and proteinuria, while all other values were unremarkable. Urine sediment did not reveal red blood cells, white blood cells, crystals, or bacteria. An IDEXX SNAP 4Dx test (IDEXX laboratories, Westbrook, Maine, USA) was negative for Borrelia burgdorferi, Ehrlichia canis, Ehrlichia ewingii, Anaplasma phagocytophilum, Anaplasma platys antibiotics, and Dirofilaria immitis antigen. Treatment with Cephalexin (500 mg, PO, q12h) was initiated and the dog was referred to the internal medicine service at Central Victoria Veterinary Hospital (CVVH).

On presentation at CVVH, the patient was moderately pyrexic (39.8°C), the remainder of her vital parameters were within normal limits, and no abnormalities were noted on physical examination. The patient was up-to-date on rabies, canine distemper, canine parvovirus, canine parainfluenza virus (DA2PP), and Leptospira spp. vaccinations and had no history of travel or known allergies. A complete blood (cell) count (CBC) revealed pancytopenia, characterized by a mild normocytic, normochromic, non-regenerative anemia (hematocrit 0.34 L/L; reference interval (RI): 0.38 to 0.57 L/L), thrombocytopenia with shift platelets (9.0 × 10⁹/L; RI: 143 to 448 × 10⁹/L), mild lymphopenia (1.0 × 10⁹/L; RI: 1.1 to 5.0 × 10⁹/L), and profound mature neutropenia (0.3 × 10⁹/L; RI: 2.9 to 12.7 × 10⁹/L) with mild toxic changes. Biochemistry revealed an increased symmetric dimethylarginine (SDMA) (0.09 µmol/L; RI: 0 to 0.07 µmol/L), total protein (77 g/L; RI: 55 to 75 g/L), aspartate transaminase (AST) (58 IU/L; RI: 16 to 55 IU/L), creatine kinase (295 IU/L; RI: 10 to 200 IU/L), hypoalbuminemia (26 g/L; RI: 27 to 39 g/L), hyperglobulinemia (51 g/L; RI: 24 to 40 g/L), and hyperbilirubinemia (6.5 µm/L; RI: 0 to 5.13 µmol/L). Total T4 was within normal limits (16.0 nmol/L; RI: 13.0 to 53.0 nmol/L). The dog urinated normally while in the clinic and urinalysis revealed a USG of 1.044, pH of 8.0, bilirubinuria, and proteinuria, while all other values were unremarkable. Urine sediment did not reveal red blood cells, white blood cells, crystals, or bacteria. An IDEXX SNAP 4Dx test (IDEXX laboratories, Westbrook, Maine, USA) was negative for Borrelia burgdorferi, Ehrlichia canis, Ehrlichia ewingii, Anaplasma phagocytophilum, Anaplasma platys antibodies, and Dirofilaria immitis antigen. Treatment with Cephalexin (500 mg, PO, q12h) was initiated and the dog was referred to the internal medicine service at Central Victoria Veterinary Hospital (CVVH).

On presentation at CVVH, the patient was moderately pyrexic (39.8°C) and lethargic. Physical examination identified prominent mandibular lymph nodes and mild dehydration. Biochemistry and CBC and biochemistry panels were repeated revealing a further decrease in hematocrit (0.25 L/L;
RI: 0.37 to 0.61 L/L), lymphocytes (0.75 × 10^9/L; RI: 1.05 to 5.10 × 10^9/L), and neutrophils (0.25 × 10^9/L; RI: 2.95 to 11.64 × 10^9/L). Albumin, bilirubin, and total protein were normal. Prothrombin time and partial thromboplastin time were within normal limits. Samples for a blood culture were collected and treatment with ampicillin (Ampicillin Sodium; Novopharm, Toronto, Ontario), 440 mg, IV, q8h, and enrofloxacin (Baytril; Bayer, Toronto, Ontario) 200 mg, IV, q24h, was initiated.

Abdominal ultrasound showed hyperechoic material with linear striations in the mid small intestine, dilating the lumen of the intestine for a distance greater than 3 cm. The wall of the intestine at this location was thickened (0.5 cm) and the mesentery surrounding this location was voluminous and hyperechoic. These findings were consistent with an intestinal foreign body — presumed to be the clothing eaten recently, causing mechanical obstruction. Intestinal wall inflammation and possible peritonitis were also identified. The splenic parenchyma contained at least 3 hyperechoic foci up to 0.8 cm in diameter. The differentials for this finding include extra-medullary hematopoesis, benign hyperplasia, or round cell neoplasia. All other abdominal organs were within normal limits. An exploratory laparotomy was recommended for removal of the suspected intestinal foreign body.

Prior to surgery, the patient's blood type was determined to be Dog Erythrocyte Antigen (DEA) 1.1+ and a fresh whole blood transfusion (500 mL) was started at a rate of 3.33 mL/min. The patient was premedicated with fentanyl (Fentanyl Citrate; Summit Veterinary Pharmacy, Richmond, British Columbia), 3 μg/kg BW, IV, and lidocaine (Xylocaine 2%; Vétouquinol), 1 mg/kg BW, IV, boluses, induced with ketamine (Ketalcan; Bimeda-MTC Animal Health, Cambridge, Ontario), 1 mg/kg BW, IV, and propofol (Propofol; Fresenius Kabi, Richmond Hill, Ontario), 10 mg/kg BW, IV, and maintained with isoflurane inhalant and oxygen on a circle circuit (fresh gas flow rate of 100 mL/kg BW per minute). Analgesia was provided throughout the surgery with a fentanyl (8 μg/kg BW per minute) continuous rate infusion (CRI). An incision was made from the xyphoid to pubis, upon which a small amount of serous peritoneal effusion was noted and collected for culture. All organs were grossly normal, although a small amount of hemosiderosis was noted on the ventral aspect of the tail of the spleen. The entire length of the small bowel was palpated and appeared grossly normal, with no foreign body identified. However, the distal colon contained firm compressible material and a foreign body could not be differentiated from fecal material. Finally, a 1 cm × 1 cm firm, purple nodule in the omentum was discovered and removed using blunt dissection for histopathology. This was later determined to be ectopic splenic tissue. A cystocentesis was performed during surgery and urine was collected for culture. The patient’s abdomen was closed using a routine three-layer closure and ampicillin, enrofloxacin, fentanyl/lidocaine CRI, and Normosol-R (2.2 mL/kg BW per hour) IV fluids were continued after surgery.

The following morning, the patient passed a small piece of rubbery, eraser-like material in her feces, which was likely the object palpated in her colon during the exploratory laparotomy. The patient’s vital parameters normalized (temperature 38.4°C); however, her lethargy and anorexia persisted. Blood, urine, and serous abdominal fluid cultures yielded no aerobic, anaerobic, or fungal growth. Metronidazole (Metronidazole; Hospira, Saint-Laurent, Quebec), 10 mg/kg BW, IV, q12h, maropitant (Cerenia; Zoetis, Kirkland, Quebec), 1 mg/kg BW, IV, q12h, sucralfate (Sulcrate Suspension Plus; Aplatlis Pharma, Mont-Saint-Hilaire, Quebec), 0.25 mL/kg BW, PO, q8h, pantoprazole (Pantoprazole Sodium; Fresenius Kabi), 1 mg/kg BW, IV, q24h, and buprenorphine (Vetergesic; Alstoe Animal Health, Whirby, Ontario), 0.01 mg/kg BW, IV, q8h, were added to her regimen and the fentanyl/lidocaine CRI was discontinued. The dog’s packed cell volume (PCV) was maintained at approximately 31.6% and her lymphopenia (0.31 × 10^9/L; RI: 1.05 to 5.10 × 10^9/L), thrombocytopenia (15 × 10^3/μL), and severe neutropenia (0.17 × 10^9/L; RI: 2.95 to 11.64 × 10^9/L) persisted.

Further diagnostics were pursued at this point, including ventral-dorsal, left and right lateral radiographs of the thorax, which were within normal limits. The tick polymerase chain reaction (PCR) performed through IDEXX (Rickettsia rickettsii, Mycoplasma haemocanis, Neorickettsia risticii, Leishmania spp., Hepatozoon spp., Ehrlichia spp., Babesia spp., Anaplasma spp., Bartonella spp., Candidatus Mycoplasma haemotaurum) was negative. The patient was premedicated for a bone marrow aspirate with buprenophine (0.01 mg/kg BW, IV) and midazolam (Midazolam; Sandoz, Boucherville, Quebec), 0.2 mg/kg BW, IV, induced with propofol (5 mg/kg BW, IV) and maintained on isoflurane inhalant and oxygen on a circle circuit (fresh gas flow rate of 100 mL/kg BW per minute). The bone marrow aspirates were reviewed by True North Veterinary Diagnostics (Langley, British Columbia) and revealed a myeloid/erythroid (M:E) ratio of 8:1, with the neutrophilic series predominating. There was a significant left shift within the neutrophilic series as well as dysplastic features, including abnormal nuclear/cyttoplasmic maturation, retention of primary granules, giant band cells, and toxic changes. Megakaryocytes were subjectively decreased with some containing irregular segmented nuclei. Macrophages were noted occasionally, containing hemosiderin and some phagocyted cellular debris. Both stem cell injury (as a result of transient insult/toxicity or immune-mediated destruction) and myelodysplastic syndrome were noted as possible causes for these findings, with stem cell injury considered more likely as evidenced by the toxic changes. Blast cells did not exceed 20% of the nucleated cell count, thereby ruling out leukemia as a possible cause for the dog’s illness.

In light of these findings, 1 dose of dexamethasone (Dexamethasone 5; Vetoquinol), 0.22 mg/kg BW, IV, was given, after which the patient was placed on prednisone (NOVO-Prednisone; Novopharm, Toronto, Ontario), 1.5 mg/kg BW, PO, q24h. The dog remained anorexic in hospital and resistant to having a liquid diet fed by syringe. Her owners elected to try managing her at home in the hopes that she would improve clinically and feel more comfortable eating in a familiar environment. She was discharged and prescribed oral prednisone (NOVO-Prednisone; Novopharm), 1 mg/kg BW, q12h for 7 d; tapering to 1 mg/kg BW, q24h for 7 d then 1 mg/kg BW, q48h for 14 d, omeprazole (Omeprazole; Sandoz), 0.5 mg/kg BW,
PO, q24h for 7 d, enrofloxacin (Baytril; Bayer), 7.5 mg/kg BW, PO, q24h for 7 d, and amoxicillin/clavulanic acid (Clavaseptin; Vетоquinol), 12.5 mg/kg BW, PO, q12h for 7 d.

After returning home, the dog’s energy level greatly improved, her appetite returned to normal, and she continued to urinate normally. A CBC and a biochemistry panel were repeated at the Island Veterinary Hospital after the patient had completed her 4-week long prednisone trial. The dog’s anemia had resolved (hematocrit 0.40 L/L; RI: 0.38 to 0.57 L/L) and a regenerative response was present (reticulocytes 188.0 × 10^9/μL; RI: 10 to 110 × 10^9/μL). Her thrombocytopenia had also resolved (186 × 10^9/L; RI: 143 to 448 × 10^9/L); however, her lymphopenia (0.2 × 10^9/L; RI: 1.1 to 5.0 × 10^9/L) and neutropenia (0.3 × 10^9/L; RI: 2.9 to 12.7 × 10^9/L) remained. Alanine transaminase (ALT; 137 IU/L; RI: 18 to 21 IU/L), alkaline phosphatase (ALP; 266 IU/L; RI: 5 to 160 IU/L), and gamma-glutamyltransferase (GGT; 17 IU/L; RI: 0 to 13 IU/L) showed mild elevations, likely as a result of corticosteroid therapy. The dog was placed on doxycycline (Teva Doxycycline; Teva Pharmaceuticals, Scarborough, Ontario), 5 mg/kg BW, PO, q12h for 14 d to combat any underlying infectious causes prior to repeating a CBC and biochemistry panel in August. Results were unavailable at the time of writing.

Discussion

Neutropenia in dogs can be due to increased use (during severe suppurative inflammation/infection), decreased production (as a result of primary or secondary insults to bone marrow neutrophilic precursor cells), or accelerated destruction of neutrophils through immune-mediated mechanisms (1). Primary immune-mediated neutropenia (IMN) is an uncommon disorder in veterinary medicine and is diagnosed clinically based on exclusion of other mechanisms that cause neutropenia, as well as response to corticosteroid immunosuppressive therapy (1–9). The disease has been documented in dogs (1–4,7–9, cats (6), and horses (10) and involves the direct targeting of neutrophils by autoantibodies, resulting in subsequent opsonization and phagocytosis of neutrophils (5,7,9–11).

In humans, several methods have been described for detecting anti-neutrophil antibodies in circulation which may provide a more definitive diagnosis for IMN when other causes have been ruled out (3–6,8–9,11). Most of these tests have proven to be unreliable for use in veterinary patients, although 1 study showed promising results using flow cytometry to detect anti-neutrophil antibodies in dogs affected with IMN (3). One of the key limitations in detecting anti-neutrophil antibodies lies within the neutrophils themselves as neutrophils are fragile cells that do not store well without activation, consequently leading to autolysis (4,7,11). Also, false positives are frequently encountered due to non-specific binding of immunoglobulin G (IgG) to their neutrophilic target cells (6,11) and false negatives may occur in severely neutropenic patients which are too neutrophil depleted to permit proper performance of the test (3,6). Therefore, there is a need for a safe, reliable, and efficient method for diagnosing immune-mediated neutropenia in veterinary patients, as arriving at a diagnosis continues to be an expensive and difficult challenge.

In veterinary patients, the process of diagnosing IMN is a tedious and often expensive process of elimination. Individuals affected by IMN typically present with non-specific signs that do not reflect the severity of their underlying disease. This commonly includes lethargy, anorexia, and vomiting (9), all of which were reported in this particular case. When a CBC is performed and reveals a profound neutrophil depletion, often accompanied by deficiencies in other cell lineages, the extent of the patient’s disease is discovered. Infectious causes of neutropenia (viral, bacterial, and fungal) can be ruled out through vaccination history, blood and urine cultures, 4Dx SNAP, and tick PCR tests, all of which were performed in the case presented here. In addition, septic peritonitis and gastric or enteric perforation due to a foreign body were definitively ruled out in this patient through gross examination of the abdominal organs and culture of the abdominal effusion.

Primary and secondary insults to bone marrow precursor cells can be excluded through obtaining a thorough medical history, including recent drug administration and eliminating gross neoplasia through thoracic and abdominal imaging as well as bone marrow analysis. An extensive list of drugs that are potentially myelotoxic was reviewed by this patient’s owners and it was determined that there was no history of any exposure prior to her clinical signs appearing in May. Her abdominal ultrasound, thoracic radiographs, and bone marrow aspirates did not support the presence of a neoplastic process. Bone marrow aspirates from IMN patients typically reveal normal erythroid and megakaryocytic cells, an abnormally high M:E ratio, and neutrophilic hyperplasia with dysplastic features (5), which were evident in this patient.

One of the consistent hallmarks of immune-mediated neutropenia in dogs and cats is a rapid response to immunosuppressive therapy (1–4,6–9), with some patients’ neutrophil count achieving normal levels as early as 3 d after initiating treatment (2). However, relapse after cessation of immunosuppressive therapy is common. Concurrent use of prednisone and azathioprine is recommended for refractory cases or those whose response is suboptimal (7). Despite resolution of clinical signs and her owner reporting that she was doing well, the patient’s neutropenia did not resolve after 4 wk of prednisone therapy.

It is worth noting that predisposition to secondary infections is most often mild to moderate in human patients with primary autoimmune neutropenia (2). Treatment in these patients aims to control secondary infections when they occur through use of antibiotics, with large doses of immunosuppressive steroids used in instances that require more aggressive treatment (2). In support of these findings, 2 dogs affected by IMN showed marked improvement in their clinical signs following administration of antibiotics alone without the use of corticosteroids, although their neutropenia remained unchanged (2). Similar results were observed in the case presented here, as the patient’s lethargy, stranguria, dysuria, and anorexia quickly resolved following antibiotic treatment although her neutropenia persisted. Interestingly, the dog’s anemia and thrombocytopenia responded completely to corticosteroid therapy. Therefore, it is possible that the dose, duration of therapy, the immunosuppressive drug chosen, or a combination of these factors were not sufficient in treating her neutropenia.
Immune-mediated neutropenia remains a challenging and complex disease. This case serves to highlight both the difficulty in establishing a diagnosis of IMN and the importance of finding a treatment regimen that is tailored to the individual animal. Further efforts are needed to validate diagnostic tests for this disease in veterinary medicine in order to establish a timely diagnosis and initiate treatment promptly. Finally, the use of various immunosuppressive drugs and treatment protocols in controlling this disease should be explored to provide veterinarians different options to use under their clinical judgment.

Acknowledgments
The author thanks Dr. Blair Gurney at Central Victoria Veterinary Hospital for his support and assistance and Dr. Jane Armstrong for her expertise. A sincere thank you to Jason Vrastak for his assistance in acquiring details for this case. A special acknowledgment to the patient’s owners for providing her with love and support and allowing me to explore her case.

References
Attracting new clients with the first phone call

Recruter des clients lors du premier appel téléphonique

Terra Shastri

Research has shown that the manner in which a veterinary team member handles a call from a telephone shopper can directly contribute to the number of new clients acquired by the hospital. Veterinary hospitals with the highest number of new clients from each province were called with an inquiry regarding the cost of an ovariohysterectomy for a small puppy. Using a customer service scorecard, the hospital representative was given a score based on the information they shared, questions they asked the caller, and their demeanour throughout the call.

All of the hospitals with the top number of new clients per full-time equivalent were included in the study. Most of those veterinary clinics which charged more for a canine spay also tended to score higher than those which charged less.

Staff who answered the telephone were asked the question “Can you please tell me how much it would be to have my puppy spayed?”, and were evaluated based on their response. All of the hospitals received scores for answering the telephone promptly and for the staff identifying themselves by name. Clinics scored higher when they asked about the pet’s name.

Research has shown that the manner in which a veterinary team member handles a call from a telephone shopper can directly contribute to the number of new clients acquired by the hospital. Veterinary hospitals with the highest number of new clients from each province were called with an inquiry regarding the cost of an ovariohysterectomy for a small puppy. Using a customer service scorecard, the hospital representative was given a score based on the information they shared, questions they asked the caller, and their demeanour throughout the call.

All of the hospitals with the top number of new clients per full-time equivalent were included in the study. Most of those veterinary clinics which charged more for a canine spay also tended to score higher than those which charged less.

Staff who answered the telephone were asked the question “Can you please tell me how much it would be to have my puppy spayed?”, and were evaluated based on their response. All of the hospitals received scores for answering the telephone promptly and for the staff identifying themselves by name. Clinics scored higher when they asked about the pet’s name.

Terra holds a degree in Communication Studies and a diploma in Business Administration from Wilfrid Laurier University, and is a graduate of the Walt Disney Institute (School of Leadership). Before joining the Ontario Veterinary Medical Association in 2008 as Manager of Business Development, Terra spent 20 years helping small businesses better market their services, improve client service, increase revenues, improve staff retention, and manage change. Terra assists OVMA members with the business side of their practice and teaches the popular JumpStart! Boot Camp workshop she created.

This article is provided as part of the CVMA Business Management Program, which is co-sponsored by IDEXX Laboratories, Petsecure Pet Health Insurance, Merck Animal Health, and Scotiabank.

Address all correspondence to the CVMA Business Management Committee; e-mail: admin@cvma-acmv.org

Use of this article is limited to a single copy for personal study. Anyone interested in obtaining reprints should contact the CVMA office (hbroughton@cvma-acmv.org) for additional copies or permission to use this material elsewhere.

Terra est titulaire d’un diplôme en communication et d’un diplôme en administration des affaires de l’Université Wilfrid Laurier et elle est diplômée du Walt Disney Institute (School of Leadership). Avant de se joindre à l’Ontario Veterinary Medical Association en 2008 en tant que gestionnaire du développement des affaires, Terra a passé 20 ans à aider les petites entreprises à mieux commercialiser leurs services, à améliorer leur service à la clientèle, à accroître les revenus, à améliorer la rétention de personnel et à gérer le changement. Terra aide les membres de l’OVMA à gérer l’aspect commercial de leur pratique et elle enseigne le populaire atelier «JumpStart! Boot Camp» qu’elle a créé.

Le présent article est rédigé dans le cadre du Programme de gestion commerciale de l’ACMV, qui est cocommandité par IDEXX Laboratories, Petsecure Insurance, Merck Santé Animale et la Banque Scotia.

Veuillez adresser toute correspondance au Comité de la gestion commerciale de l’ACMV; courriel: admin@cvma-acmv.org

L’usage du présent article se limite à un seul exemplaire pour étude personnelle. Les personnes intéressées à se procurer des réimpressions devraient communiquer avec le bureau de l’ACMV (hbroughton@cvma-acmv.org) pour obtenir des exemplaires additionnels ou la permission d’utiliser cet article ailleurs.
1. Answered the telephone promptly
2. Staff identified themselves by name
3. Engaged in conversation/built rapport by learning more about the caller
4. Found out caller's name/used caller's name
5. Found out more about caller/what they want
6. Found out more about pet
7. Described the hospital: gave 2 unique features/why pick them?
8. Explained the procedure and highlighted value and benefits
9. Offered to e-mail or send more information to the caller
10. Directed caller to website/Facebook page or invited caller to tour the hospital
11. Asked the caller if they had any other questions
12. Asked the caller to book an appointment
13. Ended call with offer to follow-up, confirm appointment, or for the caller to call back with any questions; asked for contact information

Overall
14. Friendly tone and enthusiastic during call
15. Collected caller's information for follow-up
16. Thorough with information in a way call- ers understand

Figure 1. Customer service scorecard used to evaluate each phone shopping call./Carte de pointage du service à la clientèle utilisée pour évaluer chaque appel de magasinage.

asked the caller if they had any more questions, found out more about the pet, and when they encouraged the caller to call back with any other questions (Figure 1). Some clinics charged lower fees and some charged higher fees. Figure 2 shows how new clients can be attracted with higher fees, but better service needs to be provided on the telephone in order to do so.

While the overall price provided by staff included various items (e.g., pre-anesthetic blood work, post-operative pain management), the take away from the telephone call was the price. In this exercise, most of the hospitals which charged more than others scored higher, which should be expected. When a caller inquires at a hospital, staff at the higher priced clinic should take more time to explain the procedure using a language clients understand, and should include details to show more value. Otherwise, it would make financial sense for the caller to choose the lowest priced hospital.

The amount of information provided about an ovariohysterectomy over the telephone can be confusing and difficult for pet owners to understand and make a fair comparison among veterinary clinics, but the overall price is clearly understood. Usually, pet owners do not know what questions to ask or how to compare how the surgery is conducted among various veterinary hospitals. Taking the time to educate the caller about the

1. L'employé a répondu rapidement au téléphone
2. L'employé s’est identifié par son nom
3. A entamé une conversation et établi un rapport en obtenant des renseignements à propos de l’interlocuteur
4. A demandé le nom de l’interlocuteur et a utilisé son nom
5. A demandé des renseignements à propos de l’interlocuteur et de ses besoins
6. A demandé des renseignements à propos de l’animal
7. A décrit la clinique : a donné deux avantages uniques et la raison de choisir la clinique
8. A expliqué l’intervention et a souligné la plus-value et les avantages
9. A offert d’envoyer un courriel ou d’envoyer des renseignements à l’interlocuteur
10. A demandé à l’interlocuteur de visiter le site Web ou la page Facebook ou a invité l’interlocuteur à visiter la clinique
11. A demandé à l’interlocuteur s’il avait d’autres questions
12. A demandé à l’interlocuteur de prendre rendez-vous
13. Chaque appel s’est terminé par une offre de suivi, de confirmation du rendez-vous ou en invitant l’interlocuteur à appeler de nouveau s’il avait des questions; l’employé a demandé les coordonnées de l’interlocuteur

En général
14. Ton sympathique et enthousiaste durant l’appel
15. A recueilli les coordonnées de l’interlocuteur pour effectuer un suivi
16. Renseignements complets en vue d’assurer la compréhension de l’interlocuteur

faire stériliser ma jeune chienne?» et il était évalué en fonction de sa réponse. Toutes les cliniques ont reçu des notes pour avoir répondu au téléphone rapidement et pour un employé qui s’identifiait par son nom. Les cliniques obtenaient des notes supérieures lorsqu’elles demandaient le nom de l’animal, demandaient à l’interlocuteur s’il avait d’autres questions, se renseignaient à propos de l’animal et lorsqu’elles encourageaient l’interlocuteur à appeler de nouveau s’il avait d’autres questions (figure 1). Certaines cliniques avaient des tarifs inférieurs et d’autres des tarifs supérieurs. La figure 2 montre comment les nouveaux clients peuvent être attirés par des tarifs supérieurs, mais un meilleur service doit être offert au téléphone pour atteindre cet objectif.

Tandis que le prix total fourni par l’employé incluait divers éléments (p. ex., profil sanguin pré-anesthésique, gestion de la douleur postopératoire), le message que l’on retient est le prix. Lors de cet exercice, la plupart des cliniques qui facturaient plus que les autres ont obtenu des notes supérieures, ce qui n’est pas surprenant. Lorsqu’un interlocuteur présente une demande de renseignements à une clinique, l’employé d’une clinique qui affiche des tarifs supérieurs devrait prendre plus de temps pour expliquer l’intervention en utilisant un langage compris par les clients et il devrait inclure des détails pour indiquer une
La quantité d’information fournie par téléphone à propos d’une ovario-hystérectomie peut porter à confusion et il peut être difficile pour les propriétaires d’animaux de comprendre et d’effectuer une comparaison juste entre les cliniques vétérinaires, mais le prix total est bien compris. Habituellement, les propriétaires d’animaux ne savent pas quelles questions poser ou comment comparer la façon dont la chirurgie est réalisée entre les diverses cliniques vétérinaires. Afin d’aider à prévenir des comparaisons inexactes du prix par l’interlocuteur, il est important de prendre le temps de bien l’informer à propos de l’intervention. Par exemple, certaines cliniques enverront un courriel à l’interlocuteur pour lui communiquer de l’information à propos d’une ovario-hystérectomie en indiquant ce qui est inclus dans le prix ainsi qu’en soulignant les avantages de chaque élément. On encourage l’interlocuteur à utiliser les renseignements comme une liste de contrôle lorsqu’il appelle les autres cliniques afin de s’assurer qu’il compare les mêmes éléments.

Il y a encore place à l’amélioration quant à la façon dont les cliniques gèrent les appels téléphoniques des clients potentiels. Cela présente une excellente occasion pour les équipes vétérinaires qui sont disposées à investir du temps et des efforts dans un client éventuel qui appelle pour se renseigner à propos de son animal de compagnie. Les équipes qui peuvent se distinguer de la concurrence, démontrer la plus-value, illustrer la start d’une excellente expérience à la clientèle durant le premier appel téléphonique et demander à l’interlocuteur de prendre un rendez-vous récolteront les bénéfices du recrutement de nouveaux clients.

---

Figure 2. Cost of canine ovariohysterectomy (< 10 kg) is indexed according to each province’s average cost. Illustration of the relationship between higher cost and a higher customer service score. 1 = mean. As indexed for the cost of a canine ovariohysterectomy.

Ensemble le coût de l’ovario-hystérectomie canine (< 10 kg) est indexé conformément au coût moyen dans chaque province. Illustration du rapport entre le coût supérieur et une note de service à la clientèle supérieure. 1 = moyenne. Indexé pour le coût d’une ovario-hystérectomie canine.

---

Eight practices were called from each province, except for Newfoundland and PEI for which the sample size was 3.


---

Have you been checking your e-mail inbox?

The Canadian Veterinary Medical Association (CVMA) communicates time-sensitive and relevant information and news to its members by e-mail based on the addresses we have on record in our database. If you are not receiving e-mail communication from us, it may be that we do not have a valid e-mail address for you.

Review/update your contact information and stay connected!

Also, ensure that you add us (notify@cvma-acmv.org) to your safe sender’s list so that our messages do not get blocked.

Online

Log on at www.canadianveterinarians.net and view your contact information. You can make changes directly online.

Contact CVMA

By e-mail at admin@cvma-acmv.org or by telephone at 1.800.567.2862. We will confirm the e-mail address we currently have for you and make any necessary changes.
Be exhilarated.

Travel to beautiful Charlottetown, P.E.I. to participate in the 2017 CVMA Convention. Join peers and colleagues and be exhilarated by east coast beauty and hospitality. Attend CVMA signature events, stellar CE sessions and more!
History and clinical signs

A 7-year-old spayed female Labrador retriever-cross dog was examined at the ophthalmology service at the Western College of Veterinary Medicine for evaluation of bilateral red eyes, blepharospasm, and a cloudy right eye. The dog was presented to her referring veterinarian 5 days previously and therapy was initiated in both eyes with topical diclofenac sodium 0.1% (Voltaren ophtha; Novartis, Mississauga, Ontario), q12h, atropine sulphate 1% (Isopto-atropine, Alcon Canada, Mississauga, Ontario), q12h, ciprofloxacin 0.3% (Apotex, Toronto, Ontario), q6h, and oral meloxicam (Metacam; Boehringer Ingelheim Vetmedica, St. Joseph, Missouri, USA), 37.5 kg, q24h for 5 days. At the time of presentation, the dog was lethargic and had been coughing for approximately 2 weeks. On general physical examination she was bright, alert, and responsive. Vital parameters were within normal limits and thoracic auscultation was normal. Clinical abnormalities appeared to be limited to the eyes. The menace response and dazzle reflex were absent in the right eye. Pupils were dilated bilaterally and direct and consensual pupillary light reflexes were absent bilaterally. Palpebral and oculocephalic reflexes were present bilaterally. Schirmer tear test (Schirmer Tear Test Strips; Alcon Canada, Mississauga, Ontario) values were 27 and 12 mm/min in the right and left eyes, respectively. The intraocular pressures were estimated with a rebound tonometer (Tonvet; Tiolat, Helsinki, Finland) and were 47 and 14 mmHg in the right and left eyes, respectively. Fluorescein staining (Fluorets; Bausch & Lomb Canada, Markham, Ontario) was negative bilaterally. On direct examination the right eye had moderate blepharospasm and conjunctival hyperemia, diffuse, severe corneal edema, and peripheral stromal vascularization extending 3 to 4 mm into the corneal stroma. Biomicroscopic examination of the left eye (Osetra 64222; Carl Zeiss Canada, Don Mills, Ontario) revealed semi-translucent cysts originating medially from the ciliary body and mild pigment dispersion on the anterior lens capsule with evidence of ruptured uveal cysts. Evaluation of intraocular structures of the right eye was impeded by corneal edema. Indirect ophthalmoscopic (Heine Omega 200; Heine Instruments Canada, Kitchener, Ontario) examination was normal in the left eye. Gonioscopy of the left eye revealed a normal iridocorneal angle. Photographs of the right (Figure 1a) and left (Figure 1b) eyes at presentation are provided for your assessment.

What are your clinical diagnosis, differential diagnoses, therapeutic plan, and prognosis?

Discussion

The clinical diagnoses were secondary glaucoma of the right eye and uveal cysts of the left eye. Based on the history of bilateral red eyes an underlying bilateral uveitis was suspected. Although no evidence of active inflammation was noted in the left eye at the time of presentation, this eye was currently being treated.
with topical anti-inflammatory medications which may have been controlling the uveitis. Differential diagnoses for bilateral uveitis include systemic infectious diseases (viral, bacterial, rickettsial, parasitic, algal, or mycotic infections), neoplasia, and immune-mediated inflammation. Canine uveal cysts have variable clinical manifestations and significance. Solitary to multiple, thick-walled, pigmented, usually free-floating or ruptured cysts are seen in many dog breeds and are generally thought to have little clinical significance (1). However, multiple, translucent, thin-walled cysts, attached to the ciliary epithelium, are associated with a clinical syndrome of uveitis. This syndrome is termed pigmentary uveitis and is most often seen in the golden retriever; however, it has been reported in other breeds including retriever-crosses, great Danes, and American bulldogs (2–4). A hallmark of pigmentary uveitis is a radial or multifocal pattern of pigment dispersion on the anterior lens capsule often in association with signs of uveitis; glaucoma is a common sequela (2–5).

The ocular abnormalities present in this dog made us suspicious of a pigmentary uveitis, causing secondary glaucoma. Because the dog had been lethargic and coughing, however, a minimum database of a complete blood (cell) count (CBC), serum biochemistry profile, and urinalysis were appropriate to evaluate for underlying systemic illness. These had recently been completed by the referring veterinarian and laboratory values were within normal limits. Thoracic radiographs provided by the referring veterinarian were assessed and no significant abnormalities were detected.

Treatment for uveitis had been initiated with topical non-steroidal anti-inflammatory (NSAID) drops to reduce inflammation, as well as atropine to achieve mydriasis and reduce ciliary muscle spasm. As the uveitis appeared controlled in the left eye atropine was discontinued and topical NSAIDs were continued q12h.

Treatment of glaucoma depends on the underlying cause and if the eye has potential for vision. Assessment of visual potential in glaucoma requires evaluation of the neuro-ophthalmic reflexes. Poor prognostic indicators include absence of a consensual pupillary light reflex to the contralateral eye and lack of a dazzle reflex. The dazzle reflex is a subcortical reflex initiated by shining a bright light into the affected eye and observing a reflex squint. Atropine therapy confounded the interpretation of the pupillary light reflexes; however, the lack of a dazzle reflex in the right eye was consistent with blindness and for this reason enucleation was recommended as therapy for the right eye.

The dog returned to the referring veterinarian for enucleation 3 days later. At that time the eye had ruptured at the corneoscleral junction and in-clinic cytology performed on purulent material from the globe showed presence of yeast organisms suspected to be Blastomyces dermatitidis. The enucleated globe was submitted for histopathology which confirmed the diagnosis as a pyogranulomatous panophthalmitis with secondary glaucoma due to Blastomyces dermatitidis. Systemic treatment was initiated with oral itraconazole 5 mg/kg body weight (BW), q12h. The dog was re-evaluated at the ophthalmology service 1 month after the right eye was enucleated and no evidence of ocular blastomycosis was detected in the left eye. The uveal cysts and pigment dispersion with the eye remained; however, there was no active uveitis and the frequency of topical anti-inflammatory therapy was gradually reduced and discontinued.

Blastomycosis is a systemic fungal infection caused by Blastomyces dermatitidis, a dimorphic soil fungus. The organism is endemic in central and southeastern United States, and the Canadian provinces of Quebec, Ontario, Manitoba, and Saskatchewan (6). Although direct inoculation can occur, the mode of infection is most often by inhalation and the organism may then be disseminated by hematogenous or lymphatic routes to skin, lymph nodes, subcutaneous tissues, bone, eyes, testicles, and the central nervous system (CNS) (7). Ocular lesions occur in up to 48% of infected dogs (8–10). The most common ocular manifestations are those of uveitis. Organisms reach the eye hematogenously and initiate a pyogranulomatous chorioretinitis (8,11). The intense posterior inflammation triggers an inflammatory response in the anterior ocular tissues resulting in anterior uveitis. Secondary glaucoma is a common sequela to severe anterior uveitis and is often due to development of peripheral anterior synecchia, or inflammatory cell infiltration of the iridocorneal angle (11,12). Pulmonary involvement is evident in approximately 88% of cases (7). A miliary to nodular interstitial pattern is most commonly observed on thoracic radiographs and may be diffuse or non-diffuse in distribution (9). Given the presence of a cough in this dog, pulmonary involvement was likely but was not obvious on initial radiographic assessment.

Blastomycosis may be diagnosed upon identification of yeast organisms in infected tissues or fluids via cytology or histopathology of affected tissue. Agar gel immunodiffusion tests to detect serum antibodies have low sensitivity according to some reports (13). The antigen test performed on urine has been shown to be highly reliable and has largely replaced serum antibody testing (14). Cytology and histopathology were instrumental in achieving the diagnosis in this case.

The antifungal therapy of choice for treatment of blastomycosis is itraconazole at a dose of 5 mg/kg BW, PO, q24h for at least 4 to 6 months (15). It is recommended that therapy be continued for at least 1 month following radiographic evidence that pulmonary infiltrates have resolved (15,16). The prognosis for survival of blastomycosis is good unless there is CNS involvement or severe lung disease. The prognosis for affected eyes and vision depends on location and severity of disease in the eye. Glaucoma secondary to anterior segment disease is the most common reason for enucleation (10,17).

This case highlights the importance of pursing light microscopic examination of all enucleated eyes. The presence of uveal cysts in this case may have been incidental; however, the clinical manifestations are similar to those reported for pigmentary uveitis and thus, regular monitoring of the remaining eye for development of this condition was recommended.

References

---

Wanted: Dogs, cats and cows!

Have your photo featured on a CVJ cover

Photographs for the covers of The CVJ are always in demand. We not only welcome, but encourage veterinarians, or family and friends of veterinarians, to send us photos of animals. While digital cameras make it easier to submit photos, certain guidelines must be met to make them useable for covers. Here are some specifications to remember:

- Photos for submission are required to be at least 300 dpi at 100% size which is 9 x 12 inches
- Cameras should be set to the highest resolution possible. An option is to shoot in RAW mode
- High resolution photos should be sent via CD (the files may be too large to e-mail)
- A landscape shot should be at least a 46 MB file; a portrait should be 27 MB
- Vertical shots and close-ups work best
- High quality large printed photos are still acceptable (photos will not be returned)
- Keep the photo simple!

E-mail photos to hbroughton@cvma-acmv.org or send to the CVMA office or call 1-800-567-2862.

---

Recherchés : chiens, chats et vaches!

Faites publier une de vos photos sur la couverture de La RVC

Nous sommes toujours à la recherche de photos pour la couverture de La RVC. Nous encourageons même la famille et les amis des vétérinaires à nous faire parvenir des photos d’animaux. Même si les caméras numériques facilitent la soumission de photos, il est nécessaire de respecter certains critères pour que nous puissions les utiliser pour les couvertures. Voici quelques paramètres à respecter :

- les photos doivent avoir une résolution d’au moins 300 ppp à une taille de 100 %. qui est de 9 x 12 po;
- les caméras doivent être réglées à la plus haute résolution possible. Une option consiste à prendre la photo en mode brut.
- les photos à haute résolution devraient être envoyées sur un CD (les fichiers pourraient être trop gros pour la transmission par courriel);
- la photo d’un paysage devrait être un fichier d’au moins 46 MB; un portrait devrait être de 27 MB;
- des photos verticales et des gros plans sont préférables;
- les grandes photos imprimées de haute qualité sont toujours acceptables (les photos ne seront pas retournées);
- visez la simplicité pour la photo!

Acheminez les photos par courriel (hbroughton@cvma-acmv.org), envoyez-les au bureau de l’ACMV ou appelez au 1-800-567-2862.
1. **B)** Diabetes in the dog is insulin-dependent versus non-insulin-dependent which can be seen in cats. A, C, and E would be more appropriate for a cat; answer is D is incorrect unless the diet is high in fiber.

**B)** Chez le chien, le diabète est insulinodépendant alors qu’il est non insulinodépendant chez le chat. Les réponses A, C et E seraient plus appropriées pour un chat; la réponse D est incorrecte à moins que la diète ne soit à forte teneur en fibres.

2. **A)** Terriers are predisposed to lens luxations that can lead to secondary glaucoma. A hypermature cataract without severe lens-induced uveitis would not cause glaucoma. A retinal detachment does not usually cause glaucoma unless it is very longstanding. Conjunctivitis does not explain the glaucoma.

**A)** Les Terriers sont prédisposés à la luxation du cristallin qui peut mener à du glaucome secondaire. Une cataracte hypermûre sans uvéite sévère induite par le cristallin ne causera pas de glaucome. Un décollement de la rétine ne cause pas habituellement de glaucome, à moins qu’il ne soit présent depuis fort longtemps. La conjonctivite n’explique pas le glaucome.

3. **B)** The correct answer is pars intermedia. Hypertrichosis is a consistent finding in equine hyperadrenocorticism and is associated with a functional pituitary lesion, rather than an adrenal lesion as indicated by answers A and E. Answers C and D describe the incorrect portion of the pituitary.

**B)** La bonne réponse est la partie intermédiaire. Chez le cheval, l’hypertrichose est souvent concomitante à l’hyperadrénocorticisme et elle est associée à une lésion fonctionnelle de l’hypophyse plutôt qu’à une lésion des surrénales tel qu’il est indiqué dans les réponses A et E. Les réponses C et D se rapportent aux parties incorrectes de l’hypophyse.


5. **E)** Birds usually do not recognize pellets as a food source. Withholding a recognized food from a bird for an extended period can result in starvation.

**E)** Les oiseaux ne reconnaissent pas habituellement les granulés comme source de nourriture. Le retrait d’un aliment reconnu par l’oiseau pendant une période prolongée peut se traduire par l’inanition.

---

**Answers to Quiz Corner**

**Les réponses du test éclair**

1. A) Diabetes in the dog is insulin-dependent versus non-insulin-dependent which can be seen in cats. A, C, and E would be more appropriate for a cat; answer is D is incorrect unless the diet is high in fiber.

2. A) Terriers are predisposed to lens luxations that can lead to secondary glaucoma. A hypermature cataract without severe lens-induced uveitis would not cause glaucoma. A retinal detachment does not usually cause glaucoma unless it is very longstanding. Conjunctivitis does not explain the glaucoma.

3. B) The correct answer is pars intermedia. Hypertrichosis is a consistent finding in equine hyperadrenocorticism and is associated with a functional pituitary lesion, rather than an adrenal lesion as indicated by answers A and E. Answers C and D describe the incorrect portion of the pituitary.


5. E) Birds usually do not recognize pellets as a food source. Withholding a recognized food from a bird for an extended period can result in starvation.

**Quiz Corner is generously sponsored by**

**Le test éclair est généreusement commandité par**

A: With trusted Nobivac® specialty vaccines, that provide demonstrated efficacy against specific pathogens, and offer unique features that set them apart in their category.

Nobivac® is a registered trademark of Intervet International B.V. Used under license.

MERCK® is a registered trademark of Merck Canada Inc. © 2016 Intervet Canada Corp. All rights reserved.
Classifieds Petites annonces

Business Directory

Gallant Custom Laboratories Inc.
Your Canadian Leader for Autogenous Biologics

Experts in Autogenous Bacterins and Swine Influenza Virus Vaccines
“See you in Banff”
For more information, contact: Sam Mostafa
Phone: 1-888-838-5223
e-mail: sameh@gallantcustomlaboratories.com
www.gallantcustomlaboratories.com

Animal Health Laboratory
Full service veterinary diagnostics. State of the art testing and in-house veterinary specialists to provide optimal services to you.
“Working for animal health”
Guelph (519) 824-4122 ext. 54530
Kemptville (613) 256-5520
Email ahiinfo@uoguelph.ca
Website www.aih.uoguelph.ca

---

FMS Medical Systems Ltd.

X-Ray Digital & Analog Ultrasound
ElectroSurgery & Laser Autoclave, Centrifuge & Microscope
Procedure & Surgery Light Vital Sign Monitor
IV Pump & Warmer
Anesthesia & Surgery Accessories
Stainless Steel & Veterinary Table
Dental Unit & Dental X-Ray

VetAdvise.com

Terry A. Jackson, C.P.A. - C.G.A.
Consulting, Coaching, Valuations, Negotiations, Purchase / Sale

Phone: 604.939.2323
tjackson@jandacga.com

Practice One Consulting

Practice Valuations ◆ Practice Purchase
Practice Sale ◆ Practice Management

Dr. Frank Richardson, DVM, MBA
Veterinary Management Consultant

P.O. Box 176
Western Shore, Nova Scotia
B0J 3M0

Phone: (902) 531-2617
E-mail: frank.richardsonvdvm@gmail.com
Fax: (902) 531-2618

UXR

Eric Hoffmann

T 514 695 4114  F 514 695 4926  C 514 889 1580
E eric@uxr.ca  W www.uxr.ca
227G Brunswick Blvd., Pointe-Claire, QC H9R 4X5

---

Chiron Compounding Pharmacy Inc.

Professional Precise Prompt
Speak to a Veterinary Compounding Pharmacist today!
Call Rita, Scott, Becky, or Linda
info@chironcompounding.com
Tel/Fax: (289) 644-6463

---

FOR PERSONAL USE ONLY
You Asked, We Listened!
Now featuring Specific Urine Analysis Strips for Veterinary use.

**URS 2K**
Strips are used for semi-quantitative detection of glucose and ketone.

**UPC**
Strips are used for semi-quantitative determination of protein and creatinine in urine, which can be used to detect Proteinuria.

**UAC**
Strips are used to test for albumin and creatinine in urine, which can be used to detect early onset of kidney malfunction.

You can reach Sensor Health Vet at 1-888-777-7080 (Office) or 1-519-621-8778 (Fax) or visit their website at www.sensorhealthvet.com.

---

**Reaching Canada’s Veterinarians**
Get your message into The Canadian Veterinary Journal
For more information contact:
Laima Laffitte
Advertising Manager
Tel.: (613) 673-2659
Fax: (613) 673-2462
e-mail: llaffitte@cvma-acmv.org
In-house blood diagnostics, now with Profiles to Choose From

- Canine Wellness Profile
- Comprehensive Diagnostic Profile
- Prep Profile II
- Critical Care Plus
- Kidney Profile Plus
- T4/Cholesterol Profile
- Mammalian Liver Profile
- Equine Profile Plus
- Avian/Reptilian Profile Plus
- Large Animal Profile

**VETSCAN® Electrolyte Plus**
The Electrolyte Plus allows for cost-effective monitoring of hospitalized patients on fluid therapy, early diagnostic information regarding acid-base status, and recheck examinations for different conditions.

**VETSCAN® Preventive Care Profile Plus**
The Preventive Care Profile Plus is an advanced panel for pre-surgical, general health, ill patient, geriatric, and wellness testing that includes full electrolyte values and early information regarding acid-base status.

It’s not just better diagnostics, it’s a **Better** way.

- 800.822.2947
- www.abaxis.com
- abaxisinc@abaxis.com
Lowest Fat. Period.

1.74 g fat
100 kcal

- Low Fat
- High Total Digestibility
- Prebiotic Fiber

**Purina® Pro Plan Veterinary Diets®**
**EN Gastroenteric Low Fat™ Dry Canine Formula**

Introducing a formula with the lowest fat (g/100 kcal) of any dry GI-focused, canine therapeutic diet on the market†, formulated to nutritionally manage patients when fat digestion is compromised. For patients with pancreatitis, hyperlipidemia and lymphangiectasia, a low-fat diet can make a world of difference.

Learn more at [www.ProPlanVeterinaryDiets.ca](http://www.ProPlanVeterinaryDiets.ca)

† Comparison based on values published in PPVD Product Guide 2015 (average nutrient content), Hill’s Key 2016 (average nutrient contents), Royal Canin Product Guide 2016 (typical analysis)

Purina trademarks are owned by Société des Produits Nestlé S.A.