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Antimicrobial usage in western Canadian cow-calf herds

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1. Source: Ad Hoc Research 2017, 1634 participants as main caretaker for the family cat, across Canada, USA, UK, France.

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President’s Message
Le mot de la présidente

A peaceful, caring goodbye
Des adieux paisibles et compatissants

Several years ago I had to euthanize a dog that was seized during a criminal investigation. The dog was extremely aggressive, chained in a yard and unable to be handled. After several attempts at sedation, the dog was brought to the clinic muzzled but still fighting. As we started the euthanasia, I was rubbing his shoulder and talking to him when he began to wag his tail. I will never know what his life was like before that moment, but I imagine he may have seen the worst of what people can do to each other and to the animals they should care for. Would his death be the time when we could show him the love and kindness he deserved throughout his life? I decided then that I would do euthanasia well.

In the past, if an animal was afraid, I would sedate, and we would do house call euthanasias whenever possible, wherein any and all family members could be present and the time it took to do this final appointment would not matter. Euthanasia has changed so much over my career as a veterinarian. When I graduated we never allowed owners to be present for the procedure. I still remember families saying goodbye and hugging their pets in parking lots and on the backs of trucks. I now do as many house call euthanasias as I do in clinic and almost all owners elect to stay with their pet.

How do veterinarians walk into rooms and onto farmyards time and time again to perform a procedure that for most people is unimaginable? How do we make sense of euthanizing the animals that we love so much and dedicate our lives trying to treat and cure? How do we provide animals with a dignified and peaceful ending while helping their owners make the most important decision in their pet’s life?

I believe it is by treating euthanasia as important and meaningful as every other service we have provided throughout the life of a pet. I imagine I have euthanized thousands of animals over my career and so for my own mental health I need to do this well. I need to know that euthanizing is in the best interests of the animal and I need to know that I am doing the best job I can.

It is so difficult for owners to make this final decision regarding their pet’s care. Research has shown that 70% of clients will...
be emotionally affected by the death of their pet, 30% will feel overwhelming grief, and 50% will experience guilt over the decision to euthanize (1). These numbers are no surprise as animals are viewed by most of us as beloved family members.

How we handle the conversations leading up to euthanasia can significantly impact how our clients will feel after the death of their pet. Compassionate end-of-life discussions and acknowledging the gravity of such a decision can go a long way toward making the unimaginable manageable. It is important to let owners know that it may never feel like the right time to euthanize but it is our duty to the animals we love to prevent suffering.

There are Quality of Life Scales for dogs and cats that can help us counsel owners on end-of-life decisions. I think it is crucial that owners know that they do not have to make this decision alone and that we as veterinarians will be there with them until the end. Once the decision has been made it is imperative that clients have privacy, comfort, and no distractions. Sedating the animals prior to euthanizing and placing IV catheters beforehand has certainly made the procedure less stressful for many families and their pets.

I have heard so many amazing stories about the human-animal bond as we wait for pets to become sedated — how these animals were there for their owners in the best and worst of times. I have heard whispered messages for the dog to tell loved ones when they get to heaven. I have seen grown men break down and weep and children make sure that much loved bones and balls go with their pets. I have heard of such touching going away parties — trips to McDonalds, rides down country roads with heads hanging outside car windows and the last night spent together in bed.

I am now on my 3rd generation of family animals at this clinic. I have given puppies their first vaccinations and I have held their paws as they died. Some euthanasias break my heart but they all touch me with the significance of what I have done. I have come to see my role in euthanasia as an honor and a privilege. It is a privilege for me to be able to help say goodbye to a beloved pet and ensure they have a peaceful and kind death.

I love these words from a book I read and I often repeat them to heartbroken families. “I had my arms around his neck, my face buried in his shoulder, and from above me I felt what I thought for one befuddled moment was rain, the same rain that was falling so hard out on the street, making that stones-in-a-tin-can sound. Then I realized it was my husband’s tears. I could hear our children sobbing, and suddenly, improbably, I was almost exultant at the love we had managed to muster for that old dog, and at the thought that someday, if I was very, very lucky, I might have a death as simple and serene as this one, with these same people around me’: Taken from the book, “Good Dog. Stay.” by Anna Quindlen.

**Reference**


**Terri Chotowetz**

offrons pendant la vie de l’animal. J’imagine que j’ai euthanasié des milliers d’animaux pendant ma carrière et je dois donc adopter cette approche aussi pour ma propre santé mentale. Il est important pour moi de savoir que l’euthanasie est dans l’intérêt supérieur de l’animal et que je fais le meilleur travail possible.

Il est tellement difficile pour les propriétaires de prendre cette dernière décision concernant les soins de leur animal de compagnie. La recherche a démontré que 70% des clients seront émotionnellement affectés par la mort de leur animal, que 30% ressentiront une douleur écrasante et que 50% éprouveront de la culpabilité relativement à la décision d’euthanasier l’animal (1). Ces chiffres ne sont pas surprenants car les animaux sont considérés par la plupart d’entre nous comme des membres adorés de la famille.

La façon dont nous gérons les conversations précédant l’euthanasie aura un impact important sur l’état d’esprit de nos clients après la mort de leur animal. Des discussions de fin de vie compatissantes et la reconnaissance de la gravité d’une telle décision peuvent grandement faciliter la gestion d’une situation difficile à imaginer. Il est important de dire aux propriétaires qu’il ne semblera jamais que c’est le bon moment d’euthanasier mais que c’est notre devoir envers les animaux que nous aimons de prévenir leurs souffrances.

Il existe des échelles de qualité de vie pour les chiens et les chats qui peuvent nous aider à conseiller les propriétaires concernant les décisions de fin de vie. Je crois qu’il est crucial que les propriétaires sachent qu’ils ne prennent pas cette décision seuls et que nous, les médecins vétérinaires, serons avec eux jusqu’à la fin. Une fois que la décision a été prise, il est impératif que les clients aient droit à l’intimité, au confort et au calme. La sédation des animaux avant l’euthanasie et la mise en place des cathéters intraveineux au préalable a certainement atténué le stress de l’intervention pour beaucoup de familles et leurs animaux.

J’ai entendu tellement d’histoires incroyables à propos du lien humain-animal tandis que nous attendions que les sédatifs agissent sur les animaux, comment ces animaux étaient présents pour leurs propriétaires dans les meilleurs et les pires moments. J’ai entendu chuchoter des messages au chien à communiquer aux êtres chers à leur arrivée au paradis. J’ai vu des hommes adultes craquer et pleurer et des enfants qui s’assurent que les os et les balles adorés partent aussi avec les animaux. J’ai entendu parler d’émouvantes fêtes d’adieux — de sorties au McDonald, de balades dans des chemins de campagne avec la tête sortie par la fenêtre du véhicule et la dernière nuit passée ensemble au lit.

J’en suis maintenant à ma troisième génération d’animaux de famille dans cette clinique. J’ai administré le premier vaccin aux chiots et j’en ai ensuite tenu leur partie tandis qu’ils Mourraient à la fin de leur vie. Certaines euthanasies me brisent le cœur mais elles me rappellent toutes l’importance de mon travail. J’en suis venue à considérer mon rôle dans l’euthanasie comme un honneur et un privilège. C’est un privilège pour moi de pouvoir aider à faire des adieux à un animal adoré et d’assurer qu’il a une mort paisible et compatissante.

J’adore ces paroles trouvées dans un livre que j’ai souvent répétées à des familles éprouvées. “J’avais les bras autour de son cou, mon visage enfoui dans ses épaules et j’ai senti ce qui me semblait, pendant un moment embrouillé, comme de la
pluie, la même pluie qui tombait si bruyamment dans la rue, avec un son de cailloux dans une boîte de conserve. Puis j’ai réalisé que c’était les larmes de mon mari. Je pouvais entendre nos enfants sangloter, et, soudainement et bizarrement, j’étais presque jubilante en pensant à l’amour que nous avions réussi à accumuler pour ce vieux chien et à la pensée qu’un jour, si j’étais vraiment, vraiment chanceuse, je pourrais avoir une mort aussi simple et paisible que celle-ci, avec ces mêmes personnes autour de moi.» Citation tirée du livre «Good Dog. Stay.», d’Anna Quindlen.

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Veterinary Medical Ethics
Déontologie vétérinaire

Ethical question of the month — December 2018

The keeping of exotic pets is a growing trend in North America. Reptiles, amphibians, and birds are popular among those prohibited from keeping cats or dogs in their condominiums or rental homes. Exotics are commonly non-domesticated, non-native species; essentially another country’s wildlife. In Canada, provincial governments prohibit the keeping of native wildlife as pets; however, it is often left to municipalities to decide whether exotics can be kept by residents. Although some species are banned, others are easily purchased at pet stores where these animals are promoted as low maintenance. Commonly, exotics are displayed in environments that fail to meet their needs. Inappropriate housing and substandard husbandry result in high morbidity and mortality of exotics throughout the supply chain, and in homes. Should our moral obligation to native Canadian wildlife differ from our obligations to non-native wildlife? Does providing veterinary services to exotic pets support and validate this industry?

Submitted by Megan Allore, Fergus, Ontario

La garde d’animaux exotiques est une tendance grandissante en Amérique du Nord. Les reptiles, les amphibiens et les oiseaux sont populaires parmi les personnes qui ne peuvent pas avoir de chats ou de chiens dans les condominiums ou les logements loués. Les animaux exotiques sont communément des espèces non indigènes et non domestiquées, autrement dit, la faune d’un autre pays. Au Canada, les gouvernements provinciaux interdisent la garde d’espèces sauvages indigènes comme animaux de compagnie. Cependant, ce sont souvent les municipalités qui décident si les résidents peuvent posséder des animaux exotiques. Même si certaines espèces sont interdites, on peut facilement acheter d’autres espèces dans les animaleries où l’on fait la promotion de ces animaux en disant qu’ils exigent peu de soins. Par ailleurs, les animaux exotiques sont habituellement présentés dans des environnements qui ne satisfont pas à leurs besoins. De plus, un logement inapproprié et un élevage inférieur aux normes se traduisent par un taux élevé de morbidité et de mortalité dans la chaîne d’approvisionnement et dans les foyers. Notre obligation morale envers la faune indigène canadienne devrait-elle être différente de nos obligations envers la faune non indigène? Les services vétérinaires prodigués aux animaux exotiques servent-ils à appuyer et à valider cette industrie?

Soumise par Megan Allore, Fergus (Ontario)

An ethicist’s commentary on dealing with exotic animals

I’ve had a particular soft spot in my heart for issues arising out of the selling and ownership of exotic companion animals. For 11 years I was part of a blue-ribbon advisory committee on animal welfare issues for a major international pet company. Some of the issues raised in this month’s column were problems we tackled for the company. For example, we convinced the management not to sell parrots because they can live longer than their owners, and are very easily traumatized when they are shifted to a new household. Our group also paid careful attention to confirming that animal vendors maintain the animals properly; that the animals were shipped in a minimally stressful manner; and that individual stores understood the needs and natures of the animals. For a while, the loss of aquatic animals, particularly fish, was staggering. Fortunately, one member of our committee was a world-famous fish veterinarian who was able to improve the death rate significantly, both to the benefit of the company and to the benefit of the animals’ welfare.

One finds a similar problem in many households when someone gives a child a baby chick for Easter. The initial excitement ends very quickly, and the animals are either killed or neglected. The bottom line is that animals are far too easy to acquire and equally easy to dispose of.

Whether the animal is native to the country or non-native is, in my view, irrelevant. An animal is an animal in either case. It has needs and interests determined by its nature which must be accommodated for it to enjoy positive welfare and which generate suffering when they are not accommodated. I would certainly support restricting the sale and ownership of animals whose needs are generally not understood and thence neglected. Trendy animals such as sugar gliders provide a case-in-point, and...
when such animals are acquired as pets for college dormitories, they are often abandoned when the school year ends because “my parents do not want me to bring home any animals.”

Acquiring an animal and keeping it in a moral way involves incurring significant responsibilities which too many people who acquire exotic animals never take the trouble to learn about, inevitably eventuating in suffering for these innocents. Such animals should never be acquired on a whim and without the purchaser familiarizing themselves with basic features of feeding and husbandry.

Thomas Aquinas said that while animals were not true objects of moral concern, it was grievously wrong to abuse them, as habits are created in abusers which can readily transfer to genuine objects of moral concern. It is well-known that many sadistic killers and a large percentage of violent offenders have an early history of animal abuse. Abuse of exotic animals is inevitable as a result of ignorance, and the state has an interest in restricting easy access to owning them.

As far as veterinarians are concerned, such issues as whether an animal is native or not is irrelevant to their sworn obligation to care for them. A sick sugar glider is just as much a candidate for veterinary care as a dog or cat. If veterinarians refuse to treat such animals when they are sick for arbitrary political reasons, the animals suffer and the veterinarians suffer as they possess the knowledge to help but are not allowed to do so, creating serious moral stress for practitioners. It is totally unsatisfactory for the veterinarian to turn his or her back and say “you should never have acquired such an animal.” As I have written many times, veterinarians suffer significant moral stress when they cannot exercise their art to the benefit of animals, whether failure to do so is the result of inadequate resources of the client or in the sort of situation we are discussing. There is no justification therefore for adding additional stress to practitioners growing out of not helping an animal because it is not native to an area.

Bernard E. Rollin, PhD

Ethical question of the month – March 2019

Animal welfare research often focusses on the measurement of carefully defined outcomes following specific interventions. As an example, a study may focus on laying hen preferences in regard to different litter substrates for dust bathing. The outcome variable may be the amount of time the hens spend with each substrate, or the number of obstacles they are willing to maneuver to reach the litter area. Results are regularly interpreted as demonstrating that one intervention promotes better animal welfare than another. Often, these studies are performed in university research facilities with limited numbers of animals over short time periods. Are strictly controlled, short-term intervention studies likely to improve the welfare of intensively managed livestock over the course of their lifetime on commercial farms? How can university researchers most efficiently enhance the quality of life of animals on commercial farms?

Submitted by Megan Allore, Fergus, Ontario

Response 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.
1. Concerning diarrhea, which of the following statements is NOT correct?
   A. Small bowel diarrhea is usually associated with weight loss.
   B. Mucus and hematochezia are common with small bowel diarrhea.
   C. The treatment for acute diarrhea is mainly supportive.
   D. Chronic diarrhea may be persistent or recurrent.

2. Which of the following is the most common etiology for megacolon in cats?
   A. Perineal hernia
   B. Dysautonomia
   C. Anorectal stricture
   D. Idiopathic

3. Which of the following is NOT transmitted from pets to humans?
   A. Francisella tularensis
   B. Yersinia pestis
   C. Bartonella henselae
   D. Brucella canis
   E. Borrelia burgdorferi

4. On per-rectal examination of a cow’s reproductive tract, the finding is made of a 10-cm diameter left horn which, on palpation, feels fluid-filled. There is a corpus luteum palpable on the right ovary. The cow calved 30 days ago. The most likely etiology is which of the following?
   A. Pregnancy
   B. Pyometra
   C. Mummified fetus
   D. Mucometra
   E. Neoplasia
5. Chinchillas with central nervous system signs: lethargy, anorexia, and pneumonia, are most likely infected with which of the following?
   A. Listeria monocytogenes
   B. Pasteurella pseudotuberculosis
   C. Pseudomonas
   D. Coccidia
   E. Giardia

   (See p. 321 for answers./Voir les réponses à la page 321.)
Join now and save 10% on your Commercial Insurance or Employee Benefits!
WHEN IT COMES TO PET INSURANCE, A WIN FOR PETS IS A WIN FOR VETS

For many Canadian dog and cat owners, having a pet as part of the family is a no-brainer. But what happens when the cost of veterinary care extends well beyond their financial means?

As veterinary care advances, it becomes more challenging to advocate for procedures or treatments based on what most Canadians can afford. This can result in delayed vet visits, unnecessary euthanasia for otherwise treatable conditions, or increased debt loads when your clients must overextend their credit. Ensure your clients understand that preventative and unexpected veterinary care is feasible with pet insurance.

GROW YOUR PRACTICE

You're not an insurance salesperson, but the reality is, when your clients have pet health insurance, you and your team are more likely to be able to provide the care pets deserve, when they need it – especially if there's been a serious injury or illness.

What's in it for vets? Healthy pets and retained customers. With the number of pet insurance companies in Canada, pet owners have a choice when it comes to picking coverage that works for their budget, lifestyle, and their pet's well-being. You and your front-line staff can provide the information clients need to make an informed decision. When a client decides to sign up, both the clinic and pet owner benefit!

A HEALTHY PET MEANS A HAPPY VET

It's important for pet owners to recognize signs or symptoms of a possible accident or illness, and then be proactive about veterinary care. Often, pet owners reach beyond their wallet and into their hearts to take care of their pet's health needs. This leaves the pet owner in debt, causing financial stress and potentially fewer vet visits. Pet owners who can't pay for vet bills may be left with psychological stress from the consequences.

With pet insurance, you can provide the care that's necessary and ease the burden of financial stress for your clients. Plans vary in price depending on what coverage your client is looking for, so there are options for every budget. You and your staff can offer information that comes from a unique perspective – from those who are on the front line of care. You have your finger on the pulse and can provide modern alternatives that keep animals healthier.

ENGAGE IN THE CONVERSATION

Only a handful of pet owners know that pet insurance exists, and many are skeptical about the idea of insuring their pet. Help your clients understand that as pets age, so does the likelihood of illness and the frequency of vet visits. Even with the best intentions, putting money into a savings account often isn't enough when something unexpected happens.

Engage in the conversation! Petsecure provides comprehensive coverage and reimbursement for up to 80% of vet bills, as well as special coverage, exam fees, taxes, diagnostics, medications, and more. The Petsecure representative in your area can give you materials with helpful information about pet ownership, dental care, etc. that you can display in your clinic and send home with your clients. If you're interested, you can also start your clients on Petsecure trials with 6 weeks of free coverage.

Want to know more? Visit petsecure.com and check out our products and programs.

You can also check us out on Facebook, Instagram, or Twitter.
What would your practice look like today if every client had pet insurance?

According to the Canadian Animal Health Institute, cat and dog populations – and pet ownership – in Canada are on the rise. Veterinarians are challenged with increasing demand, technological shifts, and retaining loyal customers. Understanding how pet health insurance works allows you to bridge the gap and grow your practice. It’s a win for pets and vets!

1 **GROW YOUR PRACTICE**

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Want to know more? Visit petsecure.com and check out our products and programs. You can also check us out on Facebook, Instagram, or Twitter.
Pet parents have a lot to remember. Give them one less thing to forget...

...and the longer dosing interval they prefer,* with the 12-WEEK extended flea and tick protection of BRAVECTO®.

Fewer doses per year mean fewer opportunities for late or missed doses...and fewer potential gaps in protection that can result in infestations.

Help simplify your clients’ monthly “to-do” list by offering them the only canine flea and tick product that provides 12 weeks of uninterrupted protection in a single dose.

*B. Canadian dog owner market research, Guilbault Marketing, July 2018.
BRAVECTO® is a registered trademark of Intervet International B.V. Used under license. MERCK® is a registered trademark of Merck Canada Inc. © 2019 Intervet Canada Corp. All rights reserved. CA/BN/1218/067
March is here, and it’s time to get ready for the 4th edition of National Tick Awareness Month (NTAM).

Launched in 2015 by the Canadian Veterinary Medical Association (CVMA) in partnership with Merck Animal Health, this pet-owner education campaign has helped increase public awareness about ticks, the potential health risks they pose, and measures that are available to help control them.

The 2019 NTAM campaign builds on the momentum of the 3 previous years, with the launch of TickTalkCanada.ca, a new educational website for Canadian pet owners.

Prominently featured on the new website will be material produced for the 2018 “What do you really know about ticks?” campaign, including a video animation and a series of 12 shareable “The truth about ticks” videos in which Canadian veterinarian Dr. Scott Stevenson answers common pet-owner questions about ticks.

“Last year’s campaign was inspired by what pet owners want to know about ticks. While client education remains the focus of this year’s campaign, we’ve taken things up a notch by bringing the message directly to pet owners, which was the most common request we received from veterinarians during the 3 previous campaigns,” says Dr. Terri Chotowetz, CVMA president.

“Many pet owners are already online looking for information about ticks, but don’t always know which sites to trust,” adds Dr. Chotowetz. “We created TickTalkCanada.ca to provide pet owners with a credible online resource, with the goal of initiating the ‘tick talk’ and encouraging clients to continue a meaningful tick-control conversation with their veterinarian.”

In addition to the TickTalkCanada.ca website, the 2019 NTAM campaign will also feature:

- Take the “Tick Talk” Online During National Tick Awareness Month
- New Canadian Website Helps Get the Conversation Started
En plus du site Web tiquetoccanada.com, la campagne 2019 du MNST comportera aussi :

- Une annonce bannière que les vétérinaires sont invités à afficher dans les pages des médias sociaux de leur clinique afin d’encourager les clients à visiter le nouveau site Web pour trouver des réponses à leurs questions.
- Une campagne publicitaire sur le Web pour diriger la circulation sur le site Web et vers les cliniques vétérinaires.
- Une affiche pour la salle d’attente et des images graphiques pour les médias sociaux que les cliniques pourront télécharger afin d’appuyer la campagne et d’encourager les propriétaires d’animaux à participer à la conversation sur les tiques avec leur médecin vétérinaire.


Comment l’ACMV appuie-t-elle votre exercice de la médecine vétérinaire?

L’ACMV fournit des outils et des ressources pratiques afin de vous appuyer, vous, votre équipe de soins vétérinaires et votre établissement et, dans certains cas, ces ressources contribuent également à l’une des grandes priorités de l’ACMV, l’amélioration du bien-être animal au Canada. Profitez des outils et des ressources suivants et tirez le maximum de votre adhésion à l’ACMV.

NOUVEAU! Les lignes directrices et ressources de l’ACMV sur l’utilisation des antimicrobiens vétérinaires

Lancées le 30 novembre 2018, les Lignes directrices et ressources de l’ACMV sur l’utilisation des antimicrobiens vétérinaires sont une nouvelle plateforme en ligne qui a pour but d’appuyer les médecins vétérinaires du Canada dans la prise de décisions judicieuses sur l’utilisation appropriée et responsable des antimicrobiens chez les animaux. La nouvelle plateforme remplace les Lignes directrices 2008 de l’ACMV sur l’administration judicieuse des antimicrobiens et traite de six groupes d’espèces, dont les bovins de boucherie, les bovins laitiers, la volaille, les porcs, les petits ruminants ainsi que les animaux de compagnie. Les principales caractéristiques incluent une interface interrogeable pour un accès rapide aux renseignements, des mises à jour fréquentes de l’information et l’ajout de nouvelles ressources ainsi que l’accessibilité sur tous les appareils. Une interface en français sera disponible au cours des prochains mois. Tous les médecins vétérinaires autorisés du Canada ont accès à la version intégrale de cet outil en ligne jusqu’au 1er avril 2019. Après cette date, l’accès sera limité aux membres de l’ACMV. Visitez le site Web de l’ACMV pour accéder à ce nouvel outil.

La Revue vétérinaire canadienne

La Revue vétérinaire canadienne (La RVC), qui est publiée par l’ACMV, est la « voix de la médecine vétérinaire au Canada ». Cette publication scientifique générale mensuelle, qui est évaluée par les pairs, présente un vaste éventail d’articles et de rubriques à l’intention du public vétérinaire.
be available in the coming months. All licensed veterinarians in Canada have full access to this online tool until April 1, 2019. After that date, access will be restricted to CVMA members only. Visit the CVMA website to access this new tool.

**The Canadian Veterinary Journal**
The Canadian Veterinary Journal (The CVJ), published by the CVMA, is the “voice of veterinary medicine in Canada.” This monthly, peer-reviewed, general scientific publication features a wide variety of articles and regular columns intended for the veterinary practitioner. The CVJ includes news and features of interest to CVMA members, new product information, and book reviews.

**The Canadian Journal of Veterinary Research**
The Canadian Journal of Veterinary Research (CJVR), published by the CVMA, is Canada’s only veterinary research publication. This quarterly peer-reviewed online-only journal has earned a wide international readership through the publishing of high quality scientific papers in the field of veterinary medicine. CJVR publishes the results of original research in veterinary and comparative medicine.

**Clinician’s Brief**
CVMA members receive a complimentary subscription to the monthly Global Digital Edition of Clinician’s Brief, which provides practical clinical information to companion animal practitioners. Members who prefer the print edition are entitled to a discounted subscription price.

**Plumb’s Veterinary Drugs**
CVMA members receive a 30% discount on the Individual or Practice online subscription of Plumb’s Veterinary Drugs, a practical drug information resource. In addition, available exclusively with your subscription, the Plumb’s mobile app provides you with instant, offline access to drug dosing information, any time, from any location.

**Pain Management Protocols**
Pain Management Protocols posters were developed collaboratively between the CVMA and the Sir James Dunn Animal Welfare Centre at the Atlantic Veterinary College.

These posters include:
- Anaesthetic Pain Management Protocols for Healthy Dogs and Cats
- Fundamental Points in Perioperative Pain Management, including new analgesic and anesthetic drugs and protocols
- Sedative, Anaesthetic and Pain Management Protocols for Healthy Horses, Cattle and Swine
- Principles of Effective Perioperative Pain Management.

The CVMA hopes these Guidelines and Posters will be valuable reference tools for veterinary students and practitioners, and teaching tools for faculty at Canadian veterinary colleges.

Since the release of the Code of Practice for Canadian Kennel Operations 2nd edition in 2007, both society and science have advanced with respect to the humane treatment of dogs. Over

**La Revue canadienne de recherche vétérinaire**
La Revue canadienne de recherche vétérinaire (RCRV), qui est publiée par l’ACMV, est la seule publication de recherche vétérinaire au Canada. Cette revue trimestrielle évaluée par les pairs est publiée en ligne seulement et s’est acquise un vaste lectorat international par la publication d’articles scientifiques de grande qualité dans le domaine de la médecine vétérinaire. La RCRV publie les résultats de travaux de recherche originaux en médecine vétérinaire et comparée.

**Clinician’s Brief**
Les membres de l’ACMV reçoivent un abonnement gratuit à l’édition mensuelle numérique mondiale de Clinician’s Brief qui fournit des renseignements cliniques pratiques aux praticiens pour animaux de compagnie. Les membres qui préfèrent l’édition imprimée ont droit à une réduction sur le prix d’abonnement.

**Plumb’s Veterinary Drugs**
Les membres de l’ACMV reçoivent un rabais de 30 % sur un abonnement en ligne individuel ou pour la clinique à Plumb’s Veterinary Drugs, une source d’information pratique sur les médicaments. De plus, l’appli mobile de Plumb’s, qui est offerte exclusivement avec votre abonnement, vous procure un accès instantané et hors ligne à la posologie des médicaments, en tout temps et n’importe où.

**Protocoles de gestion de la douleur**
Les affiches des protocoles sur la gestion de la douleur ont été créées dans le cadre d’une collaboration entre l’ACMV et le Sir James Dunn Animal Welfare Centre de l’Atlantic Veterinary College.

Les affiches comprennent :
- Des protocoles de gestion de la douleur anesthésique pour les chiens et les chats en santé.
- Des éléments fondamentaux pour la gestion de la douleur périopératoire, y compris des nouveaux médicaments et protocoles analgésiques et anesthésiques.
- Des protocoles de gestion des sédatifs, de l’anesthésie et de la douleur pour les chevaux, le bétail et les porcs en santé.
- Les principes d’une gestion efficace de la douleur périopératoire. L’ACMV espère que ces lignes directrices et affiches serviront d’outils de référence utiles pour les étudiants et les praticiens en médecine vétérinaire ainsi que d’outils d’enseignement pour les professeurs dans les facultés de médecine vétérinaire.

**Code de pratiques recommandées aux chenils du Canada – Troisième édition (2018)**
Depuis la publication de la deuxième édition du Code de pratiques recommandées aux chenils du Canada en 2007, la société et la science ont réalisé des progrès dans le domaine du traitement sans cruauté des chiens. Au cours des dix dernières années, de nouveaux renseignements scientifiques ont été mis au jour sur le comportement canin, l’hébergement des chiens, les questions de fin de vie, le transport, la nutrition, l’euthanasie et le bien-être.
the past 10 years, new scientific information has become available on dog behavior, housing, end-of-life issues, transport, nutrition, euthanasia, and general dog welfare. This 3rd edition of the Code of Practice for Canadian Kennel Operations (“the Kennel Code”) reflects both the new science and our evolving relationship with dogs. The Kennel Code has been updated to mirror the changing values towards animals that have emerged over the past decade. Dogs are now recognized by the public and by some legislative bodies as sentient beings that have the capacity to feel, perceive, and experience. This recognition has influenced the way people interact with dogs and the standard of care expected to be provided for them, whether a dog’s role is that of family member, working dog, or a dog kept for breeding and show.

Guidelines for the Legitimate Use of Compounded Drugs in Veterinary Medicine

These guidelines summarize and clarify all existing legislation and policy regarding the compounding and prescribing of compounded products for use in animals. For the most part, the wording is a concise reflection of the text from various pieces of legislation. However, the document is intended for guidance only; it is not to be used as a legal interpretation. The CVMA believes there is a significant need for information in this area. Concerns have been expressed about some current compounding practices. On occasions, compounding practices have crossed the line and become manufacturing. In these cases, veterinarians may unknowingly be assuming significant liability. Food safety could be placed at risk. There could be unknown threats to animal health. Inappropriate compounding practices may prove to be a disincentive to the development and approval of new animal health products. This document is intended as guidelines for veterinarians and to provide veterinary practitioners with information needed to make appropriate professional decisions when considering whether or not to use a compounded product for the treatment of a patient.

Animal abuse resources

Animal abuse is an important social issue affecting animals, families, and communities. Animal abuse includes physical abuse (non-accidental injury), sexual abuse, emotional abuse, neglect, and staging animal fights. Whether providing expert advice to the local humane authorities, visiting neglected farm animals, or treating an animal victim of violence, veterinarians are on the front lines of dealing with abuse.

Federal and provincial legislation affords animals protection from abuse, but veterinarians are sometimes concerned about disclosing information to humane authorities due to concerns regarding client confidentiality and personal liability. However, recognizing and reporting abuse is important, not only because veterinarians are charged with the welfare of animals, but also due to the link between animal abuse and human violence. Veterinarians suspicious of animal abuse need to understand how to recognize the signs of abuse and document these cases. Increasingly, veterinarians are asked to serve as expert witnesses and to assist in establishing forensic evidence.

The CVMA recognizes the vital role veterinarians play in protecting animals and creating safe and humane communities.
The Animal Abuse section of the CVMA website is intended to serve as a helpful resource for veterinary practitioners faced with animal abuse. The CVMA also created a 2-page poster “Animal Abuse — What Veterinarians Can Do.” This includes the CVMA position statement, which recognizes that veterinarians are in a position to observe occasions of animal abuse and have a moral obligation to report suspected cases.

**CVMA online education portal**
CVMA members have access to a global network of education resources from veterinary experts and education institutions from around the world. Choose from over 900 e-learning sessions on this exclusive continuing education (CE) portal from the comfort of your computer. You can select sessions based on refined search criteria such as specialty, accreditation, minimum duration, type of education, free or paid, and use the tracker tool to record your completed CE activities.

**CVMA Annual Convention**
CVMA members receive a discounted rate on the registration fee for the Convention. Take advantage of an excellent CE program, practical workshops and networking opportunities for you and your health care team. Plan to join us in Toronto for the joint 2019 World Small Animal Veterinary Association and CVMA Congress.

To learn more about these resources, visit the CVMA website (www.canadianveterinarians.net), or if you have any questions or require more information, contact the CVMA (admin@cvma-acmv.org).

**Portail d’éducation en ligne de l’ACMV**
Les membres de l’ACMV ont accès à un réseau mondial de ressources éducatives créées par des experts et des établissements d’enseignement de toutes les régions du monde. Vous pouvez choisir parmi plus de 900 ateliers de cyberapprentissage sur ce portail exclusif de formation continue à partir de votre ordinateur. Vous pouvez choisir des ateliers selon des critères de recherche précis tels que la spécialisation, l’agrément, la durée minimum, le type de formation, une formation gratuite ou payante et utiliser l’outil de suivi pour enregistrer les activités formation continue que vous avez terminées.

**Congrès annuel de l’ACMV**
Les membres de l’ACMV reçoivent un tarif réduit pour l’inscription aux congrès. Profitez d’un excellent programme de formation continue, d’ateliers pratiques et d’occasions de réseautage pour vous et votre équipe de soins vétérinaires. Planifiez de vous joindre à nous à Toronto lors du congrès 2019 conjoint de la World Small Animal Veterinary Association et de l’ACMV.

Pour en apprendre davantage à propos de ces ressources, visitez le site Web de l’ACMV (www.veterinairesaucanada.net) ou si vous avez des questions ou avez besoin de plus amples renseignements, contactez l’ACMV (admin@cvma-acmv.org).
A new partnership between LifeLearn Animal Health and the Canadian Veterinary Medical Association (CVMA) now entitles CVMA members to a 10% savings on 4 LifeLearn products:

• **WebDVM** websites, custom-built to rank veterinary practices higher on search engines, attract more pet owners and convert those pet owners into clients.

• **ALLYDVM**, the simple and flexible system for veterinary clinics to easily track, schedule and automate appointment reminders, reduce the risk of no-shows and boost clinic profitability. Add ALLYDVM’s optional Loyalty Program to keep clients engaged and returning to your practice.

• **ClientEd**, LifeLearn’s trusted online library of over 2000 pet health articles, written, edited and reviewed by animal health experts to facilitate effective client education in veterinary practices and improve patient outcomes.

• **Sofie**, the most advanced veterinary medical search tool available, created by veterinarians for the sole purpose of empowering veterinarians and their teams with faster, easier access to the most current, trusted and credible veterinary medical information. CVMA members can also get a free 30-day trial of Sofie prior to purchase.

**Claim your CVMA membership discount today. Membership does have its privileges!**

For more information about LifeLearn’s suite of customizable online solutions for veterinary practices and animal health organizations, visit the website (www.lifelearn.com).

LifeLearn, Inc. empowers animal health organizations to optimize client communications, maximize efficiency, and improve profitability with the LifeLearn ECOsystem. This comprehensive suite of customizable solutions advances animal health and education worldwide. For 25 years, LifeLearn has expanded its range of products and services by embracing innovation and excellence. LifeLearn was named one of Canada’s fastest-growing companies from 2015 to 2017 by PROFIT 500 and GROWTH 500 in 2018.
With you, whenever you need us. Insurance that works for you.

As a member of CVMA, you not only get access to exclusive group rates on your home and auto insurance, but you could enjoy online and mobile services that make insurance work for you.

Get a quote today. Discover insurance that works for you.
1-866-860-2862 cvmainsurance.com

Avec vous, partout et en tout temps. L’assurance pensée pour vous.

En tant que membre de l’ACMV, vous avez accès à des tarifs de groupe exclusifs pour vos assurances auto et habitation, en plus de services en ligne et mobiles pensés pour vous simplifier la vie.

Demandez une soumission. Découvrez l’assurance pensée pour vous.
1 866 860-2862 cvmainsurance.com/fr

The Personal refers to The Personal Insurance Company. Certain conditions, limitations and exclusions may apply. Auto insurance is not available in MB, SK and BC due to government-run plans.

La Personnelle désigne La Personnelle, compagnie d’assurances. Certaines conditions, exclusions et limitations peuvent s’appliquer. L’assurance auto n’est pas offerte au Man., en Sask. ni en C.-B., où il existe des régimes d’assurance gouvernementaux.
Experience Toronto: Discover the World
July 16–19, 2019

The Canadian Veterinary Medical Association (CVMA) is bringing the world to Canada in this joint Congress between the World Small Animal Veterinary Association (WSAVA) and the CVMA.

Online registration for the congress is already open. Be sure to visit the CVMA website for a breakdown of pricing and how you can save as much as 20% on your registration if you register prior to April 10, 2019. Registration fees are in Canadian dollars and include taxes.

The CVMA is hosting the Global CVMA Summit, chaired by Dr. Melanie Hicks, CVMA president-elect, and will focus on The Gold Standard of Animal Welfare — Positive and Negative Impact on Animals and Veterinarians, as well as the CVMA Global Forum presenting Telehealth and Animal Welfare — Pros, Cons and Implications for Veterinary Patients. Both of these CVMA signature events will take place on Tuesday, July 16. Visit the CVMA Convention website for more details on the speaker line-up.

The 2019 WSAVA/CVMA Congress will offer many events pre-, during and post-congress. The Community Outreach Program taking place on Saturday July 13, will include a 2.5-hour workshop session where Community Veterinary Outreach (CVO) will provide background on its One-Health model and approaches, along with presentations by both human and animal partners, followed by a CVO One Health Clinic. Delegates will be supervised by licensed veterinarians. Registration details to come.

Be sure to save the date for the WSAVA/CVMA social evening on Thursday, July 18 at the Evergreen Brickworks in Toronto. Evergreen Brick Works is one of Toronto’s most sought-after reception and event facilities. Experience local food, drinks, live entertainment and more. Stay tuned for more details.

If you have not done so already, the 2019 Congress has negotiated room blocks in 9 hotels near the Metro Toronto Convention Centre. Please visit the website (https://hotel.kenes.com/en/congress/wsva19) to make your hotel reservations.

(by Sarah Cunningham, Manager, Conventions, CVMA)

Faites l’expérience de Toronto :
Découvrez le monde
Du 16 au 19 juillet 2019

L’Association canadienne des médecins vétérinaires (ACMV) invite le monde au Canada lors de ce congrès conjoint entre la World Small Animal Veterinary Association (WSAVA) et l’ACMV. L’inscription en ligne pour le congrès est déjà ouverte. Assurez-vous de visiter le site Web de l’ACMV pour vous renseigner à propos du tarif et de la façon dont vous pouvez économiser jusqu’à 20 % sur votre inscription si vous vous inscrivez avant le 10 avril 2019. Les tarifs d’inscription sont en dollars canadiens et incluent les taxes.


Le congrès 2019 de la WSAVA/ACMV offrira beaucoup d’activités avant, durant et après le congrès. Le programme de rayonnement communautaire aura lieu le samedi 13 juillet et inclura un atelier de 2,5 heures au cours duquel Community Veterinary Outreach (CVO) communiquera des informations sur son modèle et ses approches d’Une santé ainsi que des présentations par des partenaires humains et animaux, suivies d’une clinique Une santé de CVO. Les délégués seront supervisés par des médecins vétérinaires autorisés. Les détails sur l’inscription seront communiqués ultérieurement.


Si vous n’avez pas encore réservé votre chambre, veuillez noter que le congrès 2019 a négocié des blocs de chambres dans neuf hôtels près du Metro Toronto Convention Centre. Veuillez visiter le site Web (https://hotel.kenes.com/en/congress/wsva19) pour faire la réservation d’hôtel.

(par Sarah Cunningham, gestionnaire, Congrès, ACMV)
My world just isn’t the same when I have ticks and fleas. Credelio™ (lotilaner) is a small, tasty* chewable tablet that acts fast²,³ to protect puppies and dogs* like me all month long.

*Puppies and dogs 8 weeks of age and older and 1.4 kg and greater

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The label contains complete use information, including cautions, and warnings. Always read, understand and follow the label, and use directions.


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Special Report  Rapport spécial

Veterinary Antimicrobial Stewardship in Australia

John Prescott

I visited Australia in November 2018 to present at 2 conferences on antimicrobial stewardship, the first a “One Health” conference organized by the National Centre for Antimicrobial Stewardship at the University of Melbourne, and the second the inaugural Australian Veterinary Antimicrobial Stewardship conference near Brisbane. The following are reflections on the current state of veterinary antimicrobial stewardship in Australia. I was very impressed by the high quality and level of engagement of people at these conferences.

National Antimicrobial Resistance and Stewardship Forum: The National Centre for Antimicrobial Stewardship (NCAS)

The NCAS is a nationally funded Australian Research Council Centre of Excellence that is approaching the end of its 5-year funding. It has a One Health approach to antimicrobial stewardship (AMS) but the core of its work relates to the use and development of a world-class information system, Guidance, to monitor and benchmark antimicrobial use in human hospitals in Australia, with recent expansion into homes for the aged. The system is being applied even in smaller hospitals, and seems to be largely self-funding. The critical impetus for its success has been the national requirement for hospitals to develop AMS programs as part of their certification. There is interest in Canada in this work, and active links to the major medical centres and the medical antimicrobial stewards in Canada. The NCAS would like to expand the Guidance software into general medical practice but this is a challenge because the informatics are not there. Australia is at the high end of antibiotic use in human medicine in the developed countries, described as a “culture of addiction to antibiotics in Australia;” Australians consume 4 times more antibiotics than do their animals. There was talk of developing a veterinary version of Guidance but that doesn’t seem likely.

The conference was well-organized, and had several parallel sessions including a veterinary session: https://www.ncas-australia.org/forum2018

One interesting aspect was Hand Hygiene Australia, a national hand hygiene initiative program developed through the Australian Commission on Safety and Quality in Health Care (ACSQHC): https://www.hha.org.au/ An article on the effectiveness of this 8-year program has just been published in the Lancet Infectious Diseases: “The 2016 NHHI (National Hand Hygiene Initiative) budget was equivalent to AUD$0·06 per inpatient admission nationally. Among Australia’s major public hospitals (n = 132), improved hand hygiene compliance was associated with declines in the incidence of hospital acquired Staphylococcus aureus bacteremia (HA-SAB); for every 10% increase in hand hygiene compliance, the incidence of HA-SAB decreased by 15%.” This emphasizes the importance of infection control as a critical part of AMS. There is a national (Australian Veterinary Association) infection control manual for veterinary practices but its uptake and implementation is unclear and is probably marginal currently.

The veterinary side of NCAS is largely an energetic and productive group of researchers from the University of Melbourne veterinary school. A recent PhD project by Laura Hardefeldt includes a stellar and productive analysis of antimicrobial use in different types of veterinary practice, an analysis of problematic drug labelling dosages, an analysis of the totally uncoordinated and highly variable veterinary diagnostic bacteriology systems in Australia, and an analysis of antimicrobial use in companion animals based on pet insurance data. In interesting on-going work on the veterinary side, antimicrobial use data from the practice software of 130 or so Australian veterinary clinics is being analyzed through the VetCompass program, a Royal Veterinary College-owned system for analysis of data from practices: https://www.vetcompass.org/ This program is being improved at NCAS as part of a PhD program to develop “natural language” software, with the potential, as has been shown in Britain, for benchmarking of antimicrobial drug choice and stewardship. Veterinary software analysis is a rapidly growing global business with considerable potential for national antimicrobial stewardship programs.

The NCAS veterinary program included discussion of how to obtain resistance data from veterinary diagnostic labs (“Why is it so difficult?”), use surveillance, and infection control. Agriculture is under fire in Australia because of live export of sheep to Muslim countries, with antimicrobial use another potential whipping boy, so there has been reluctance to present food animal use data publicly even though it is available. Although there was discussion of companion animal practice as a black box in which antimicrobial witchcraft is practiced, the data on lack of use of “high end” antimicrobials (e.g., carbapenems) don’t support this.

Currently, Australia has no public system for acquiring and reporting antimicrobial resistance (AMR) in animal pathogens or indicator bacteria, though the AURA system reports AMR in
resistant endemic and special concern human pathogens: https://www.safetyandquality.gov.au/antimicrobial-use-and-resistance-in-australia/about-aura/ There was interesting discussion about reporting veterinary diagnostic data under a green-orange-red traffic light coding, depending on the category of the antibiotic, a great idea, although the 3 lights would have different antimicrobials in North America. This approach, if adopted nationally, could be a simple way to remind veterinarians about AMR and enhance the value of diagnostic lab reporting, since there seems to be confusion by veterinarians about the meaning of some reports and limited knowledge about antibiotic importance rankings. Bizarrely, 4 of the 18 Australian veterinary diagnostic labs report zone diameters to practitioners and the use of CLSI interpretations by most labs means that some reports have no interpretation provided by CLSI. Since diagnostic labs have a central role in AMR surveillance there is clearly work to be done in this area and plans to improve this in Australia are under discussion.

One interesting discussion issue, which Americans and Canadians will appreciate, is that veterinary medicine is regulated at the State and not Commonwealth (federal) level. Some of the veterinary boards have been effectively neutered through various deregulation processes, among other issues, so that issues of VCPR (“under the care of a veterinarian”) are highly problematic in potentially regulating or evaluating practice standards of AMS. Throughout both conferences, I wasn’t aware of the role of the Australian Veterinary Association (AVA) in AMS, although clearly it is interested because of the involvement of the AVA at the AVAMS conference. I sent someone a copy of the CVMA-CCCVR “Veterinary Oversight of Antimicrobial Use: A pan-Canadian Framework of Professional Standards,” for which he seemed grateful since national harmonization is being discussed under his chairmanship. Further information about plans for harmonization is at www.agriculture.gov.au/ag-farm-food/ag-vet-chemicals/domestic-policy/harmonisation-min-vet-prescribing-reg-requirements

**Australian Veterinary Antimicrobial Stewardship Conference 2018**

This was the first conference of its type in Australia, with 175 people attending. The AVAMS conference was largely the major animal industries getting together for the first time around the resistance issue. The AVAMS was very well-organized with excellent presentations, and great discussion and interactions among the delegates: http://avams2018.w.yrd.currimda.com/

Australia is among the world’s lowest users of antimicrobials in food animals, falling slightly below Sweden but increasingly to its dismay being challenged by the United Kingdom. The surprise about this challenge by the UK is that, unlike the UK, most of Australian animal agriculture is extensive beef and sheep production; there are 6 sheep and 1 cow for every Australian. Beef cattle are often finished in a feedlot. The chicken industry is largely self-sufficient (and not an exporter) and the swine industry is tiny and struggling. Drought is an increasingly serious and intractable problem which threatens grain production and therefore expansion of intensive animal agriculture (but not marine aquaculture). Australia is an island that only imports animals under extremely strict conditions so that the threat to animal AMR is probably largely from humans, for which there are no such rigid quarantine requirements, or from seagulls. One of the themes of the conference, based on the O’Neill Report global agricultural antibiotic use figure, was that “Australia has a good news story” as far as antimicrobial use is concerned. Part of the good news theme is that fluoroquinolones are not used in food animals and use of third-generation cephalosporins in food animals is minimal. The data on resistance in food animal indicator bacteria and pathogens do not show resistance to these drugs. My theme was “this is great, but you need to prove this and publish this” and use the data to promote Australian animal agriculture nationally and internationally as “Respected, Responsible, Reactive (or similar).” The data on AMU and AMR are clearly available but the industries have been unwilling to publish it, partly for fear of public kickback by its enemies and partly for competitive reasons, since there is a limited number of significant actors in the major intensive animal producers (including beef feedlots). I repeatedly said that AMU and AMR surveillance doesn’t have to be expensive, or even annual, once baseline data are obtained and recognized as reliable. I also pushed the importance of benchmarking at the industry level, farm level, and country level, as well as resistance surveillance, as a way of identifying problems and of measuring and proving success. Conference participants were vividly aware of the impact on Australia as an animal product exporting country of changes in the EU not to import animal products from countries in which medically important antibiotics are used as growth promoters or for long term “preventive” use in the absence of evidence of infection.

National coordination and leadership of AMS are clearly an issue in Australia, just as they are in Canada. Getting buy-in from the Australian states and territories on AMR has been tough, as I think it has been in Canada. However, at least Australia, unlike Canada, has a national action plan. Australia is now starting to prepare its second 5-year plan, and has good links between the Chief Medical and Veterinary Officers. Everyone at both conferences was astonished that antimicrobial drug use in food animals in Canada and the US had only now become vet script only, and medically important antimicrobials only now been banned. This has been the case in Australia for decades.

National AMU data are available as tonnage because all antimicrobials are imported, but there were questions about the validity of the data, which don’t seem to capture all imports, and it wasn’t clear where all AMs were ending up. For example, some chicken-licensed products end up in pigs. Mark Schipp, the Chief Veterinary Officer, is President of OIE for the next 3 years and, very impressively because I’ve never seen this in Canada, sat through and participated in the entire conference (as well as in NCAS). Clearly there are plans being hatched to improve and report AMU collection as well as to implement a national AMR surveillance system for animals, including pathogen surveillance, but this will need to be funded as part of the second national action plan. I think the industries came around to recognizing the importance of national and international reporting of AMU and AMR and framing this both as a good news story and as
an important baseline against which to measure changes. The point was made in discussion that focusing national resources to obtain AMU and AMR data simply to meet WHO or OIE requirements could seriously detract from national efforts to actually improve stewardship, which has many more dimensions than AMU and AMR measurement. Glenn Browning said that not measuring AMU “is like using sea level changes [AMR] to monitor carbon dioxide levels”; everyone sees AMR issues as having the dimensions and complexity of climate change, though it’s probably easier to address.

Because of the work of Stephen Page, the Weese et al’s (1) continuous improvement “5Rs” of antimicrobial stewardship (Responsibility, Reduce, Refine, Replace, Review) has been accepted by most of the industries so it has given them a valuable common framework and language around which to develop their stewardship programs. An excellent summary of AMS in Australian livestock, prominently featuring the 5Rs, has just been published:

There was discussion of the different importance ratings of antimicrobials between the WHO, OIE, and different countries. I hadn’t realized that WHO ranks macrolides as critically important because of their possible effect in promoting resistance to Campylobacter jejuni; I’d never previously understood the reason why they (and several other antibiotics) were of such high importance. Health Canada has categorized them as Category 2. The WHO recognizes that country specific lists are legitimate; one speaker at the conference applauded the Health Canada list. The WHO list is problematic generally and may detract from the message the WHO wants to give. The same can be said of the WHO Guidelines for antimicrobial use in food animals. It looks as though the WHO may divide macrolides into 15-member lactone ring groups (azolides, e.g., azithromycin) as critically important and 16-member ring groups (e.g., tylosin) as of lower importance, which would be helpful and would increase credibility. There was a neat mantra that “important diseases do not require important antibiotics,” a good message to get across.

It’s hard to capture all the talks without going on too long, and people interested can look at the summaries of talks in the conference booklet that can be downloaded from the conference website. It was a great conference. Leigh Nind from the Department of Agriculture and Water Resources in Canberra gave a very clear and prophetic talk laying out future international directions for veterinary AMS. There was a very funny talk by Jessica Ramsden of Elanco Australasia of global consumer understanding of antimicrobial use in animals. Jacqui Norris from the University of Sydney has led development of an online antimicrobial stewardship training program for veterinarians as part of a national collaborative effort by the veterinary schools, with 6 modules. It is available at http://www.vetams.org. An interesting talk by Sam Abraham described the very frequent carriage by seagulls of human MDR ESBL E. coli, with the suggestion that sources might be untreated human sewage or diapers from infants or aged home patients obtained at garbage dumps. Such a finding further emphasizes the complexity of the movement of antibiotic resistant bacteria.

In summary, Australia is slightly lagging Canada and the United States in veterinary antimicrobial stewardship but will catch up fast in the next 2 years. We’re probably all close to the intermission after Act 1 of what will be a 3- to 4-Act play, with a long way to go and many still not convinced that there’s really a problem. We still don’t know whether the play is a tragedy, a comedy or, most likely, a tragicomedy.

Reference
Use of protective hand shielding by veterinary workers during small animal radiography

Monique N. Mayer, Niels K. Koehncke, Narinder Sidhu, Trevor Gallagher, Cheryl L. Waldner

Abstract — Federal government guidelines recommend wearing hand shielding that provides full protection for the entire hand during manual restraint of animals for radiography. The primary objective of this cross-sectional survey of 143 Saskatchewan veterinary workers was to describe behaviors of workers who do not follow guidelines for effective hand shielding, and to examine the factors associated with these behaviors. An electronic invitation to complete an online questionnaire was sent to 1261 members of the provincial veterinary medical and veterinary technologist associations. More than half of the workers reported that their hand protection was visible on a radiograph at least once a month, and 1/5 reported visible unshielded body parts at least once a month. More than 1/3 of workers never used shielding that fully enclosed their hands. Use of fully enclosing gloves or mittens was more likely for workers in academic workplaces ($P < 0.001$).

Résumé — Usage d'une protection pour les mains par les préposés vétérinaires durant la radiographie des petits animaux. Les lignes directrices du gouvernement fédéral recommandent le port d'une protection pour les mains qui offre une protection complète pour l'ensemble de la main durant la retenue manuelle des animaux lors de la radiographie. L'objectif primaire de cette enquête ponctuelle auprès de 143 préposés vétérinaires de la Saskatchewan consistait à décrire les comportements des préposés qui ne respectent pas les lignes directrices en matière de protection efficace des mains et à examiner les facteurs associés avec ces comportements. Une invitation électronique à répondre au questionnaire en ligne a été envoyée aux 1261 membres des associations provinciales de médecins vétérinaires et de technologues vétérinaires. Plus de la moitié des préposés ont signalé que leur protection était visible sur une radiographie au moins une fois par mois et 1/5 a signalé des parties du corps visibles non protégées au moins une fois par mois. Plus de 1/3 des préposés n'utilisait jamais une protection complète des mains. L'usage de gants ou de mitaines entièrement fermées était plus probable pour les préposés travaillant en milieu universitaire ($P < 0.001$).

(Traduit par Isabelle Vallières)

Can Vet J 2019;60:249–254

Introduction

In Canada, federal government guidelines state that a worker restraining an animal for radiography must wear protective gloves that provide protection throughout the glove, including fingers and wrist, and that irradiation by the X-ray beam must be avoided, whether or not gloves are worn (1). These are recommendations only; radiation protection for occupational exposure to X-rays is legislated at the provincial or territorial level. Current Saskatchewan legislation requires that employers ensure that the radiation dose to a worker is as low as reasonably achievable, and that workers use personal protective equipment provided by an employer, although no reference is made in the provincial legislation to the specific type of leaded hand shielding to be used (2,3).

Despite these guidelines and legislation, previous studies have found that Canadian veterinary workers do not consistently use leaded hand protection when restraining animals during small animal radiography (4–6). A 2017 survey of 331 Saskatchewan veterinary workers also reported inconsistent use of leaded gloves; only 6% of workers reported that they always wore gloves on both hands, while 35% of workers reported that they never wore gloves on both hands (7). Of the workers who did wear
gloves, 34% reported never wearing gloves that fully enclosed their fingers and hands (7). Leaded hand protection that does not fully enclose the hand includes mittens with single or multiple openings on the palmar surface and hand shields with a fully open palm, and is intended to facilitate manual restraint of animals by allowing workers to grasp patients directly. These types of hand shielding do not provide effective protection from radiation. Most radiation dose to workers is from X-rays scattered from the patient, and therefore any part of the worker that is not shielded from the patient will not be protected (Figure 1) (8). To the authors’ knowledge, there are no published data on the workplace availability and factors affecting use of different types of hand shielding during small animal radiography.

In addition to use of hand shielding that does not fully protect the fingers and wrist, other behaviors previously described in veterinary workplaces do not adhere to regulatory requirements to keep the dose as low as reasonably achievable. In a 2017 observational study of workers in a veterinary teaching hospital that used motion-triggered video cameras in a radiology room to observe use of personal protective equipment during manual restraint for small animal radiography, workers were observed laying gloves over the top of their hands during exposures, and also placing their gloved hands into the primary beam (6). Gloves laid over the top of hands will not protect a worker from X-rays scattered from the patient, and leaded hand protection does not effectively protect against primary beam radiation, which has a higher average energy than scattered radiation (9). In the authors’ experience, unshielded worker body parts are also included in the radiograph at times. To our knowledge, the frequency of shielded and unshielded body parts in the primary beam has not been described in private veterinary practice.

Hand doses are not monitored for most veterinary workers involved in diagnostic radiography. Whole body doses of ionizing radiation are monitored for some veterinary workers (37% of Canadian veterinarians and veterinary technicians in 2006); however, the whole body dose is usually measured using a dosimeter worn underneath a leaded apron, and the dose to unshielded hands would be expected to be much higher (10). The limit on dose from occupational exposure to ionizing radiation for extremities is based on the estimated amount of radiation that is required to cause skin reaction in 1% of individuals (11). This dose limitation also provides what is judged to be sufficient protection for the skin against cancer. In contrast to the risk of skin reaction, however, the risk of stochastic effects such as cancer has no dose threshold, meaning that with any dose some finite risk exists (11). This is the reason that radiation dose should be kept as low as reasonably achievable, even when worker doses are expected to be well below dose limits. These studies have identified a wide gap between the recommended and actual worker use of leaded hand shielding in veterinary workplaces, and the aim of this cross-sectional survey study was to answer questions raised by these previous studies (6,7).

The first objective of this study was to determine availability and use of different types of hand shielding, and factors that affect worker use of these types of hand shielding. The second objective was to describe the frequency of behaviors, such as placing shielded or unshielded body parts into the primary beam, which would result in higher worker dose. Finally, we planned to determine the most important reasons individual workers decide not to wear leaded hand shielding.

Materials and methods

The study protocol was submitted to the University of Saskatchewan’s Behavioral Research Ethics Board and was determined to be exempt from review as per Article 2.5 of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, December 2014 (BEH 16-127).

An electronic invitation to complete the online questionnaire was sent to all members of the Saskatchewan Veterinary Medical Association with an electronic mail address (750 veterinarians), and to all members of the Saskatchewan Association of Veterinary Technologists (458 veterinary technologists, 89 veterinary clinics, and 53 student members). Membership in these professional associations is mandatory for all veterinarians and technologists practicing in the province. An initial invitation to complete the questionnaire and a second invitation 10 d later were sent by electronic mail. Recipients were asked to share the electronic survey link with any workers involved in taking radiographs at their clinic who were not veterinarians or veterinary technologists.

The questionnaire was developed by 4 authors (MM, NK, TG, CW). The questionnaire first asked workers if they had been involved in taking a radiograph of a small animal (including companion animals, exotics, and wildlife) in the last year, and only workers who answered yes were asked to complete the remainder of the questionnaire. Workers were asked how many X-ray exposures on average they were involved in acquiring in 1 month, as well as for how many X-ray exposures on average the glove(s) they wore or an unshielded body part was visible on the radiograph in 1 month. They were also asked if leaded
hand shielding was available at their practice, and what type of leaded hand shielding was available (gloves that fully enclose hands and fingers, mittens that fully enclose hands and fingers, mittens with a slit or small opening in the palm, hand shields with a fully open palm, other) (Figure 2).

Workers were then asked how often they wore different types of hand shielding (gloves or mittens that fully enclose hands and fingers, mittens with a slit or small opening in the palm, hand shields with a fully open palm, other) and how often they used no hand shielding.

Workers were also asked to describe their knowledge of the risks of ionizing radiation, and to select the 3 most important reasons they sometimes did not use hand shielding when taking an X-ray, with reason 1 being most important. Seven reasons were available: i) gloves interfere with restraint of the animal; ii) I am not concerned about adverse health effects; iii) gloves are unhygienic; iv) gloves are not required by my employer; v) gloves do not fit properly; vi) not enough gloves for all workers; and vii) my coworkers do not wear gloves. The available reasons were developed from open text suggestions to increase use of leaded hand shielding were worn, worker knowledge of the risks of exposure to ionizing radiation, practice type, and worker position, and practice type were evaluated as potential confounders. As this was an exploratory analysis no interactions were examined. Categorical risk factors considered included: how many X-ray exposures the worker acquired per month, employer requirement that leaded hand shielding be worn, worker knowledge of the risks of exposure to ionizing radiation, practice type, and worker position, age and gender. Employer requirement that leaded hand shielding be worn was examined only for the percentage of time any type of hand shielding was used.

The association between the type of hand shielding workers had access to (only fully enclosing hand shielding or both fully enclosing and other types) and the percentage of time no hand shielding was used was examined with linear regression.

Results

Fifteen percent (183/1261) of workers who were sent an e-mail invitation completed a questionnaire. The overall response rate is an approximation as the number of non-veterinarian, non-technologist workers who were forwarded the questionnaire is unknown, and the questionnaire was sent to 89 veterinary clinic electronic mail addresses in addition to the individual members of the 2 professional associations.

Of the workers who completed a questionnaire, 22% (40/183) had not been involved in taking a radiograph of a small animal in the last year, and their questionnaire was terminated after the first question. Seventy-eight percent (143/183) of workers who completed a questionnaire had been involved in taking a radiograph of a small animal in the last year, and their questionnaire was terminated after the first question.

Characteristics of these 143 workers are described in Table 1.

![Figure 2. Examples of leaded hand shielding used by veterinary workers. A — a glove that fully encloses the hand; B — a mitten with openings in the palm; and C — a hand shield with a fully open palm.](image)

<table>
<thead>
<tr>
<th>Practice type</th>
<th>n</th>
<th>% (n/143)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Academic institution</td>
<td>10% (15/143)</td>
<td></td>
</tr>
<tr>
<td>Small animal exclusive private</td>
<td>48% (68/143)</td>
<td></td>
</tr>
<tr>
<td>Mixed animal private</td>
<td>38% (55/143)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3% (5/143)</td>
<td></td>
</tr>
<tr>
<td>Position</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Veterinarian</td>
<td>31% (44/143)</td>
<td></td>
</tr>
<tr>
<td>Technologist</td>
<td>63% (90/143)</td>
<td></td>
</tr>
<tr>
<td>Veterinary student</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Technologist student</td>
<td>&lt; 1% (1/143)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6% (8/143)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Greater than 65</td>
<td>&lt; 1% (1/143)</td>
<td></td>
</tr>
<tr>
<td>45 to 65</td>
<td>20% (28/143)</td>
<td></td>
</tr>
<tr>
<td>25 to 44</td>
<td>66% (94/143)</td>
<td></td>
</tr>
<tr>
<td>18 to 24</td>
<td>14% (20/143)</td>
<td></td>
</tr>
<tr>
<td>&lt; 18</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>94% (134/142)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6% (8/142)</td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Types of leaded hand shielding used by Saskatchewan veterinary workers during small animal radiography.

<table>
<thead>
<tr>
<th>Practice type</th>
<th>Number of exposures per month</th>
<th>Use no gloves</th>
<th>Mittens with a slit opening</th>
<th>Hand shields with open palm</th>
<th>Gloves or mittens that fully enclose hands with no openings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Academic institution</td>
<td>(6/137)</td>
<td>54/141 (38%)</td>
<td>11/141 (8%)</td>
<td>2/141 (1%)</td>
<td>29/143 (20%)</td>
</tr>
<tr>
<td>Small animal exclusive private</td>
<td>(8/137)</td>
<td>54/141 (38%)</td>
<td>11/141 (8%)</td>
<td>2/141 (1%)</td>
<td>29/143 (20%)</td>
</tr>
<tr>
<td>Mixed animal private</td>
<td>(8/137)</td>
<td>54/141 (38%)</td>
<td>11/141 (8%)</td>
<td>2/141 (1%)</td>
<td>29/143 (20%)</td>
</tr>
<tr>
<td>Other</td>
<td>(8/137)</td>
<td>54/141 (38%)</td>
<td>11/141 (8%)</td>
<td>2/141 (1%)</td>
<td>29/143 (20%)</td>
</tr>
</tbody>
</table>

Table 3. Report by Saskatchewan veterinary workers of average number of radiographs per month on which lead gloves and unshielded body parts were visible during small animal radiography.

<table>
<thead>
<tr>
<th>Number of radiographs/month</th>
<th>Glove use</th>
<th>Body part visible</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>2/141 (1%)</td>
<td>2/141 (1%)</td>
</tr>
<tr>
<td>1 to 5</td>
<td>2/141 (1%)</td>
<td>2/141 (1%)</td>
</tr>
<tr>
<td>6 to 10</td>
<td>2/141 (1%)</td>
<td>2/141 (1%)</td>
</tr>
<tr>
<td>11 to 15</td>
<td>2/141 (1%)</td>
<td>2/141 (1%)</td>
</tr>
<tr>
<td>16 to 20</td>
<td>2/141 (1%)</td>
<td>2/141 (1%)</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>2/141 (1%)</td>
<td>2/141 (1%)</td>
</tr>
</tbody>
</table>

31-50 X-ray exposures a month, 8% (12/143) 51-70 X-ray exposures a month, and 3% (5/143) > 70 X-ray exposures a month.

Ninety-eight percent (140/143) of workers reported that leaded gloves were available at their practice, 1% (2/143) did not have leaded gloves available, and 1% (1/143) did not know if leaded gloves were available. Seventy percent (97/139) of workers reported that hand protection that did not fully enclose the hand was available at their workplace; mittens with a slit or small opening in the palm were available to 45% (63/139) of workers, and hand shields with a fully open palm were available to 32% (44/139) of workers. Twenty-seven percent (37/139) of workers reported that the only hand protection available at their workplace were types that did not fully enclose the hand.

Excluding workers who did not have leaded gloves available and workers who were the employer, 47% (62/133) of workers reported that their employer required them to wear leaded gloves when taking radiographs of an animal, 50% (67/133) reported that their employer did not require them to wear leaded gloves, and 3% (4/133) did not know if their employer required them to wear leaded gloves.

Reported use of different types of leaded hand shielding is presented in Table 2. Twenty-eight percent (38/137) of workers used mittens with a slit or small opening in the palm at least 50% of the time, and 14% (19/137) used hand shields with an open palm at least 50% of the time. Thirty-six percent (49/137) of workers never used gloves that fully enclosed the hand and fingers.

The number of radiographs, on average, on which workers reported visible leaded gloves or unshielded body parts are presented in Table 3.

Eleven percent (16/143) of workers described their knowledge of the risks of exposure to ionizing radiation as poor, 29% (41/143) described their knowledge as fair, 46% (66/143) described their knowledge as good, and 14% (20/143) described their knowledge as excellent.

Factors associated with use of fully enclosing hand shielding

In the final multivariable model, use of fully enclosing gloves or mittens was significantly more likely for workers in academic workplaces than in small animal or mixed private practice (P < 0.001) (Table 4). Risk factors that were not associated with the use of fully enclosing gloves or mittens included the number of exposures acquired per month (P = 0.80), a knowledge of risks of ionizing radiation (P = 0.31), position (P = 0.80), age (P = 0.07), and gender (P = 0.20).

Factors associated with use of any type of hand shielding

In unconditional analysis, risk factors that were significantly associated with use of any type of hand shielding included employer requirement that hand shielding be worn (P < 0.001), knowledge of risks of ionizing radiation (P = 0.009), practice type (P < 0.001), and age (P = 0.02). Risk factors that were not associated with the use of hand shielding included the number of exposures acquired per month (P = 0.46), position (P = 0.44), and gender (P = 0.33).

The risk factors that were significantly associated with use of any type of hand shielding in the final multivariable analysis are presented in Table 5. Practice type was included in the multivariable analysis and was a significant risk factor (P = 0.005). However, significant differences were found only between practice type “other” and the other categories. For all respondents selecting “other,” the practice type consisted of > 1 of academic, small, and mixed private practice; therefore, it was felt that this finding was not important.

There was no difference in the use of any type of hand shielding between workers with access to only fully enclosing hand shielding and workers with access to both fully enclosing and other types of hand shielding (P = 0.86).

The most important reasons selected by workers for not wearing leaded gloves when taking a radiograph are presented in Table 6. Ninety-three percent (113/122) of workers selected “gloves interfere with restraint of the animal” as the most important reason they do not wear gloves.
Table 5. Final multivariable model of the associations between significant risk factors of interest and whether any type of hand shielding was used by veterinary workers.

<table>
<thead>
<tr>
<th>Employer requires*</th>
<th>Relative frequency of workers in category</th>
<th>Mean</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>44% (62/140)</td>
<td>0.89</td>
<td>0.82 to 0.95</td>
<td>reference</td>
</tr>
<tr>
<td>No</td>
<td>48% (67/140)</td>
<td>0.27</td>
<td>0.21 to 0.33</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>I don't know</td>
<td>3% (4/140)</td>
<td>0.45</td>
<td>0.19 to 0.70</td>
<td>0.003</td>
</tr>
<tr>
<td>I am the employer</td>
<td>5% (7/140)</td>
<td>0.48</td>
<td>0.29 to 0.67</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Knowledge of risksa

<table>
<thead>
<tr>
<th></th>
<th>Relative frequency of workers in category</th>
<th>Mean</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor</td>
<td>11% (16/143)</td>
<td>0.51</td>
<td>0.38 to 0.64</td>
<td>0.761</td>
</tr>
<tr>
<td>Fair</td>
<td>29% (41/143)</td>
<td>0.49</td>
<td>0.41 to 0.56</td>
<td>reference</td>
</tr>
<tr>
<td>Good</td>
<td>46% (66/143)</td>
<td>0.58</td>
<td>0.52 to 0.65</td>
<td>0.058</td>
</tr>
<tr>
<td>Excellent</td>
<td>14% (20/143)</td>
<td>0.67</td>
<td>0.56 to 0.79</td>
<td>0.006</td>
</tr>
</tbody>
</table>

a Results adjusted for confounding by practice type. CI — Confidence interval.

Discussion

Health Canada and the National Council on Radiation Protection and Measurements have developed guidelines for radiation protection in veterinary medicine (1,12). While both organizations recommend that veterinary workers always use gloves that fully enclose the hand when holding patients during radiographic imaging, our results demonstrate that this does not happen consistently in clinical practice. When workers do use hand protection, more than 1/3 never use shielding that fully encloses the hand. Forty percent of workers use hand shields with an open palm, or mittens with an opening for fingers, at least half of the time. Mittens with an opening to allow fingers to grasp the patient are marketed to veterinary employers to facilitate manual restraint. However, if portions of the hand or fingers extend through openings during the exposure, they will not be shielded from scattered radiation. In order for mittens with an opening to provide full protection, the worker would need to pull the portion of the animal that they are holding with their fingers through the opening back into the mitten. This could work for the lower portion of a leg or the foot of a smaller sized animal; however, in the authors’ experience, workers do not use mittens with openings in this manner.

Of workers with access to both fully enclosing hand shielding and hand shielding with openings, workers at an academic institution reported using fully enclosing hand shielding more often than workers in small animal and mixed animal private practice. It is possible that this difference was due to the type of hand shielding that is readily available to academic workers. For example, at the veterinary teaching hospital in Saskatchewan, radiology technologists store hand shielding with openings out of sight of workers in an attempt to limit use, while fully enclosing hand shielding is stored in open view next to the radiology table.

While a greater knowledge of risks of ionizing radiation was associated with more frequent use of any type of hand shielding, knowledge of risks was not associated with use of fully enclosing gloves or mittens. It may be that workers with more knowledge understand the reduction in dose that leaded shielding provides, but are unaware that the main source of dose is scattered X-rays from the patient, and that the level of protection is therefore not equivalent between the different types of hand shielding. If multiple types of hand shielding are made available by their employer, workers may infer that all types provide equal protection, and there is no impetus to wear fully enclosing hand shielding. In addition, veterinary supply companies offer hand shielding with openings specifically for use with veterinary patients, and this may suggest efficacy to workers.

An obvious recommendation to decrease use of hand shielding that does not provide full protection to fingers and wrist would be for employers to only make fully enclosing gloves or mittens available to employees. However, in contrast to hand shielding with openings for fingers, fully enclosing gloves or mittens do not allow workers to use their fingers to grasp patients, and workers in previous studies have identified interference with restraint as a reason they choose not to wear gloves (6,7). For this reason, we examined whether workers with access to only fully enclosing gloves or mittens were less likely to wear hand shielding than workers who also had access to hand shielding that did not fully enclose the hand. Our results showed no difference in use of hand shielding between these 2 groups, and we therefore recommend that employers make only fully enclosing gloves or mittens readily accessible to workers.

Half of veterinary workers reported that the glove they were wearing was visible on at least 1 radiograph a month, and 1 in 20 workers reported that a glove was visible on > 11 radiographs a month. Leaded apparel is designed to protect workers from the energies composing scattered radiation; the primary beam has a higher average energy and the effectiveness of protection is therefore much lower (9). One-fifth of workers reported unshielded body parts visible in the field at least once a month, while 2 workers reported unshielded body parts visible in the field > 20 times a month. Our findings may underestimate the true frequency of gloves and unshielded body parts visible on radiographs as not all workers view the radiographs for which they restrain animals, and therefore may be unaware that gloves or body parts are visible. A study using a canine cadaver and an anthropomorphic phantom found that the dose within the primary beam was on the order of 100 times higher than the scattered radiation dose measured at the position of the restrainer’s hands (13). We therefore recommend that both unshielded and shielded hands never be placed in the primary

Table 6. Three most important reasons (with reason 1 being most important) Saskatchewan veterinary workers do not wear leaded gloves when taking a radiograph.a

<table>
<thead>
<tr>
<th>Reason</th>
<th>Number of workers selecting the reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gloves interfere with restraint of the animal (n = 122 respondents)</td>
<td>(n = 113)</td>
</tr>
<tr>
<td>Gloves do not fit properly (n = 89 respondents)</td>
<td>Gloves interfere with restraint of the animal (n = 16)</td>
</tr>
<tr>
<td>My coworkers do not wear gloves (n = 22)</td>
<td>Gloves are not required by my employer (n = 18)</td>
</tr>
<tr>
<td>Not enough gloves for all workers (n = 12)</td>
<td>Gloves interfere with restraint of the animal (n = 11)</td>
</tr>
</tbody>
</table>

a Only reasons selected by > 10 respondents are presented.
beam. Employers are legally responsible for this safety behavior; an employer must ensure that the dose to a worker is kept as low as reasonably achievable (3). If a worker is still likely to engage in this practice, we recommend that a ring dosimeter be worn to monitor dose.

Based on our findings, employers can increase worker use of any type of hand shielding by requiring that hand shielding be worn when manual restraint is used for radiographs, and by educating their employees on the risks of exposure to ionizing radiation. Employers should ensure that all workers are aware that hand shielding is required, that shielding with openings does not provide equal protection to shielding that fully encloses the hand, and that hands must not be placed in the primary beam even when shielding is worn. The probability of harmful effects caused by exposure to ionizing radiation associated with diagnostic radiography has been described for veterinary workers, and educational materials designed specifically for veterinary workers are available to employers (14–16).

Workers identified hand shielding interfering with restraint of an animal as the most important reason they chose to sometimes not wear hand shielding. This is consistent with the findings of a study carried out in 2015 in a veterinary teaching hospital in which 73% of workers reported that glove use would increase if they could use less cumbersome gloves that would allow them to grasp and position animals more easily (6). The lack of flexibility is due to the minimum lead attenuation equivalent that is required to reduce the percentage of X-rays passing through the material. Reduction in the lead attenuation equivalent could increase flexibility; however, the percentage of X-rays reaching the worker's hands would increase. The second most important reason that workers identified for not wearing hand shielding was fit. In the past, personal protective equipment has been sized based on measurements for men, and this equipment may not provide a good fit for women, who on average have smaller and narrower hands than men (17). Employers can address this reason by providing leaded gloves or mittens in different sizes for workers, and ensuring that leaded gloves or mittens are available that fit all employees.

In addition to unwieldiness and poor fit, workers reported that their decision to use hand shielding was influenced by their coworkers, suggesting that modelling of appropriate radiation safety practices by employers may increase employee's use of hand shielding. As well, employers should ensure that adequate numbers of gloves or mittens are available, as some workers reported that there were not enough gloves or mittens for all workers.

A limitation of this study is that an exact response rate cannot be reported, as we asked recipients of the e-mailed questionnaire to share it with other workers who were not technologists or veterinarians. There is also the potential for reporting bias, or selective suppression of information about behaviors that do not follow radiation safety guidelines by respondents. This could result in an underestimation of behaviors that increase dose to workers.

In conclusion, less than 1/3 of veterinary workers who do use hand shielding during small animal radiography always use fully enclosing gloves or mittens. Hand shielding that does not fully enclose the hands does not provide effective protection against scatter radiation, and therefore we recommend that employers supply only fully enclosing hand shielding to veterinary workers. Employers can increase the use of any type of hand shielding by requiring and modelling use, by educating workers on the risks of ionizing radiation exposure, and by providing well-fitting gloves or mittens for all employees.

References

Antimicrobial usage in western Canadian cow-calf herds
Cheryl L. Waldner, Sarah Parker, Sheryl Gow, Devon J. Wilson, John R. Campbell

Abstract — While ongoing surveillance and research initiatives have provided some information on antimicrobial use (AMU) in many livestock commodities, there are no recent reports for Canadian cow-calf herds. Antimicrobial use data were collected in 2014 for bulls, cows, and calves from 100 herds participating in the Western Canadian Cow-Calf Surveillance Network. Lameness was the most common reason for treatment in cows and bulls, with oxytetracycline being the treatment of choice. Herd owners were most likely to treat calves before weaning with florfenicol, oxytetracycline, and sulfamethazine for respiratory disease or diarrhea. The most frequently reported reason for antimicrobial use in weaned calves was respiratory disease and the most reported product was florfenicol. While 98% of herds reported treating ≥ 1 animal with antimicrobials, most cattle did not receive antimicrobials for either treatment or disease prevention on participating cow-calf operations.

Résumé — Usage des antimicrobiens dans les troupeaux d'élevage-naissage de l'Ouest canadien. Même si les initiatives continues de surveillance et de recherche ont fourni certaines données sur le recours aux antimicrobiens (RAM) pour de nombreux types d'élevage, il n'y a pas de rapport récent sur les troupeaux bovins d'élevage-naissage canadiens. Des données sur l'utilisation des antimicrobiens ont été recueillies en 2014 pour les taureaux, les vaches et les veaux provenant de 100 troupeaux participant au Réseau de surveillance d'élevage-naissage de l'Ouest canadien. La boiterie a été la raison la plus courante du traitement des vaches et des taureaux et l'oxytétracycline était le traitement de choix. Avant le sevrage, il était plus probable que les propriétaires de troupeau traitent les veaux à l'aide du florfenicol, de l'oxytétracycline et de la sulfaméthazine pour les maladies respiratoires ou la diarrhée. La raison la plus fréquemment signalée pour l'utilisation des antimicrobiens chez les veaux sevrés était la maladie respiratoire et le produit le plus souvent signalé était le florfenicol. Même si 98 % des troupeaux ont signalé le traitement de ≥ 1 animal avec des antimicrobiens, la plupart des animaux d'élevage n'avaient pas reçu d'antimicrobiens soin pour le traitement ou la prévention d'une maladie dans les exploitations d'élevage-naissage participantes.

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Introduction

There is growing global recognition of the importance of antimicrobial resistance (AMR) and the need for antimicrobial stewardship in human and veterinary medicine (1,2). In response to the AMR threat, Health Canada revised Canada's regulatory framework for veterinary antimicrobials (3). One objective of these changes was to increase veterinary oversight of antimicrobial use (AMU) such that all medically important antimicrobials (MIA) require a prescription. Previously, some MIA approved for veterinary use before 2004 had not required a prescription (3) and these included many products commonly used for disease management. To evaluate the impact of these regulatory changes and other antimicrobial stewardship initiatives, reliable baseline data are needed for AMU practices in the Canadian livestock industry.

While the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) reports annual data from the Canadian Animal Health Institute on antimicrobial sales (4), specific information on why these products are being used and in what commodities is more limited. To address this gap CIPARS has implemented programs and is examining new frameworks for collection of on-farm data from several commodities. For instance, the 2015 CIPARS report contains farm surveillance AMU for broiler chickens and grower-finisher pigs (4). Since 2015, other surveillance programs have been initiated for turkeys and research on data collection frameworks is underway for nursery pigs, and dairy and feedlot animals.
However, there is currently no national surveillance program for on-farm AMU data from cow-calf operations. Antimicrobial use and resistance in cow-calf operations are of interest as cull cows and bulls are typically sold directly to slaughter. As well, AMU in cow-calf herds is a potential determinant of AMR in calves entering the feedlot.

Information on the types of antimicrobials used and reasons for use in North American cow-calf herds is limited, and the reported product-specific data for cow-calf herds were collected more than a decade ago. Carson et al (5) reported individual animal treatment records and a garbage can audit of AMU for 8 cow-calf herds from Ontario in 1999 to 2002. In 2002, Gow and Waldner (6) collected data from 36,634 cows and heifers and 28,573 calves from herds in western Canada. The 203 participants provided individual animal records for AMU and reason for use and herd-level data on the types of products used. The 2007–2008 National Animal Health Monitoring System (NAHMS) Beef project surveyed AMU in 470 US cow-calf herds for 2007 (7). More recently, a 2010 mail survey of 310 producers in western Canada described AMU data and reasons for treatment (8). However, the types of antimicrobials used were not reported.

In 2014, the Western Canadian Cow-Calf Surveillance Network provided an opportunity to collect baseline farm-level AMU data before the December 2018 changes to “prescription only” status. The primary objective of this study was to describe the types of antimicrobials used and the most common reasons for use in different production groups (cows, bulls, and weaned and unweaned calves) within western Canadian cow-calf herds. The secondary objective of this study was to determine if AMU for the most common disease problems in cows or in calves before weaning varied based on herd size, timing of calving season, and between purebred and commercial beef operations.

Materials and methods
Survey design
A paper-based survey to assess AMU was developed and tested with 20 producers and veterinarians. Changes were made in response to comments from the test group. Producers were provided with a handbook that included commercial and generic drug names and color photographs of product packaging for antimicrobials approved for use in cattle in Canada. The handbook was reviewed by 6 veterinarians including pharmaceutical representatives.

Survey content
The survey consisted of 2 sections. The first collected AMU information between July 1, 2013 and June 30, 2014 in 4 production groups: bulls, cows, unweaned calves, and weaned calves. Questions for each group were presented in separate tables and included data on whether any animals were administered antimicrobials for treatment or prevention for a list of common indications. If AMU was reported for the condition, the next questions addressed which antimicrobials were used and the percentage of animals treated (<5%, 6% to 30%, 31% to 70%, >70%). The second section of the survey asked about producer attitudes to AMU and decision-making strategies for AMU; the results are presented in a second paper (9).

Participant recruitment and survey distribution
Cow-calf producers were recruited from Alberta, Saskatchewan, and Manitoba participating in a cattle health and productivity surveillance network. National census data (10) were used to target selection of herds within each province to match the reported distribution of herd sizes and herd density.

Veterinarians were asked to identify interested clients who pregnancy-checked and kept basic calving and production records. Producers were offered a small honorarium. Producers returning the consent form and initial survey with baseline information from the 2013 calving season and management data were eligible for this study.

In July 2014, a survey requesting AMU information was distributed to the 104 participants enrolled to date; reminders were sent in August and 100 responses were returned between July 2014 and March 2015 for a return rate of 96%. Another survey on 2014 calving outcomes and herd management was distributed in February 2015. This survey was returned between March 2015 and January 2016. Selected data from subsequent surveys in the same cohort in 2015 and early 2016 were also used.

Data management and statistical analysis
Data from the AMU survey were merged with herd attribute information collected at the time of enrollment and herd management and production information from calving season 2014, record-keeping practices and dart gun use using a commercial database program (Microsoft Access; Microsoft, St. Louis, Missouri, USA).

The study population was described using appropriate statistics. Herd size was categorized as large (having >300 cows on January 1, 2014) or moderate, whether or not they sold any purebred animals, and if calving started before March 1, 2014.

Outcomes examined in the risk factor analysis included whether >5% of calves were treated for diarrhea or respiratory disease before weaning and if >5% of cows were treated for lameness. The associations between herd size, selling purebred cattle, starting to calve before March, and each treatment outcome were investigated using generalized linear models (GLM). The models used a Poisson distribution and log link function with a robust variance estimate to facilitate the direct estimation of relative risk (RR) with 95% confidence interval (CI) (11). This model was chosen to provide an unbiased estimation of RR (12) and avoid the overestimation of effect expected from odds ratios (OR) and logistic regression when the event of interest is common. P-values from this analysis were compared to those from logistic regression (data not reported).

All potential risk factors were screened with unconditional analysis; factors with \( P < 0.2 \) were considered for inclusion in the final multivariable models. Continuous predictors were examined to assess the linearity assumption. Manual step-wise backward selection was used to develop a main effects model, retaining only variables in which \( P < 0.05 \). As no variables were significant at \( P < 0.05 \) either alone or in the multivariable models, additional steps in the model building process were not described.
Table 1a. Summary of the antimicrobials used and reasons for use in bulls from July 2013 to June 2014 in 100 cow-calf herds.

<table>
<thead>
<tr>
<th>Generic antimicrobial</th>
<th>Use for ≥ 1 reason</th>
<th>Disease prevention</th>
<th>Eye</th>
<th>Lameness</th>
<th>Other</th>
<th>Reproductive tract</th>
<th>Respiratory</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bulls</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzyl penicillin procaine</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Benzylpenicillin procaine/benzathine</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ceftiofur crystalline free acid</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ceftiofur sodium</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Florfenicol</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Florfenicol, flunixin meglumine</td>
<td>8</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Monensin</td>
<td>7</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Oxytetracycline</td>
<td>57</td>
<td>1</td>
<td>15</td>
<td>51</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Penicill G procaine</td>
<td>17</td>
<td>0</td>
<td>2</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Polymyxin B*</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sulfadoxine/trimethoprim</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tilmicosin</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Tulathromycin</td>
<td>11</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td>0</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total herds reporting use of any antimicrobial in bulls</strong></td>
<td><strong>72</strong></td>
<td><strong>7</strong></td>
<td><strong>19</strong></td>
<td><strong>68</strong></td>
<td><strong>4</strong></td>
<td><strong>7</strong></td>
<td><strong>13</strong></td>
</tr>
</tbody>
</table>

a Contained in intramammary preparation (Special Formula 17900-Forte Suspension).

b Total does not reflect a sum of the column as some herds used more than one product for a particular reason within a particular age class.

Table 1b. Summary of the antimicrobials used and reasons for use in cows from July 2013 to June 2014 in 100 cow-calf herds.

<table>
<thead>
<tr>
<th>Generic antimicrobial</th>
<th>Use for ≥ 1 reason</th>
<th>Disease prevention</th>
<th>Eye</th>
<th>Lameness</th>
<th>Mastitis</th>
<th>Other</th>
<th>Reproductive tract</th>
<th>Respiratory</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cows</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzyl penicillin procaine</td>
<td>4</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Benzylpenicillin procaine/benzathine</td>
<td>5</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Ceftiofur crystalline free acid</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ceftiofur hydrochloride</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ceftiofur sodium</td>
<td>5</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Cepahipirin sodium</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Florfenicol</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Florfenicol, flunixin meglumine</td>
<td>20</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>Lasalocid</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Monensin</td>
<td>11</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neomycin</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Oxytetracycline</td>
<td>80</td>
<td>4</td>
<td>28</td>
<td>66</td>
<td>9</td>
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<td>7</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>3</td>
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<td><strong>Total herds reporting use of any type of antimicrobial in cows</strong></td>
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<td><strong>15</strong></td>
<td><strong>45</strong></td>
<td><strong>80</strong></td>
<td><strong>34</strong></td>
<td><strong>13</strong></td>
<td><strong>49</strong></td>
<td><strong>31</strong></td>
</tr>
</tbody>
</table>

a Contained in intramammary preparation (Special Formula 17900-Forte Suspension).

b Total does not reflect a sum of the column as some herds used more than one product for a particular reason within a particular age class.

Results

Study population

The median herd size was 359 animals (range: 125 to 7435). This included all cows, bulls, calves, steers, and replacement heifers present on the operation as of January 1, 2014. Typical herd size was 234 cows (median) [interquartile range (IQR): 160 to 359], 9 breeding bulls (IQR: 6 to 16), 66 replacement heifers (IQR: 30 to 121), and 17 steers (IQR: 1 to 140); 34% of the 100 had > 300 cows. Most survey participants (95%) reported having commercial cattle; 23% reported having purebred cattle with 18 of the 23 reporting both. Calving began between December 2013 and May 2014. In 2014, 42% of herds started calving before March 1st. Of the 37% of producers that retained any calves after weaning, 35% reported backgrounding (5% with stockers, 6% with feedlot, 1% with stockers and feedlot), 6% having stockers (5% backgrounding, 1% backgrounding and feedlot), and 9% having a feedlot (6% backgrounding and 1% backgrounding and stockers).
Sixty of the 100 producers described their herd record-keeping practices on a 2015 survey; 49 (82%) had health records.

### Most commonly reported antimicrobials and reasons for treatment

Ninety-eight producers (n = 100 completed surveys) reported AMU at least once. The antimicrobials most likely to be used at least once were: oxytetracycline (84%), florfenicol (81%), sulfonamides (50%), penicillin (34%), sulfadoxine/trimethoprim (SXT) (34%), tulathromycin (28%), and tilmicosin (19%).

Lameness was the most common reason for AMU in adult bulls and cows (Tables 1a, b). Herd owners also reported AMU in bulls for eye, respiratory, and reproductive infections. The most common drug used to treat lameness and ocular disease in bulls was oxytetracycline (Table 1a) and to treat respiratory disease was florfenicol with or without flunixin meglumine.

After lameness, the most common reasons for AMU in cows were reproductive tract infections, eye infections, mastitis, and respiratory disease (Table 1b). Oxytetracycline was the most commonly reported antimicrobial used for treating lameness, reproductive infections, and ocular disease in cows. Other reasons reported for AMU in cows included: injuries and abscess (6%), assisted calvings, and Cesarean-sections (6%), lumpy jaw (3%), and peritonitis/pericarditis (2%).

Before weaning, producers were most likely to report AMU in ≥ 1 calf for respiratory disease as well as for diarrhea followed by navel ill and then arthritis (Table 1c). Producers (n = 100) were also most likely to report using ≥ 2 antimicrobials at least once for treating diarrhea (38%) or respiratory disease (35%), as well as using ≥ 3 antimicrobials for diarrhea (13%) or respiratory disease (9%). Other reasons reported for AMU before weaning included: pinkeye (6%), foot rot (3%), abscesses (3%), cocciidiosis (3%), calf diphtheria (1%), and castration (1%). The antimicrobials most likely to be used in calves before weaning were: penicillic (florfenicol), tetracyclines (oxytetracycline) and oral boluses (sulfamethazine) (Table 1c).

The most commonly reported reason for AMU in weaned calves was respiratory disease with 69% of producers (n = 100) using ≥ 1 antimicrobial, 34% using ≥ 2, and 8% using ≥ 3. The second and third most common reasons for AMU in weaned calves were ocular infections, such as pink eye, and arthritis or lameness (Table 1d). The antimicrobial used most frequently for respiratory disease was florfenicol with or without flunixin meglumine. For ocular disease and arthritis, the most used antimicrobial was oxytetracycline. Other reasons reported for AMU in weaned calves included: injuries and abscess (3%), foot rot (1%), castration (1%), and ear infection (1%).

Regarding AMU for disease prevention, 7% of 100 herds reported disease prevention use in bulls, 15% in cows, 16% in unweaned calves and 27% in weaned calves (Tables 1a, b, c, d). Medically important antimicrobials were used for disease prevention in a smaller proportion of herds: 1% in bulls, 5% in cows, 10% in unweaned calves and 11% in weaned calves. No producers reported using ≥ 2 antimicrobials for disease prevention in bulls and only 2% reported use of ≥ 2 antimicrobials for disease prevention in cows, and 3% in unweaned calves and 4% in weaned calves.

### Route of administration

Most products reported were approved for subcutaneous or intramuscular injection. Most injectable MIA were used for...
Table 1d. Summary of the antimicrobials used and reasons for use in calves after weaning from July 2013 to June 2014 in 100 cow-calf herds.

<table>
<thead>
<tr>
<th>Generic antimicrobial</th>
<th>Total number and percentage of herds reporting AMU in calves after weaning (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Use for ≥ 1 reason</td>
</tr>
<tr>
<td>Post-weaned calves</td>
<td></td>
</tr>
<tr>
<td>Benzyl penicillin procaine</td>
<td>2</td>
</tr>
<tr>
<td>Benzylpenicillin procaine/Benzathine</td>
<td>3</td>
</tr>
<tr>
<td>Cefotiofur crystalline free acid</td>
<td>1</td>
</tr>
<tr>
<td>Cefotiofur sodium</td>
<td>3</td>
</tr>
<tr>
<td>Chlorotetracycline</td>
<td>2</td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>2</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>1</td>
</tr>
<tr>
<td>Florfenicol</td>
<td>19</td>
</tr>
<tr>
<td>Florfenicol, flunixin meglumine</td>
<td>44</td>
</tr>
<tr>
<td>Ganimethromycin</td>
<td>2</td>
</tr>
<tr>
<td>Lasalocid</td>
<td>1</td>
</tr>
<tr>
<td>Monensin</td>
<td>21</td>
</tr>
<tr>
<td>Neomycin</td>
<td>2</td>
</tr>
<tr>
<td>Oxytetracycline</td>
<td>53</td>
</tr>
<tr>
<td>Penicillin G procaine</td>
<td>18</td>
</tr>
<tr>
<td>Polymyxin B*</td>
<td>6</td>
</tr>
<tr>
<td>Sulfadoxine/trimethoprim</td>
<td>7</td>
</tr>
<tr>
<td>Sulfamethazine</td>
<td>4</td>
</tr>
<tr>
<td>Tildipirosin</td>
<td>1</td>
</tr>
<tr>
<td>Tilmicosin</td>
<td>7</td>
</tr>
<tr>
<td>Tulathromycin</td>
<td>19</td>
</tr>
<tr>
<td><strong>Total herds reporting use of any type of antimicrobial in calves after weaning</strong></td>
<td><strong>85</strong></td>
</tr>
</tbody>
</table>

* Contains in intramammary preparation (Special Formula 17900-Forte Suspension).

† Total does not reflect a sum of the column as some herds used more than one product for a particular reason within a particular age class.

Treatment of disease: 70% of herds used injectable MIA in bulls, 93% in cows, 93% in preweaned calves, and 79% in weaned calves. The use of injectable MIA for disease prevention was reported in only 1% of herds for bulls, 5% of herds for cows, 9% of herds for preweaned calves, and 8% of herds for weaned calves. Injectable tetracyclines were used for disease prevention in 10% of herds, and injectable macrolides were used for disease prevention in 6% of herds (Tables 3a, b, c, d).

Of the 82 producers who answered a question on a later survey about treatment while on pasture, 23 described using 1 or more types of equipment to inject cattle at a distance with 15 (18%) using a dart gun, 8 (10%) using a crossbow, and 1 (1%) using a pole syringe.

The use of oral antimicrobials in any form was reported in bulls in 8% of herds, in cows in 15%, in unweaned calves in 54%, and in weaned calves in 28%. In-feed antimicrobials (including monensin and lasalocid) were used in bulls in 8% of herds, in cows in 15%, in unweaned calves in 9%, and in weaned calves in 24% of herds. Water soluble antimicrobials were not used in bulls or cows, but were used in unweaned calves in 5% of herds and in weaned calves in 1% of herds. Similarly, oral boluses were also not used in bulls or cows, but were administered to unweaned calves in 51% of herds and in weaned calves in 3% of herds.

In-feed products not considered as MIA included monensin, which was used in 25% of herds, and lasalocid in 2% of herds. Medically important antimicrobials including oxytetracycline were used in feed in 4% of herds and chlorotetracycline was used in 2% of herds; 1 herd used both. Three herds reported using in-feed MIA to treat lameness in cows and 2 herds reported use for disease prevention in weaned calves. Other reported reasons for use of MIA in feed were: lameness in bulls (1 herd), disease prevention in unweaned calves (1 herd), and diarrhea in weaned (1 herd) and unweaned calves (1 herd). Water soluble sulfamethazine was used in 3% of herds, tetracycline hydrochloride in 2%, and oxytetracycline in 1%. The reported reasons for use of MIA in water were for treating diarrhea in unweaned calves (5 herds) and disease prevention in weaned calves (1 herd).

Use of oral sulfamethazine boluses was reported in 45% of herds. Oral boluses with neomycin sulfate were used by 11% of herd owners for unweaned calves. Calf diarrhea (87%) was the most commonly reported reason for using oral boluses.

Frequency of antimicrobial use

Most herds reported treating < 5% of animals in each group with MIA for any reason other than disease prevention: bulls (90%), cows (89%), unweaned calves (57%), and weaned calves (78%). These values decreased slightly when AMU for disease prevention was also considered: bulls (89%), cows (88%), unweaned calves (53%), and weaned calves (68%).

The MIAs most likely to be used in > 5% of animals for any reason were: oxytetracycline and penicillin in bulls; oxytetracycline and penicillin in cows; florfenicol, oxytetracycline, sulfamethazine, and SXT in calves before weaning; and oxytetracycline, florfenicol, tulathromycin, and tilmicosin in calves after weaning (Table 2).
Table 2. Summary of the frequency of reported AMU in bulls, cows, unweaned and weaned calves for participating herds. Reported as the number of herds and percentage of herds (n = 100) that used each antimicrobial in each production category for any reason and the highest reported percentage of the production class from each herd that was given the antimicrobial for any reason.

<table>
<thead>
<tr>
<th>Generic antimicrobial</th>
<th>Total herds reporting AMU (%)</th>
<th>&lt; 5%</th>
<th>6% to 30%</th>
<th>31% to 69%</th>
<th>70% to 100%</th>
<th>% treated not reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Benzylpenicillin procaine/benzathine</td>
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<td>2</td>
<td>2</td>
<td>0</td>
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<tr>
<td>Ceftiofur crystalline free acid</td>
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<td>0</td>
</tr>
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<td>Cefitofur sodium</td>
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<td>Florfenicol, flunixin meglumine</td>
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</tr>
<tr>
<td>Total herds reporting cows that received any antimicrobial&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>71</td>
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</tr>
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<td>Calves before weaning</td>
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<td>0</td>
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<td>Sulfadoxine/trimethoprim</td>
<td>30</td>
<td>19</td>
<td>9</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Sulfamethazine</td>
<td>45</td>
<td>31</td>
<td>12</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Tetracycline hydrochloride</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tilmicosin</td>
<td>11</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Tulathromycin</td>
<td>12</td>
<td>9</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total herds reporting calves that received any antimicrobial before weaning&lt;sup&gt;b&lt;/sup&gt;</td>
<td>95</td>
<td>46</td>
<td>26</td>
<td>7</td>
<td>16</td>
<td>0</td>
</tr>
</tbody>
</table>
The frequency of AMU varied by reason for use and type of antimicrobial across all participating herds ($n = 100$) (Tables 3a, b, c, d). Nine herds treated > 5% of bulls for lameness and 2 herds treated for ocular disease (Table 3a). Similarly, 10 herds treated > 5% of cows for lameness and 5 herds treated for ocular disease (Table 3b). Twenty-six percent of all herds treated > 5% of calves before weaning with antimicrobials for diarrhea, 28% treated > 5% for respiratory disease, and 9% of herd owners treated > 5% of calves for navel ill (Table 3c). Only 4% of all herds treated > 30% of calves before weaning for diarrhea, respiratory disease, or navel ill (Table 3c). For calves after weaning, 15% of herds treated > 5% of calves for respiratory disease (Table 3d).

### Association between herd attributes and treating > 5% of calves or cows for conditions of interest

Herd size was not significantly associated with the risk of treating either calves or cows for the most commonly reported conditions. Herds with > 300 cows were not significantly more likely than herds with ≤ 300 cows to treat > 5% of their calves with antimicrobials for diarrhea ($P = 0.30$) or respiratory disease (RR: 1.68, 95% CI: 0.91 to 3.13, $P = 0.10$). There was also no difference based on herd size in the risk of treating > 5% of cows for lameness ($P = 0.67$).

Similarly, there was no difference between herds with purebreds or cattle and those without in the risk of AMU for diarrhea ($P = 0.61$) or respiratory disease ($P = 0.40$) in calves before weaning, or lameness ($P = 0.81$) in cows. Finally, herds that started calving before March were not significantly more likely to use antimicrobials for treatment of diarrhea in calves ($P = 0.26$), respiratory disease in calves (RR: 1.70, 95% CI: 0.91 to 3.17, $P = 0.09$), or lameness in cows ($P = 0.84$) than those that had a later calving season.

### Discussion

This is the first Canadian study in more than a decade to report on the types of products and reasons for AMU in cow-calf herds. The most commonly reported antimicrobials used at least once across all age classes are considered of medium importance to human health by PHAC (Category III) (4) and included oxytetracyclines, florfenicol, and sulfonamides. The next most frequently recorded antimicrobials across all production classes were penicillin, SXT, and macrolides, which are all considered of high importance to human health by PHAC (Category II) (4). Penicillin use was most common in cows, SXT in unweaned calves, and macrolides in weaned calves. The most used macrolide was tulathromycin followed closely by tilmicosin. Overall, AMU differed only slightly from the most common previously described antimicrobials across all age classes in Canadian cow-calf herds; oxytetracycline, sulfonamides, florfenicol, and penicillin (6) and oxytetracycline, penicillin, florfenicol, and SXT (5).

Data on AMU in breeding bulls have not previously been reported in Canada, while AMU in beef cows was described for.

---

### Table 2. Summary of the frequency of reported AMU in bulls, cows, unweaned and weaned calves for participating herds. Reported as the number of herds and percentage of herds ($n = 100$) that used each antimicrobial in each production category for any reason and the highest reported percentage of the production class from each herd that was given the antimicrobial for any reason (continued).

<table>
<thead>
<tr>
<th>Generic antimicrobial</th>
<th>Total herds reporting AMU (%)</th>
<th>Reported percentage of animals within class receiving antimicrobials in each herd [Number (%) of herds ($n = 100$) for each category]</th>
<th>&lt; 5%</th>
<th>6% to 30%</th>
<th>31% to 69%</th>
<th>70% to 100%</th>
<th>% treated not reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calves after weaning</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzyl penicillin procaine</td>
<td>2</td>
<td></td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Benzylpenicillin procaine/benzathine</td>
<td>3</td>
<td></td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ceftirofur crystalline free acid</td>
<td>1</td>
<td></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Ceftiofur sodium</td>
<td>3</td>
<td></td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chlorotetracycline</td>
<td>2</td>
<td></td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>2</td>
<td></td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>1</td>
<td></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Florfenicol</td>
<td>19</td>
<td></td>
<td>14</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Florfenicol, flunixin meglumine</td>
<td>44</td>
<td></td>
<td>34</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Gamithromycin</td>
<td>2</td>
<td></td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lasaclid</td>
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<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Monensin</td>
<td>21</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>Neomycin</td>
<td>2</td>
<td></td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Oxytetracycline</td>
<td>53</td>
<td></td>
<td>40</td>
<td>6</td>
<td>3</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Penicillin G procaine</td>
<td>18</td>
<td></td>
<td>18</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Polymyxin B*</td>
<td>6</td>
<td></td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sulfadiazine/trimethoprim</td>
<td>7</td>
<td></td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Sulfamerazine</td>
<td>4</td>
<td></td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tildipirosin</td>
<td>1</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Tilmicosin</td>
<td>7</td>
<td></td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Tulathromycin</td>
<td>19</td>
<td></td>
<td>10</td>
<td>5</td>
<td>1</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total herds reporting calves that received any antimicrobial after weaning</strong></td>
<td><strong>85</strong></td>
<td><strong>38</strong></td>
<td><strong>16</strong></td>
<td><strong>7</strong></td>
<td><strong>24</strong></td>
<td><strong>0</strong></td>
<td></td>
</tr>
</tbody>
</table>

---

* ^a Contained in intramammary preparation (Special Formula 17900-Forte Suspension).  
^b Total does not reflect a sum of the column as some herds used more than one product for a particular reason within a particular age class. The value that is reported in each case is the maximum treatment frequency for the herd.
Table 3a. Summary of the frequency of reported AMU in bulls for participating herds. Reported as the number of herds and percentage of herds (n = 100) that used each category of antimicrobial in bulls and the highest reported percentage of bulls in each herd that received antimicrobials stratified by reason for use.

<table>
<thead>
<tr>
<th>Antimicrobial category</th>
<th>Total herds reporting AMU (%)</th>
<th>Reported percentage of bulls given an antimicrobial in each herd (Number (%) of herds (n = 100) for each category)</th>
<th>% treated not reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease prevention</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>1</td>
<td>0                                                                  0                                                                  0                                                                  1</td>
<td></td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>6</td>
<td>0                                                                  0                                                                  0                                                                  5</td>
<td></td>
</tr>
<tr>
<td>Any antimicrobial for disease prevention*</td>
<td>7</td>
<td>0                                                                  0                                                                  0                                                                  6</td>
<td></td>
</tr>
<tr>
<td>Ocular disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>1</td>
<td>1                                                                  0                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>3</td>
<td>2                                                                  0                                                                  1                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>15</td>
<td>13                                                                0                                                                  0                                                                  1</td>
<td></td>
</tr>
<tr>
<td>Topical antimicrobial</td>
<td>1</td>
<td>1                                                                  0                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Any antimicrobial for ocular disease*</td>
<td>19</td>
<td>16                                                                0                                                                  1                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Lameness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable cephalosporin (3rd gen)</td>
<td>2</td>
<td>2                                                                  0                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>12</td>
<td>9                                                                 3                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>19</td>
<td>15                                                                2                                                                  0                                                                  2</td>
<td></td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>5</td>
<td>4                                                                 1                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>50</td>
<td>43                                                                4                                                                  1                                                                  1</td>
<td></td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>1</td>
<td>0                                                                  1                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Any antimicrobial for lameness*</td>
<td>68</td>
<td>58                                                                7                                                                  1                                                                  1</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>1</td>
<td>0                                                                  0                                                                  0                                                                  1</td>
<td></td>
</tr>
<tr>
<td>Injectable sulfonamide</td>
<td>1</td>
<td>1                                                                  0                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>1</td>
<td>1                                                                  0                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>1</td>
<td>0                                                                  0                                                                  0                                                                  1</td>
<td></td>
</tr>
<tr>
<td>Any antimicrobial for other*</td>
<td>4</td>
<td>2                                                                  0                                                                  0                                                                  1</td>
<td></td>
</tr>
<tr>
<td>Reproductive tract disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable cephalosporin (3rd gen)</td>
<td>1</td>
<td>1                                                                  0                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>5</td>
<td>5                                                                  0                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>1</td>
<td>1                                                                  0                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Any antimicrobial for reproductive disease*</td>
<td>7</td>
<td>7                                                                  0                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Respiratory tract disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>1</td>
<td>1                                                                  0                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>8</td>
<td>8                                                                  0                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>5</td>
<td>4                                                                  0                                                                  1                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Any antimicrobial for respiratory disease*</td>
<td>13</td>
<td>12                                                                0                                                                  0                                                                  0</td>
<td></td>
</tr>
<tr>
<td>Total herds reporting bulls given any antimicrobial*</td>
<td>72</td>
<td>53                                                                7                                                                  2                                                                  8</td>
<td></td>
</tr>
</tbody>
</table>

* Total does not reflect a sum of the column as some herds used more than one product for a particular reason within a particular age class.

2002 (6). In both the present and a previous study from western Canada (6), the most commonly used antimicrobials in cows were oxytetracycline and penicillin. However, in the previous study the use of a long-acting penicillin was more common. Oxytetracycline was also the product most likely to be administered to cows in the USA (7).

The top 4 choices for treating preweaning calves were also the same as reported earlier, although the rank varied slightly. In the present study the rank order of most common products used for any reason in preweaned calves were florfenicol, oxytetracycline, oral sulfonamides, and SXT. Gow and Waldner (6) reported the most common treatment choice in preweaning calves in 2002 to be oral sulfonamides, followed by florfenicol, oxytetracycline, and SXT. Injectable tetracyclines were the top choices for respiratory disease and diarrhea in preweaned calves in the American Beef 2007–2008 survey (7). However, while florfenicol was the second most common choice for treating respiratory disease, fluoroquinolones were the second most common choice for treating calf diarrhea in American calves in the Beef 2007–2008 report (7). Fluoroquinolones are considered of very high importance to human health by the Public Health Agency of Canada (PHAC) (4).

While almost all herds reported treating at least 1 animal with antimicrobials, most animals were not administered antimicrobials for either treatment or disease prevention. Likewise, in the 2007–2008 NAHMS study ~90% of herds of similar size to those included in this survey reported using oral or injectable antimicrobials to treat disease, only 7.2% of unweaned calves, 6.0% of replacement heifers, and 1.9% of cows were treated at least once with antimicrobials in 2007 (7). This was slightly lower than the earlier western Canadian study based on individual animal records in which 14% of calves and 2.7% of cows and heifers were treated at least once (6). While this is not definitive evidence that AMU is decreasing, it provides some assurance that AMU practices have not dramatically increased during this period.
The table lists the frequency of reported antimicrobial use (AMU) in cows for participating herds. It reports the number of herds and percentage of herds that used each category of antimicrobial in cows and the highest frequency of reported AMU in cows for participating herds. The frequency of reported AMU is summarized as the number of herds and percentage of cows in each herd that received an antimicrobial stratified by reason for use.

### Table 3b.

<table>
<thead>
<tr>
<th>Antimicrobial category</th>
<th>Total herds reporting AMU (%)</th>
<th>Reported percentage of cows given an antimicrobial in each herd [Number (%) of herds (n = 100) for each category]</th>
<th>% treated not reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease prevention</td>
<td></td>
<td>&lt; 5%</td>
<td>6% to 30%</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>4</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Any antimicrobial for disease prevention*</td>
<td>15</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Ocular disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable cephalosporin (3rd gen)</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>14</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>28</td>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>Topical antimicrobial</td>
<td>8</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Any antimicrobial for ocular disease*</td>
<td>45</td>
<td>40</td>
<td>3</td>
</tr>
<tr>
<td>Lameness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>11</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>18</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Injectable sulfonamide</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>63</td>
<td>54</td>
<td>6</td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Any antimicrobial for lameness*</td>
<td>80</td>
<td>68</td>
<td>8</td>
</tr>
<tr>
<td>Mastitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable cephalosporin (3rd gen)</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>10</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Injectable sulfonamide</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>9</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Intramammary</td>
<td>18</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Any antimicrobial for mastitis*</td>
<td>34</td>
<td>32</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable cephalosporin (3rd gen)</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>6</td>
<td>6</td>
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</tr>
<tr>
<td>Oral antimicrobial</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Any antimicrobial for other*</td>
<td>13</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Reproductive tract disease</td>
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<td></td>
</tr>
<tr>
<td>Injectable cephalosporin (3rd gen)</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Injectable penicillin</td>
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<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Injectable sulfonamide</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
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<td>28</td>
<td>0</td>
</tr>
<tr>
<td>Intraterine bolus</td>
<td>7</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Any antimicrobial for reproductive disease*</td>
<td>49</td>
<td>48</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory tract disease</td>
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<td></td>
<td></td>
</tr>
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<td>Injectable cephalosporin (3rd gen)</td>
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<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>5</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>20</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Injectable sulfonamide</td>
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<tr>
<td>Injectable tetracycline</td>
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<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Any antimicrobial for respiratory disease*</td>
<td>31</td>
<td>30</td>
<td>0</td>
</tr>
<tr>
<td>Total herds reporting cows given any antimicrobial*</td>
<td>95</td>
<td>71</td>
<td>9</td>
</tr>
</tbody>
</table>

* Total does not reflect a sum of the column as some herds used more than one product for a particular reason within a particular age class.
Table 3c. Summary of the frequency of reported AMU in calves before weaning for participating herds. Reported as the number of herds and percentage of herds (n = 100) that used each category of antimicrobial in calves before weaning and the maximum reported percentage of calves in each herd given an antimicrobial stratified by reason for use.

<table>
<thead>
<tr>
<th>Antimicrobial category</th>
<th>Total herds reporting AMU (%)</th>
<th>Reported percentage of calves given an antimicrobial in each herd (Number (%) of herds (n = 100) for each category)</th>
<th>% treated not reported</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt; 5%</td>
<td>6% to 30%</td>
</tr>
<tr>
<td>Arthritis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable fluoroquinolone</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>5</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>14</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Injectable sulfonamide</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>23</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Any antimicrobial for arthritis</strong></td>
<td><strong>40</strong></td>
<td><strong>37</strong></td>
<td><strong>2</strong></td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable cephalosporin (3rd gen)</td>
<td>10</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Injectable fluoroquinolone</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>21</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Injectable sulfonamide</td>
<td>23</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>53</td>
<td>35</td>
<td>15</td>
</tr>
<tr>
<td><strong>Any antimicrobial for diarrhea</strong></td>
<td><strong>73</strong></td>
<td><strong>46</strong></td>
<td><strong>22</strong></td>
</tr>
<tr>
<td>Disease prevention</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable fluoroquinolone</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
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<td>0</td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>12</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Any antimicrobial for disease prevention</strong></td>
<td><strong>17</strong></td>
<td><strong>1</strong></td>
<td><strong>0</strong></td>
</tr>
<tr>
<td>Navel ill</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable cephalosporin (3rd gen)</td>
<td>4</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>8</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>47</td>
<td>40</td>
<td>5</td>
</tr>
<tr>
<td>Injectable sulfonamide</td>
<td>5</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>19</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Any antimicrobial for navel ill</strong></td>
<td><strong>68</strong></td>
<td><strong>59</strong></td>
<td><strong>5</strong></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable cephalosporin (3rd gen)</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>7</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Injectable sulfonamide</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>9</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Topical antimicrobial</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Any antimicrobial for other</strong></td>
<td><strong>19</strong></td>
<td><strong>17</strong></td>
<td><strong>0</strong></td>
</tr>
<tr>
<td>Respiratory tract disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable cephalosporin (3rd gen)</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Injectable fluoroquinolone</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>20</td>
<td>13</td>
<td>4</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>68</td>
<td>49</td>
<td>17</td>
</tr>
<tr>
<td>Injectable sulfonamide</td>
<td>6</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>15</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>3</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>Any antimicrobial for respiratory disease</strong></td>
<td><strong>77</strong></td>
<td><strong>48</strong></td>
<td><strong>24</strong></td>
</tr>
<tr>
<td>Total herds reporting calves given any antimicrobial before weaning</td>
<td>95</td>
<td>46</td>
<td>26</td>
</tr>
</tbody>
</table>

* Total does not reflect a sum of the column as some herds used more than one product for a particular reason within a particular age class.
Lameness and reproductive disease were the most commonly reported reasons for AMU in cows. The Beef 2007–2008 study (7) and Gow and Waldner (6) also identified lameness as the most common reason for AMU for treating cows. The most frequently reported reasons for AMU in preweaned calves herein were respiratory disease and diarrhea, and in weaned calves, AMU was for respiratory disease. Respiratory disease was also slightly more likely than diarrhea to account for a higher percentage of calves treated within each herd. Similar to the current study, the American Beef 2007–2008 (7) survey reported respiratory disease was more common than calf diarrhea as a reason for herd owners reporting AMU in preweaned calves. Most of the products reported across all production groups were approved for injection. This is consistent with previous findings in which injectable treatments were much more frequent than oral antimicrobial use in both calves and cows (6,8). The current study did not collect specific information on the proportion of treatments by route of administration (subcutaneous versus intramuscular). However, in a 2016 survey of the same cohort, 28% of participants described using dart guns or crossbows on pasture. Other estimates of the frequency of dart gun and crossbow use were not identified.

The use of injectable MIA for disease prevention was uncommon in the study herds. Only injectable tetracyclines and

### Table 3d. Summary of the frequency of reported AMU in calves after weaning for participating herds. Reported as the number of herds and percentage of herds (n = 100) that used each category of antimicrobial in calves after weaning and the maximum reported percentage of calves in each herd given an antimicrobial after weaning stratified by reason for use.

<table>
<thead>
<tr>
<th>Antimicrobial category</th>
<th>Total herds reporting AMU (%)</th>
<th>Reported percentage of calves given an antimicrobial in each herd (Number (% of herds (n = 100) for each category)</th>
<th>% treated not reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthritis</td>
<td></td>
<td>&lt; 5%</td>
<td>6% to 30%</td>
</tr>
<tr>
<td>Injectable cephalosporin (3rd gen)</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Injectable fluoroquinolone</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>11</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>6</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>26</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>Any antimicrobial for arthritis*</td>
<td>38</td>
<td>37</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Injectable sulfonamide</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>5</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Any antimicrobial for diarrhea*</td>
<td>8</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Disease prevention</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable macrolide</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
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<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>21</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Any antimicrobial for disease prevention*</td>
<td>27</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Ocular disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable cephalosporin (3rd gen)</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>12</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>26</td>
<td>22</td>
<td>2</td>
</tr>
<tr>
<td>Topical antimicrobial</td>
<td>9</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Any antimicrobial for ocular disease*</td>
<td>39</td>
<td>35</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Topical antimicrobial</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Any antimicrobial for other*</td>
<td>10</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory tract disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectable cephalosporin (3rd gen)</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Injectable fluoroquinolone</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Injectable macrolide</td>
<td>18</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Injectable penicillin</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Injectable phenicol</td>
<td>54</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>Injectable sulfonamide</td>
<td>4</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Injectable tetracycline</td>
<td>22</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>Oral antimicrobial</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Any antimicrobial for respiratory disease*</td>
<td>69</td>
<td>53</td>
<td>9</td>
</tr>
<tr>
<td>Total herds reporting calves given any antimicrobial after weaning*</td>
<td>85</td>
<td>38</td>
<td>16</td>
</tr>
</tbody>
</table>

* Total does not reflect a sum of the column as some herds used more than one product for a particular reason within a particular age class.
penicillins were used for disease prevention in cows and in just 4% of herds. The most commonly used products for disease prevention were injectable tetracyclines in unweaned calves and injectable macrolides in weaned calves. While injectable tetracyclines were used for disease prevention in calves before weaning in 7% of herds, injectable macrolides and fluoroquinolones were used in unweaned calves in only 1% of herds for disease prevention. This was substantially lower than the 14% of herd owners who reported using long-acting antibiotics at birth in a 2010 survey (8). Macrolides were used for disease prevention in only 6% of herds in any class of cattle. Three of these 6 herds backgrounded their calves and 2 had their own feedlot. Macrolide use was of interest as resistance has been reported to be a concern when treating bovine respiratory pathogens in the feedlot, but was not common in either cows or preweaned calves in this group of herds (13).

While oral boluses were used in many herds to treat diarrhea in preweaned calves (54% of herds), the frequency of oral bolus use appears to have decreased from 2002 when 85% of all herds reported at least some bolus use in calves before Spring pasture (6). In contrast, MIA in feed or water were used in a small percentage of each production group and were more likely to be used for treatment than disease prevention. In feed antimicrobials were most likely to be reported in cows for lameness. Treatment of diarrhea in unweaned calves was the most commonly reported reason for use of MIA in water. Specific data on use of MIA in feed and water were previously limited to 11 Canadian herds from an Ontario study (5), but have been described for the USA (7).

Herd size, operation type, and time of calving were not associated with treating > 5% of calves or cows for the most commonly reported conditions in these herds. A 2010 study in western Canada found that the odds of treating calves for pneumonia and treating > 10% of calves for scour decreased for each additional month later that calving started (8). The odds of having to treat > 10% of calves for scour also decreased for each additional 50 cow increase in herd size. In the present study, the risk of treating > 5% of the calves for respiratory disease was not significantly associated with larger herd sizes or calving earlier; however, both P-values were < 0.10 and the confidence intervals reflected the limited study power. While this study provides estimates of the importance of some herd factors that might influence AMU, more detailed information on the frequency of treatments and risk factors would increase the precision of these estimates.

While data quality is always a challenge with surveys, several features were intended to minimize bias. The treatment survey was administered immediately after the 1-year period of interest. Color booklets with photographs of all products licensed for use were provided to aid participant recall. The survey also had suggestions to consult purchase receipts and the herd veterinarian. Producers were not asked if they kept individual treatment record; however, on a subsequent survey of the same cohort, 82% indicated they had health records. The lack of individual records limits the accuracy of data on the frequency of use although most producers should have been able to differentiate between products that were used in < 5% of animals from others used in > 30%, especially if aided by purchase receipts. Nevertheless, even the quality of individual animal records has been recognized as an issue in collecting treatment data from some cow-calf herds (5,6).

Most animals from cow-calf herds in western Canada are not exposed to antimicrobials and when MIA are used they are primarily intended for treatment rather than disease prevention. In particular, the use of MIA for disease prevention was not a common practice. Three of the 4 antimicrobials that were most commonly used at the time of this study were available without a prescription and included oxytetracycline, sulfonamides, and penicillin. Only florfenicol had to be prescribed by a veterinarian. The changing regulations for increased veterinary oversight will require all of these products to have a prescription from a veterinarian who has a valid Veterinary Client Patient Relationship with the herd. This may result in challenges for some cow-calf herds in particular where relationships with veterinarians have often been more sporadic than for other livestock commodities such as feedlot, dairy, and swine (3,4).

There is some evidence that AMU is improving with fewer herds reporting injectable antibiotics for disease prevention in calves before weaning, oral drugs for treatment of scours, and long-acting penicillin use in cows. Ongoing systematic surveillance is needed to determine if the changes in the regulatory framework for veterinary antimicrobials in Canada and other stewardship initiatives will have an impact on AMU in cow-calf herds.

References


Book Review
Compte rendu de livre

Comparative Anatomy of the Mouse and the Rat: A Color Atlas and Text


As the title suggests, this is an in-depth anatomy textbook. It is ring bound, so it lies flat and fits nicely on a Mayo stand in surgery, or on a counter during a postmortem evaluation. The general sections include: Body Regions; Juvenile Features and Sex Differentiation; External Features; Mammary Glands; Structures of the Head and Neck; Heart, Vascular Tree and Respiratory Tract; Abdominal Structures; Male Urogenital Apparatus; Female Urogenital Apparatus; Pelvic Limb Vessels and Nerves; Structures of the Tail; and Skeletal Structures. This book is visually appealing as it has many detailed, well-done, full color drawings of mouse and rat anatomy throughout. Following the side-by-side annotated drawings of each species, there is a description of the structure featured, including the differences between the mouse and the rat. Topics are covered that I didn’t expect, such as the detailed section on Juvenile Features, which includes drawings of mouse and rat pups at < 24 hours, 5 days, 11 days, 21 days, and adult, explaining how you would sex each species at each age. In the Heart, Vascular Tree and Respiratory Tract section, the book seems to have every conceivable projection of the thoracic structures — with ribs and without ribs, in situ from left and right, in situ from ventral and dorsal, longitudinal sections, etc. As I said, it is very detailed.

This book is endorsed by the American Association of Laboratory Animal Science (AALAS), and the value of this book for laboratory animal veterinarians is clear. I do, however, feel that this book could also be a valuable resource for clinical practitioners. As an exotic animal veterinarian, for example, I was very interested to see the detailed drawings of the mammary glands. Mammary gland tumors are a common issue in mice and rats, so it is good to be able to appreciate how far that tissue extends from the ventral area and the actual papillae. Many of the other sections would be useful in establishing the locations of structures for radiographs, surgery, sample collection, catheter placement, etc.

The only comment I have is that I did find the order of some of the drawings to be a little bit random. As previously mentioned, the first section of this book is Body Regions, which makes sense to give an overall picture before diving into specifics. However, within this first section, somewhat randomly, is the very specific: “Landmarks for access to cervicothoracic vessels (ventral aspect) showed in a rat.” This is an interesting and potentially useful drawing, but it just struck me as odd that it would be in this general section. Perhaps the author or editors felt that this particular drawing would be referenced frequently, and as such, it was placed near the beginning of the book.

Overall, I found this book to be very interesting, visually appealing, and a detailed exploration of the anatomy of the mouse and rat, with the differences between the species clearly highlighted in the text. This textbook would be a useful reference for laboratory animal veterinarians and exotic animal practitioners.

Reviewed by Teresa Bousquet, DVM, Park Veterinary Centre, Sherwood Park, Alberta T8H 2A8.
Article

Assessment of dog owners’ knowledge relating to the diagnosis and treatment of canine food allergies

Siarra Tiffany, Jacqueline M. Parr, James Templeman, Anna K. Shoveller, Rachel Manjos, Anthony Yu, Adronie Verbrugghe

Abstract — Canine food allergies are the result of an immune-mediated hypersensitivity reaction to dietary proteins and can manifest as a variety of dermatologic and/or gastrointestinal clinical signs. Food elimination trials followed by provocation tests are used to diagnose food allergies; however, no research has been conducted to determine whether elimination trials and provocation tests are being properly implemented by pet owners. The objectives of this study were to determine the level of knowledge of dog owners regarding food allergies, and to investigate how dog owners approach diagnosis and treatment with their veterinarians. This information will provide veterinary teams with insight on how to work with dog owners to obtain successful diagnosis and treatment. The results indicate that appropriate diet selection for the food elimination trial, owner education on compliance during the trial, and re-challenging with the previous diet should be the focal points for veterinarians suspecting food allergies in a canine patient.

Résumé — Évaluation des connaissances des propriétaires de chiens portant sur le diagnostic et le traitement des allergies alimentaires canines. Les allergies alimentaires canines sont le résultat d’une réaction d’hypersensibilité à médiation immunitaire face aux protéines alimentaires et elles peuvent se manifester par divers signes cliniques dermatologiques et/ou gastro-intestinaux. Les essais d’élimination d’aliments suivis de tests de provocation sont utilisés pour diagnostiquer les allergies alimentaires. Cependant, aucune recherche n’a été réalisée pour déterminer si les essais d’élimination et les tests de provocation sont mis en place de façon adéquate par les propriétaires. Les objectifs de cette étude étaient de déterminer le niveau de connaissances des propriétaires de chiens concernant les allergies alimentaires et d’étudier la façon dont les propriétaires de chiens envisagent le diagnostic et le traitement avec leur médecin vétérinaire. Ces enseignements permettront aux équipes vétérinaires de constater comment travailler avec les propriétaires de chiens afin d’obtenir un diagnostic et un traitement réussi. Les résultats indiquent que le bon choix d’alimentation pour les essais d’élimination des aliments, l’éducation des propriétaires pour la conformité durant les essais et de nouveaux tests avec l’alimentation antérieure devraient être les principaux sujets pour les médecins vétérinaires soupçonnant des allergies alimentaires chez un patient canin.

(Traduit par Isabelle Vallières)

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Introduction

Food allergies in dogs result from an immune-mediated hypersensitivity reaction to dietary proteins and manifest as various dermatologic and/or gastrointestinal clinical signs. Food allergies are one type of adverse food reaction (AFR) that occurs in dogs. Canine AFR can be categorized as either non-immune-mediated food reactions (e.g., lactose intolerance) or immune-mediated food reactions (e.g., food allergies); however, distinction between various types of AFR is difficult (1–5). Typical acute dermatological clinical signs may include erythema and pruritus, which may be intense. Lesions are typically localized to the paws, face, ears, abdomen, and/or perianal area (5,6). Chronic dermatological clinical signs may include recurrent ear infections, self-induced alopecia, excoriations, and lichenification (5,6). A median prevalence of 6% of all skin diseases in dogs and 20% of all allergic dermatological signs in dogs, have been attributed to AFR, although the exact pathogenesis has not been determined (7). Of the commonly reported gastrointestinal clinical signs in dogs, 10% to 15% are attributed to AFRs, including irregular bowel movements, halitosis, excessive gas, borborygmus, and nausea (5,6).

Food allergies are predominantly mediated through acute, intermediate, or late-phase immunoglobulin E (IgE) mechanisms, and as a result, a wide range of serum IgE levels are reported during serum allergy testing in dogs (1,2,4,8,9). Food allergies have also been found to be mediated through delayed immune mechanisms, known as a type III or IV hypersensitivity, although the exact pathogenesis is unclear (2,4,8). Olivery and Mueller (7) reviewed serum testing as a method of diagnosing food allergies in dogs and reported that the accuracy of serum IgE testing ranges from 58% to 87%, with positive predictive values ranging from 15% to 100%, which means serum IgE testing cannot accurately predict food allergies. Also, other laboratory assays, skin biopsies, saliva testing, as well as intradermal testing, and endoscopic provocation tests are considered unreliable and are not suitable as screening tests for AFR in dogs (2,10). The gold standard to accurately diagnose food allergies is a food elimination trial (3,8,9), although this gives no information about the underlying immunologic mechanism and cannot discriminate between non-immune-mediated food reactions and food allergy. A food elimination trial consists of 3 steps: i) elimination of the offending food allergen (i.e., dietary protein); ii) a trial period with a strict elimination diet containing either a novel or hydrolyzed protein source; and iii) a re-challenge period (i.e., provocation testing) with previous food to observe for recurrence of clinical signs. Selecting a novel protein diet relies on the ability of the veterinary team to obtain a lifetime nutritional history from the dog owner to ensure the protein is in fact novel. When considering novel ingredient selection, the most common allergenic animal-based protein sources identified for dogs include beef, dairy products, chicken, and lamb, with other proteins being reported less often (e.g., eggs, fish, and pork) (2,5). While less common than animal-based proteins, the most common allergenic plant-based protein for dogs is wheat, with other plant proteins being reported less often (e.g., soy, rice, and corn) (2,5). Commercially available diets with hydrolyzed proteins are typically soy- or chicken-based and vary in how extensively the proteins have been hydrolyzed.

The objectives of this survey were to i) determine the level of knowledge of dog owners regarding canine food allergies, and to ii) investigate how dog owners approach diagnosis and treatment with their veterinarians. The aim was to use this information to provide veterinary teams with insights on how to work with dog owners to obtain successful diagnosis and treatment of food allergies. To our knowledge, a survey of this scope has not been previously done, and may highlight areas for improvement of veterinarian-owner communication on diagnosis and treatment of food allergies in dogs.

Materials and methods

Study population

Dog owners were recruited throughout Ontario, Canada. Participation was voluntary, and participants were able to withdraw from the study at any point. Inclusion criteria for participation included: owners 18 y of age or older, with a dog 1 y of age or older that had suspected or confirmed food allergies. The dogs were divided by size into small (0.0 to 10.0 kg), medium (10.1 to 35.0 kg), and large (>35 kg) breeds. The survey focused on an adult population as only few elimination diets are commercially available for growing dogs. Owners were instructed that the survey must be filled out before their first visit with a veterinary dermatologist. Owners provided their dog’s previous nutritional history, current nutrition plan (including how the current food was selected), and the method of diagnosing their dog’s food allergies.

Survey design and distribution

The Canine Food Allergies Survey (available upon request from the corresponding author), created and distributed online using LimeSurvey (LimeSurvey, Hamburg, Germany), consisted of 57 questions in multiple choice, multiple response, Likert, closed-ended, and open-ended format and was divided into 9 sections: i) general information about your dog; ii) medical information for your dog; iii) current commercial dog food(s); iv) previous commercial dog food(s); v) current homemade diet recipe(s); vi) treats and human foods; vii) medications/supplements; viii) personal beliefs/knowledge; and ix) owner demographics. The study was approved by the University of Guelph Research Ethics Board (REB Approval #14AP035, June 3, 2014).

The survey was open from June 2014 to December 2015 and was distributed by e-mail to veterinary practices in Ontario, social media, and postcard distribution at 3 local veterinary hospitals and at local veterinary conferences.

Statistical analysis

All categorical data were analyzed using SAS software (version 9.2; SAS institute, Cary, North Carolina, USA). The parametric survey data were analyzed using a Chi-squared test to compare the predicted values to the actual values for each survey question. Significance was declared at \( P < 0.05 \).

Results

When the online survey was closed, 166 online responses were recorded. Due to a lack of responses, sections vii, viii, and ix were removed from analysis. The results presented are based upon the
Table 1. Suspicion and diagnosis of canine food allergies.

<table>
<thead>
<tr>
<th>Question</th>
<th>Frequency</th>
<th>Chi-squared</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Who first suspected your dog's food allergy? (n = 93)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Veterinarian</td>
<td>35.48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B. Myself (dog owner)</td>
<td>60.22</td>
<td>5.11</td>
<td>0.7458</td>
</tr>
<tr>
<td>C. Family/Friend</td>
<td>2.15</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>D. Nutritionist</td>
<td>1.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. Groomer</td>
<td>1.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>How old was your dog when the concern of food allergies was FIRST suspected? (n = 93)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Less than 6 months of age</td>
<td>11.83</td>
<td>12.78</td>
<td>0.0467</td>
</tr>
<tr>
<td>B. 6 months to 1 year of age</td>
<td>24.73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. 1 year to 6 years of age</td>
<td>55.91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. Older than 6 years of age</td>
<td>7.53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were any of the following tests done to diagnose your dog with food allergies? (n = 93)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Blood testing for food allergies</td>
<td>37.93</td>
<td>6.78</td>
<td>0.5606</td>
</tr>
<tr>
<td>B. Muscle strength testing for food allergies (i.e., kinesiology)</td>
<td>0.00</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>C. Saliva testing for food allergies</td>
<td>3.45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. Other:</td>
<td>58.62</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Including: Food elimination trial</td>
<td>32.97</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Significance declared at $P < 0.05$. NS — not significant at $P > 0.05$.

**Canine demographics**

Owner-reported demographic characteristics of the dog population are available upon request. Clients reported a wide variation in the means by which they obtained their pets [breeder — 42%; shelter/rescue — 30.1%; other (e.g., family friend or previous owners), 25.8%]. Of all dogs included in the study, 17% were small breed, 28% medium breed, and 55% large breed. Owners reported the dogs as 48% male and 52% female, with ages ranging from 1 to 13 y, and a median age of 5 y. Most dogs were owner-reported as spayed/neutered (85%) as opposed to intact (15%).

**Suspicion and diagnosis of food allergies**

When dog owners were asked who suspected a potential food allergy first, most owners reported themselves (60%), followed by the family veterinarian (35%) (Table 1; $P > 0.05$). The most common age range reported for the onset of clinical signs that led to a suspicion of food allergy was 1 to 6 y (56%), followed by 6 mo to 1 y (25%) (Table 1; $P = 0.0467$).

The frequency of dermatological signs of food allergy reported by the owners, is presented in Figure 1. The 3 most frequent dermatological variables found were: licking and chewing their paws (72%), bilateral ear infections (48%), and diagnosed skin infections (40%). Paw licking/chewing was the most common dermatological sign for all breed sizes; however, there seemed to be variation in breed size in regard to the second and third most common dermatological signs.

The frequency of gastrointestinal signs of food allergies reported by the owners, is presented in Figure 1. The most common gastrointestinal signs were: excessive gas (46%), soft stools (44%), and vomiting (38%).

Most owners reported that they opted for an alternative testing type (other, 59%) compared with using blood serum testing (38%) or saliva testing (3%) for the diagnosis of food allergies (Table 1; $P > 0.05$). The most common response for “other” was food elimination trial or single ingredient elimination trial, with additional responses being skin biopsies and intradermal testing.

**Treatment of food allergies**

When suspecting food allergies, dog owners, family veterinarians, or veterinary specialists (other than dermatologists) responded by changing the dog’s food. The type of food selected depended on who changed the food (Table 2; $P < 0.0001$). If the dog owner changed the food on their own, 47% chose to switch to an over-the-counter (OTC) brand (e.g., pet store brand or wholesale brand), 33% switched to a raw or homemade diet, and 20% changed to a veterinary diet (Table 2). When the veterinarian was responsible for changing the diet, 85% switched the dog to a veterinary diet, 7% chose to switch to an OTC brand, and 7% chose to switch to a raw or homemade diet (Table 2). Finally, when a veterinary specialist switched the dog’s food, 57% chose to change to a veterinary diet, 29% chose...
to switch to a raw or homemade diet, with the remaining 14% switching to an OTC diet (Table 2).

Participants reported that 82% of dogs suffering with dermatologic signs improved within 3 mo of changing the diet, while dogs with gastrointestinal clinical signs had a shorter recovery time, with 61% improving within 1 mo (Table 2; \( P > 0.05 \)).

Discussion with a veterinarian on importance of re-challenging with the previous diet to confirm a diagnosis of food allergies (i.e., provocation testing) occurred for only 33% of dog owners (Figure 2); however, 17% of dog owners were unable to recall this information. Only 10% of dog owners reported re-challenging their dog with the previous diet to confirm the diagnosis of a food allergy (Table 2; \( P > 0.05 \)). Of the 8 pet owners who re-challenged, both dermatological and gastrointestinal clinical signs returned at variable times after re-challenging (< 24 h, 12.5%; 1 to 3 d, 37.5%; 4 to 7 d, 25%; 8 to 14 d, 25%; Table 2; \( P > 0.05 \)). Half of the participants revealed that their veterinarian did not inquire about diet at every visit, and only 1/3 of participants stated that their veterinarian recommended their current diet (Figure 2).

Dietary indiscretions during the food elimination trial was reported by 75% of dog owners to include human foods such as:

Table 2. Dietary selection, duration for amelioration of clinical signs, and re-challenging with the previous diet to confirm food allergies.

<table>
<thead>
<tr>
<th>Question</th>
<th>Frequency</th>
<th>Chi-squared</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Which statement below BEST reflects how your dog was treated/is being treated for food allergies? ( (n = 93) )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I changed my dog’s food on my own:</td>
<td>34.75</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>A. To a grocery store brand of food</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B. To a homemade diet recipe</td>
<td>2.22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. To a pet store brand of food</td>
<td>42.22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. To a veterinary brand of food</td>
<td>20.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. To a wholesale brand of food</td>
<td>4.44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F. Other</td>
<td>31.12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>My family veterinarian changed my dog’s food:</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. To a grocery store brand of food</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B. To a homemade diet recipe</td>
<td>2.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. To a pet store brand of food</td>
<td>7.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. To a veterinary brand of food</td>
<td>85.37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. To a wholesale brand of food</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F. Other</td>
<td>4.88</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A veterinary specialist changed my dog’s food:</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. To a grocery store brand of food</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B. To a homemade diet recipe</td>
<td>28.57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. To a pet store brand of food</td>
<td>14.29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. To a veterinary brand of food</td>
<td>57.14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. To a wholesale brand of food</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F. Other</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>How long after the last dietary change did it take for your dog’s skin signs to improve? ( (n = 77) )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Less than 2 weeks</td>
<td>16.88</td>
<td>13.2522</td>
<td>0.1035</td>
</tr>
<tr>
<td>B. From 2 weeks to 1 month</td>
<td>33.77</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>C. From 1 month to 3 months</td>
<td>31.17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. Greater than 3 months</td>
<td>9.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. My dog did not have skin signs</td>
<td>9.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>How long after the last dietary change did it take for your dog’s gastrointestinal signs to improve? ( (n = 77) )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Less than 2 weeks</td>
<td>42.86</td>
<td>11.0217</td>
<td>0.2005</td>
</tr>
<tr>
<td>B. From 2 weeks to 1 month</td>
<td>18.18</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>C. From 1 month to 3 months</td>
<td>12.99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. Greater than 3 months</td>
<td>5.19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. My dog did not have gastrointestinal signs</td>
<td>20.78</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AFTER your dog’s skin and/or gastrointestinal signs improved did you feed your dog the diet he/she originally had skin and/or gastrointestinal signs on? ( (n = 77) )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Yes</td>
<td>10.39</td>
<td>1.9939</td>
<td>0.3690</td>
</tr>
<tr>
<td>B. No</td>
<td>89.61</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>If yes, how quickly did the skin/gastrointestinal signs reoccur after feeding the original diet? ( (n = 8) )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Less than 24 hours after</td>
<td>12.50</td>
<td>3.7838</td>
<td>0.1508</td>
</tr>
<tr>
<td>B. 1 to 3 days after</td>
<td>37.50</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>C. 4 to 7 days after</td>
<td>25.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. 8 to 14 days after</td>
<td>25.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. Do not recall time frame</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F. Skin/gastrointestinal signs did not reoccur</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Significance declared at \( P < 0.05 \). NS — not significant at \( P > 0.05 \).
as fruits and vegetables, meats, dairy products, egg products, breads and cereals, and other (Table 3; \(P > 0.05\)). Provision of additional food sources during the trial was also reported by 51% of dog owners to include: dental chews, rawhides, flavored bones, jerky treats, meaty bones, animal-based treats (e.g., pigs’ ears, pizzle sticks), and toys infused with flavors (Table 3; \(P > 0.05\)). Participants reported that 25% of dogs had access to unmonitored food sources including cat litter boxes, prey that was hunted/killed, and garbage (Table 3; \(P > 0.05\)).

**Discussion**

This survey revealed a lack of routine nutritional assessment during veterinary consultations and a lack of owner compliance with proper food elimination trial protocols (e.g., provision of additional foods and access to unmonitored food sources). In addition, it is clear from the survey data that re-challenging with the previous diet was a limiting step to confirm the diagnosis of food allergy as half of the study participants did not discuss re-challenging with their veterinarian. The survey, however, did not clarify whether owners would have been willing to do a re-challenge using the previous diet.

As per recommendation of the World Small Animal Veterinary Association (WSAVA) and the American Animal Hospital Association (AAHA), an extended nutritional assessment should be performed for any animal suspected/at risk of a nutrition-related problem (11,12). However, many owners reported that their veterinarian was not aware and/or did not recommend their dog’s current diet. This is an area that deserves more focus in veterinary practice in order to communicate the importance of an appropriate elimination diet (e.g., novel protein or hydrolyzed protein) in diagnosing canine food allergies. Providing this information to the dog owner when food allergies are first suspected ensures a diagnosis is made using the gold standard, rather than subjecting the dog to reported ineffective testing methods for food allergies such as serum, saliva, hair, or intradermal testing (3,10,13–15). Not only are these tests ineffective for diagnosing food allergies, they are costly and in the authors’ experience they may actually impede diagnosis of the true food allergies once the dog owner has these test results. Although allergy testing performed by intradermal testing or allergen-specific IgE serology testing is not recommended as a screening test, it is an effective tool for confirming environmental allergies (16). Also, flea combing, skin scraping, hair plucking, cytological examination of skin, ear smears, and skin biopsies are useful to rule out etiologies of skin disease other than food allergies (16).

Food elimination trials begin with elimination of the offending food and selection of a new diet containing novel or hydrolyzed protein. When reviewing who was responsible for changing the diet after suspicion of a food allergy, most owners switched to an OTC diet on their own, while veterinarians and veterinary specialists were more likely to change the diet to a veterinary diet formulated for diagnosing and treating food allergies. Several recent studies have found when comparing the ingredient list to the actual ingredients within an OTC diet, there have been many incidences of ingredient cross-contamination. Raditic et al (17) analyzed 4 OTC diets, all of which contained venison as a protein source. Enzyme-linked immunosorbent assay (ELISA) testing revealed that 3 of the diets tested positive for soy proteins, which were not part of the ingredient lists. Willis-Mahn et al (18) used ELISA testing to analyze 4 OTC diets that had “no soy” claims and found that 3 of these diets tested positive for soy proteins. Two of the diets tested had >25 ppm for soy, which was above the upper limit of detection (18). These studies reflect the variability and higher potential for cross-contamination with protein sources in OTC diets. It is important to point out that OTC diets are not intended to diagnose or treat diseases, such as food allergies, and cross-contamination is not a concern for healthy animals. Therefore, the selection of an OTC diet for a food elimination trial is not recommended and may actually preclude the diagnosis of food allergies. Veterinary diets have been found to have minimal incidence of cross-contamination, but still should be carefully selected based on the previous diet history of the dog for a food elimination trial diet (17). A veterinary diet formulated to treat or diagnose food allergies, or a complete and balanced homemade diet should be used. The veterinary diet can be either novel protein (based on the dog’s lifetime nutritional history) or hydrolyzed protein, whereas a homemade diet will need to be formulated with novel protein and carbohydrate sources by a Board-certified veterinary clinical nutritionist. The homemade diet recipe must contain multivitamin and mineral supplements to avoid nutritional deficiencies. There are pros and cons to both dietary approaches, but those are beyond the scope of this paper. These recommendations are in agreement with those made by WSAVA, stating that diet choices should be restricted to formulations created for disease-associated nutritional disorders of the animal, rather than providing OTC diets (11,12).

For dermatological signs, most owners reported that the time for amelioration of clinical signs was approximately 12 wk from the beginning the food elimination trial. The rate of cell turnover for skin tissue rejuvenation can vary among breeds, due to differences in the dogs, their protein and lipid turnover, and the environment in which they live (7,19). The longest duration of cell turnover of healthy skin in dogs is 20 to 21 d, with damaged skin or skin infections taking a longer time to heal (19,20). This is measured by the duration it takes for 1 cell layer to move from the stratum basale to the stratum corneum (19,20). In comparison to humans with an epithelial
layer of 10 to 15 cells, a dog only possesses an epithelial layer 3 to 5 cells thick. With this turnover rate, a food elimination trial duration of a minimum of 8 wk for complete amelioration of dermatological symptoms is consistent with the findings of the current study, though various breeds may need longer for complete amelioration of all clinical signs (3,10,19,20). Olivry et al (21) described complete remission of dermatologic signs of food allergies in 90% of dogs when the elimination trial was a minimum of 8 wk long.

For gastrointestinal signs, the duration of amelioration reported by owners was much more rapid, with recovery times varying from < 2 wk at minimum, and most clinical signs ameliorated by 4 wk. This is most likely due to the high cell turnover rate. Newly generated intestinal epithelial cells migrate from the base of the crypts toward the villus tip region, where loss of senescent epithelial cells occurs. Complete renewal of the villus epithelium takes 2 to 6 d in most mammals (20,22). Due to more rapid amelioration of gastrointestinal signs, compared with dermatological signs, a food elimination trial duration for complete resolution of gastrointestinal signs is recommended to be 6 to 8 wk (10,20).

The final step of the elimination trial is the re-challenge with the previous diet, to observe for the reoccurrence of clinical signs and to confirm the diagnosis of food allergies. Clinical signs typically occur within minutes to hours of re-feeding, with the longest duration up to 14 d (23). Although this is an important step to confirm the diagnosis of food allergies, many owners reported that they did not recall any discussion with their veterinarian regarding re-challenging their dog with the previous diet. It is important to inform owners that the previous diet is not re-fed until the symptoms reoccur with the same severity as at the beginning of the trial, but only until the first appearance of clinical signs (2). At that point, the diagnosis of food allergies is confirmed and the dog owner must be instructed to stop feeding the offending food. Owner compliance with a strict food elimination trial is essential to guarantee a successful diagnosis of food allergies by ensuring diet consistency and no provision of confounding food sources, as well as at the step of re-challenging. Diet consistency during the trials was shown to be poor, as many owners still provided human food or treats, or their dogs had access to unmonitored food sources, such as the litterbox or garbage. Owner compliance was reported by Bethlehem et al (3) as the limiting factor for diagnosis of food allergies.

The authors acknowledge that this survey had several limitations. First, the sample size was small, which did not allow statistical analyses to assess differences between small, medium, and large breeds. Moreover, dog owners were asked to recall information on nutrition history for their own dogs, which could have been from many years ago, and as such, may not have been accurate. Dog owners were also asked to recall conversations that took place with their veterinarians. Their recall may not have been accurate or their interpretation of the conversations may not have been the same as what their veterinarian intended. Additionally, it was not possible to separate suspected food allergic dogs from confirmed food allergic dogs without obtaining medical records for individual dogs; which was not possible with anonymous survey data. Future research should include review of medical records to verify information provided by dog owners. Lastly, not all dog owners completed the survey or responded to all questions, which could have biased the results.

After determining the level of owner knowledge regarding food allergies, and the method by which diagnosis and treatment were carried out, the findings of this survey indicate that a strict food elimination trial often did not occur or was not performed appropriately. During client communication, avoidance of potential confounders such as commercial treats and

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Table 3. Owner-reported exposure of their dogs to additional foods and unmonitored food sources during food elimination trial.

<table>
<thead>
<tr>
<th>Question</th>
<th>Frequency</th>
<th>Chi-squared</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are you giving any of the following to your dog? (check all that apply)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Dental chews</td>
<td>22.58</td>
<td>5.1162</td>
<td>0.2756</td>
</tr>
<tr>
<td>B. Rawhides</td>
<td>7.53</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>C. Flavored bones</td>
<td>9.68</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. Jerky treats</td>
<td>9.68</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. Meaty bones</td>
<td>17.20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F. Pigs ears/pizzle sticks/other animal-based treats</td>
<td>11.83</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G. Toys infused with flavors</td>
<td>2.15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Are you feeding any human foods or table scraps to your dog as treats? (check all that apply)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Vegetables</td>
<td>52.69</td>
<td>5.5556</td>
<td>0.4748</td>
</tr>
<tr>
<td>B. Fruits</td>
<td>33.33</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>C. Breads/cereals</td>
<td>9.68</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. Meats</td>
<td>29.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. Eggs</td>
<td>8.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F. Dairy products</td>
<td>7.53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G. Other</td>
<td>7.53</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Does your pet have access to unmonitored food sources? (n = 93)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Yes</td>
<td>24.73</td>
<td>0.4127</td>
<td>0.8135</td>
</tr>
<tr>
<td>B. No</td>
<td>75.27</td>
<td></td>
<td>NS</td>
</tr>
</tbody>
</table>

Significance declared at P < 0.05; NS — not significant at P > 0.05.
unmonitored food sources during the trial, and the importance of re-challenging with the previous food at the end of the trial should be highlighted. Full compliance at each step in the trial should result in improved accuracy of diagnosis and treatment of food allergies in dogs. 

References
Sensitivities of a bulk-tank milk ELISA and composite fecal qPCR to detect various seroprevalence levels of paratuberculosis in cattle herds in Normandy, France

Arnaud Delafosse, Eric Meens, Thomas Rambaud, François Hanoy, Hamid Achour

Abstract — This study evaluated an ELISA on bulk tank milk (BTM) samples and a qPCR on a single composite fecal sample to detect paratuberculosis seropositive cattle dairy herds. Individual serum (n = 15372), BTM and composite fecal samples were obtained from 192 herds. The within-herd apparent seroprevalence was categorized and compared with BTM ELISA and fecal qPCR results. The BTM ELISA had poor overall sensitivity (16%) to detect seropositive herds but higher sensitivity (53%) in the higher apparent seroprevalence group of > 9%. Using an optimized cut-off point (5.0% S/P), sensitivities overall and in the high apparent seroprevalence group were 53% and 88%, respectively. The BTM ELISA gave 5% positive results in seronegative herds and 25% using the optimized cut-off. Fecal qPCR had 72% sensitivity to detect seropositive herds and 88% in the higher apparent seroprevalence group, but gave 25% positive results in fully seronegative herds. The combination of BTM ELISA and composite fecal qPCR improved the sensitivity to detect seropositive herds.

Résumé — Sensibilités d’un test ELISA sur lait de réservoir et d’une qPCR sur prélèvement composite de fèces pour le dépistage de cheptels bovins à différents niveaux de séroprévalence en paratuberculose en Normandie, France. L’étude a été entreprise pour évaluer les performances diagnostiques d’un test ELISA, effectué sur un échantillon de lait de réservoir (BTM), et d’une qPCR, réalisée sur un échantillon composite de fèces (CF), pour détecter les troupeaux de bovins séropositifs pour la paratuberculose. Les sérum individuels (n = 15372), les échantillons de BTM et de CF ont été collectés dans 192 troupeaux. La séroprévalence apparente intra-troupeau a été calculée puis catégorisée avant d’être comparée aux résultats de l’ELISA sur BTM et de la qPCR sur CF. Le test ELISA sur BTM a montré une faible sensibilité globale (16 %) mais celle-ci était plus élevée dans les élevages les plus fortement séropositifs > 9 % (53 %). En utilisant un seuil optimisé (E/P 5,0 %), les sensibilités étaient de 53 % et 88 %, respectivement. Le test ELISA sur BTM a donné 5 % de résultats positifs sur des troupeaux entièrement séronégatifs et 25 % en utilisant le seuil optimisé. La qPCR sur CF avait une bonne sensibilité (72 %), en particulier dans les élevages fortement séropositifs (88 %), et a donné 25 % de résultats positifs sur des cheptels entièrement séronégatifs. L’utilisation combinée de BTM ELISA et CF qPCR a permis d’améliorer la sensibilité à dépister des cheptels séropositifs.

(Traduit par Docteur Serge Messier)

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Introduction

Paratuberculosis (Johne’s disease, JD) is a contagious chronic enteritis of ruminants caused by Mycobacterium avium subspecies paratuberculosis (MAP) and is present in most countries across the globe (1). Control of JD is motivated by the production-limiting effects of the disease, most notably decline in milk production (2,3), reduced fertility in high-shedding animals (4), and premature culling of those with reduced weight (5,6). Mycobacterium avium ssp. paratuberculosis may also have zoonotic potential (7). Indirect costs through trading restrictions, and the less apparent loss of genetic potential due to the early culling of animals, may also occur (8).

The estimated true prevalence of infected herds ranges from 10% to 70%, although the prevalence of infected animals is...
generally less than 5% (9–11). However, a review of JD across Europe reported that its incidence was underestimated due to the low sensitivity of tests, and that the true prevalence of infected animals could be nearer to 20% (12).

Antemortem diagnostic tests have sensitivities estimated at 23% to 29% for fecal culture and 7% to 22% for serum enzyme-linked immunosorbent assay (ELISA) in infected or infectious cattle before high shedding (13). Repeated testing in herds increases the diagnostic performance; however, individual tests can be costly when screening large numbers of cattle.

Several approaches have been taken at the herd level to estimate the within-herd prevalence to help farmers and veterinary practitioners make decisions about appropriate control measures and promotion of exchanges of cattle between uninfected or low-risk herds.

Environmental (composite) fecal cultures can be used to assess the prevalence of herd-level MAJ and this method has appeal because it is relatively cost-effective and non-invasive (14,15). This approach involves taking samples from several strategic sites around the farm to determine the presence of MAP. Lombard et al (16) used a Bayesian approach on 96 United States dairy herds to estimate the herd sensitivity (HSe) for environmental fecal cultures, relative to individual fecal cultures, and concluded that culture of 5 composite fecal samples across all herds had an HSe of 77.2%. There are no reports on the use of polymerase chain reaction (PCR) on environmental fecal samples with the aim of identifying infected herds.

Detection of MAP-specific antibody in bulk-tank milk (BTM) samples is an inexpensive and automatable tool. In a study of MAP-free and seropositive herds in the Netherlands, specificity for Pourquier/IDEXX ELISA was 100%, and sensitivity to detect herds with ≥2 seropositive cows was 24% (17). A previous study of BTM ELISA, using fecal culture as reference test, reported similar results but the authors concluded that BTM ELISA was not a suitable tool for surveillance because shifts in the optical densities of samples could cause errors in classification (18). Both studies concluded that sensitivity of BTM testing can be strongly improved by using a revised cut-off. More recently, Nielsen and Toft (19) conducted a study to determine the association between the BTM antibody ELISA-level and the within-herd prevalence of antibody-positive cows. This study demonstrated that the BTM test response was significantly associated with the within-herd prevalence of antibody positive cattle. However, the authors concluded that the magnitude of the test values made it difficult to use this test for surveillance of MAP infections in practice.

The objective of this study was to evaluate the performance of BTM ELISA and quantitative PCR (qPCR) performed on a single composite feces sample to identify MAP non-negative (i.e., MAP-positive or doubtful) dairy herds using individual serology as reference. Diagnostic performance was estimated for both tests, interpreted separately and in parallel, at pre-specified and exploratory cut-off values. The final focus was to detect herds suspected of being infected by MAP in the context of an intensive dairy farming area in western France to integrate them into a control program.

Materials and methods

Target population, study population, and period

The target population was dairy herds located in Normandy (western France). Cattle were Normande and Holstein breeds and their crossbreeds. The study population was the 283 participating herds of a voluntary MAP monitoring program using individual serology and aiming to eliminate bacteria from infected farms by detection and culling of all non-negative animals and improving hygiene to prevent exposure of calves.

A cross-sectional study was conducted between November 2010 and May 2011 on 192 non-randomly selected herds. The inclusion criterion was availability of breeders and veterinary practitioners to submit all the expected samples.

Sample collection

Blood samples were taken from all adult cattle (>24 mo) and allowed to clot at environmental temperature. Samples were then transported to the laboratory, where they were centrifuged at 1500 × g for 10 min. The BTM and composite fecal samples were taken simultaneously from each farm by the local veterinary practitioner, but BTM samples could not be collected at 3 farms.

Composite fecal samples were taken according to a standardized protocol similar to that of the US voluntary control bovine Johne’s disease program (20). Four sites were selected for collecting composite fecal samples: 1 from the manure storage areas (pits or manure piles), 2 from the mature cow concentration areas (1 from the waiting area before milking and 1 from the feeding corridor), and 1 from the cow maternity area. Four samples were taken from each site using a clean latex glove, collected into clean 250-mL specimen cups, and chilled for transportation to the laboratory. The contents of the 16 cups were then combined, mixed, and homogenized in the laboratory to form a single composite fecal sample for each farm. If samples could not be processed immediately, they were frozen at ~20°C and processed within 2 wk of collection.

Sample analysis

Analyses were conducted by 2 public veterinary laboratories in Normandy. Bulk-tank milk ELISA and fecal qPCR were conducted independently and results were not available to the performers of the individual serum ELISA used as a reference test.

Absorbed ELISA

All individual serum and BTM samples were analyzed using a commercially available ELISA kit (Institut Pourquier/IDEXX, ELISA Paratuberculosis Antibody Screening, Westbrook, Maine, USA) according to the manufacturer’s instructions; optical density (OD) for each sample was measured using a spectrophotometer. The ELISA kit has a specificity of ≥99.8% and an overall relative sensitivity to detect infectious cattle (i.e., compared with fecal cultures) of 40.8% (17,21). For infected cattle, sensitivity is more difficult to assess in the absence of a gold standard but could be close to 15% (22). The individual ELISA serum test was retained as the reference standard because it is widely used in France for the management of paratuberculosis.
Results were calculated as follows: Sample/Positive (S/P) ratio = 100 × (OD value of the sample − the OD value of the negative control)/(OD value of the positive control − the OD value of the negative control), and the S/P ratio was expressed as a percentage. Cut-off points for serum sample results were < 45% – S/P negative, 45% to 55% – S/P doubtful and > 55% – S/P positive, and for milk samples ≤ 20% – S/P negative, > 20% and < 30% S/P – doubtful and ≥ 30% – S/P positive, according to the manufacturer’s recommendations. For milk samples, 2 exploratory cut-offs were selected, one for a target specificity of 95%, and the other using the Youden’s J Index in a Receiver Operating Characteristic (ROC) analysis.

qPCR
Composite fecal samples were analyzed by qPCR according to the manufacturer’s instructions (ADIAVETTM ParaTB Real Time, Saint-Brieuc, France). Fecal samples (6 g each) were diluted with 40 mL sterile deionized water and then 10 mL of supernatant was passed through an ADIAFILTER. Purified DNA was added with specific primers for amplification of the IS900 MAP sequence. A cut-off recommended by the manufacturer was used (Ct 45, i.e., 45 cycles). Moreover, 2 exploratory cut-offs (Ct38 and Ct35), were arbitrarily retained and then tested.

Statistical analyses
The within-herd prevalence of serum ELISA non-negative results was calculated and then categorized using 4 cut-off points: 0%; > 0% to ≤ 3% – very low; > 3% to ≤ 6% – low; > 6% to ≤ 9% – medium; > 9% – high. Cut-off points were arbitrarily chosen at inflection points of the quantitative scale in order to obtain balanced classes. Sensitivities for BTM ELISA and composite fecal qPCR were estimated, distinguishing pre-specified and exploratory thresholds, for each apparent seroprevalence within the herd, i.e., > 0% to ≤ 3%; > 3% to ≤ 6%; > 6% to ≤ 9%, and > 9%. Results obtained on the 0% apparent seroprevalence class were used to approximate the specificities, although the low sensitivity of the individual serum ELISA probably resulted in the misclassification of very low prevalence herds in this negative reference group.

The 95% confidence intervals (CI) were calculated using the Wilson method, as recommended by Brown et al (23), using EpiTools (24). Receiver operating characteristic (ROC) analysis was performed in EpiTools. Mean comparisons were made using the nonparametric Wilcoxon (or Mann-Whitney) test. Box plots and Wilcoxon analyses were performed using R 3.0.0 (25).

Results
Descriptive data and within-herd apparent prevalence obtained by serology
Individual serum samples (n = 15372) were obtained from 192 dairy herds. The median adult herd size was 73 cattle, and the mean was 80 (range: 20 to 268).

Screening of serum samples by ELISA indicated that 838 (5.5%) cattle were doubtful or positive for MAP antibodies. The apparent prevalence of non-negative results within herds ranged from 0% to 23.1% (mean: 5.3%; first quartile: 2.0%; median: 5.3%; third quartile: 10.1%). The MAP antibodies were not detected in 20 herds (10%) and 60 (31%) had an apparent prevalence of 3%. By contrast, 32 farms (17%) had an apparent prevalence > 9%. Thirty herds had only 1 positive or doubtful animal, 29 (97%) of which had a prevalence > 0 and ≤ 3%. Thirty-four herds had 2 positive or doubtful cattle, 33 (97%) of which had a prevalence ≤ 6%. One hundred and eight herds had > 2 positive or doubtful cattle, 102 (94%) of which had a prevalence > 3%. The number of adult cattle was significantly lower in the test negative farms than in the test non-negative farms (Table 1).

Diagnostic performance of ELISA for bulk milk samples related to within-herd seroprevalence
The BTM samples were taken from 189 of the 192 dairy herds. The distribution of BTM ELISA values by within-herd apparent prevalence classes failed to discriminate fully seronegative herds from those with very low apparent prevalence (> 0% to 3%) and low apparent prevalence (> 3% to 6%). The magnitude of the results increased markedly for herds in the high apparent prevalence class > 9% (Figure 1).
Sensitivity values and specificity approximations for the positive and negative reference materials at different cut-off (S/P) values are presented in Table 2. Sensitivity was increased using a modified cut-off of 10% S/P without loss of specificity. The use of an even lower cut-off (5% S/P), close to the optimum AUC value in a ROC analysis (Youden's J Index, 4.4% S/P), further enhances the sensitivity but degrades the specificity from 95% to 75% (Table 2).

### Diagnostic performance of qPCR for fecal samples related to within-herd seroprevalence

Composite fecal samples were obtained from 192 dairy herds. The distribution of qPCR Ct values for the within-herd apparent prevalence classes showed a general shift in detection that increased in line with increasing MAP antibody detection by ELISA in serum (Figure 2).

Sensitivity values and specificity approximations for fecal sample qPCR were calculated using positive and negative reference material at different cut-offs (Ct values). These are presented in Table 3. The qPCR sensitivity for fecal samples decreased when lower Ct values were used, with an improvement in specificity only with the lowest threshold (Ct = 35) (Table 3).

### Diagnostic performance of ELISA for bulk milk samples interpreted in parallel with qPCR for fecal samples related to within-herd seroprevalence

The parallel interpretation of ELISA and qPCR was done using threshold values that provide the best sensitivity and specificity values, i.e., BTM ELISA S/P value of 5% and Ct 45 for fecal sample qPCR.

The parallel interpretation of both tests improved the sensitivity to detect seropositive herds, in comparison with values obtained when each method was used alone, particularly for the classes > 3% to 6% (Se = 76% to 86%) and > 6% to 9% (Se = 77% to 93%) without marked loss of specificity (Sp = 75% to 70%) (Table 4).

### Discussion

The study population was composed of herds monitored for JD for several years and may not represent all dairy herds in the Normandy region. MAP monitoring could change the relative proportions of exposed, infected, infectious, and affected cattle with an impact to test characteristics at the herd level. In particular, the sample does not represent all zero-seroprevalence herds of the target population, and accordingly the estimates of specificities in this study may be an underestimate. The accuracy of the results is also limited by the low number of herds sampled, and the large confidence intervals. Finally, the study design used a modified serological test on BTM to detect serologically positive herds, which could have biased the results in favor of BTM ELISA relatively to fecal qPCR.

With these restrictions, the specificity of the ELISA for BTM related to within-herd seroprevalence was 95% (85% to 100%) at the cut-off value recommended by the manufacturer and 75% (53% to 89%) at the optimized level (S/P 5%).

By contrast, BTM ELISA had a poor sensitivity, 16% (11% to 22%), for detection in seropositive herds at the cut-off defined by the manufacturer, particularly in the low-seroprevalence groups of > 0% to 3% (Se = 2%, 95% CI: 0% to 9%) and > 3% to 6% (Se = 4%, 95% CI: 1% to 14%). The method provided better sensitivity for the high-seroprevalence group (> 9%). Using a revised cut-off at 5.0% S/P, the overall
sensitivity was 53% (95% CI: 46% to 61%) and 88% (95% CI: 72% to 95%) for detecting herds with high apparent prevalence. Therefore, BTM ELISA does not seem to be useful for detecting herds with seroprevalence < 10%.

Beyerbach et al (26) used a modification of non-absorbed LAM ELISA for BTM testing and compared the test results to the within-herd prevalence for individual milk samples. Sensitivity of the BTM ELISA was poor at a low apparent prevalence (< 3% seroprevalence in a herd), even when a lower cut-off was used. At a within-herd apparent prevalence of 5%, sensitivity was 75%, and specificity was 84%.

In a study in the Netherlands of MAP-free and seropositive herds, the specificity for Pourquier/IDEXX MAP antibody ELISA kit for Bulk Tank Milk (BTM) (cut-off S/P 5%) and the qPCR of composite fecal samples (CT 45) (n = 189) in herds of different seroprevalence (number of herds in brackets).

<table>
<thead>
<tr>
<th>Within-herd apparent seroprevalence class</th>
<th>BTM+ or/qPCR+</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0% (20)</td>
<td>30%</td>
<td>15% to 52%</td>
</tr>
<tr>
<td>&gt; 0% to 3% (58)</td>
<td>59%</td>
<td>46% to 70%</td>
</tr>
<tr>
<td>&gt; 3% to 1% (49)</td>
<td>86%</td>
<td>73% to 93%</td>
</tr>
<tr>
<td>&gt; 6% to 9% (30)</td>
<td>93%</td>
<td>79% to 98%</td>
</tr>
<tr>
<td>&gt; 9% (32)</td>
<td>97%</td>
<td>84% to 99%</td>
</tr>
<tr>
<td>All &gt; 0% (169)</td>
<td>80%</td>
<td>73% to 85%</td>
</tr>
</tbody>
</table>

Table 3. Percentage (%) of positive results using qPCR to detect MAP in composite fecal samples (n = 192) at 3 different cut-offs in herds of different seroprevalence (number of herds in brackets).

More recently, Nielsen and Toft (19) conducted a study with repeated samples on 108 Danish Holstein herds to determine the association between the BTM antibody ELISA-level and the within-herd prevalence of antibody-positive cows. Results showed that the BTM results were relatively consistent and correlated with the within-herd seroprevalence but the authors concluded that the magnitude of the test-values makes it difficult to use this tool for surveillance of MAP infections in practice.

In our study, the specificity of qPCR using composite fecal samples was 75% (95% CI: 53% to 89%) at the recommended cut-off (CT = 45). The PCR amplification of genes is a finely tuned technique, and under certain conditions a specificity of 100% may be anticipated. The lower specificity of the environment samples may be due to the lack of discrimination from dead MAP cells, or naked DNA. This theory may be tested by comparison of the positive fecal qPCR results with those of cultures.

qPCR is a sensitive diagnostic test for detecting low numbers of target genes. This can explain why herds with a low prevalence of MAP can provide positive environmental fecal qPCR results in combination with individual seronegative ELISA. This may be due to the residual presence of MAP in herds with a history of JD, and the improved sensitivity of qPCR compared with previous approaches. It is more likely that the lack of specificity of the fecal qPCR in this study is due to better sensitivity than individual ELISA for detection of herds, rather than false positive classifications.

Analysis of environmental fecal culture (EC) samples from material taken from around farm sites hosting cattle has provided supporting data, and in some cases revealed new positive results. For example, in a study of 28 herds that were historically classified as uninfected, one of them tested positive for MAP after environmental samples were taken (15). Lombard et al (27) reported that after EC sampling of 10 herds considered negative, 2 of them were positive for MAP, and similarly Lavers et al (28) reported that from 18 MAP-negative herds, 1 was positive after EC sampling.

In our study, qPCR showed good sensitivity (72%, 95% CI: 65% to 78%) for detection in seropositive herds, particularly where the apparent prevalence was > 9% (88%, 95% CI: 72% to 95%). The method provided lower sensitivity when the apparent prevalence was > 0 to 3% (58%, 95% CI: 46% to 70%).
Several studies have been conducted to assess environmental fecal samples but only with fecal cultures and with a variable number of samples collected on farms. 

Lombard et al (16) used a Bayesian approach to estimate the HSe of composite fecal culture relatively to individual fecal cultures on 96 United States dairy herds. Their study concluded that the number of composite samples tested in a herd and the within-herd prevalence impacted HSe. Thus, for all herds, HSe increased from 49% with 1 sample per farm to 77% with 5 samples. For 5 samples per farm, HSe increased from 56% in low-prevalence herds (> 0% to 12.0%) to 90% in high-prevalence herds (> 25.0%).

Lavers et al (28) evaluated ECs in 32 Canadian herds. Relative to a MAP herd status based on all pooled fecal culture results collected during the study, the specificity of a set of 6 EC-samples was 71% and the specificity was 99%.

Previous studies of composite cultures reported lower HSe values of 40% to 74% but values were higher in high-prevalence herds (14,27,29,30).

Our results indicated that sensitive qPCR performed on 1 composite fecal sample, representative and concentrated, provided similar results to those previously obtained with 5 or 6 EC-samples, with a reduced cost as only 1 analysis was required. Nevertheless, previous studies had generally used individual fecal culture as a reference test versus individual serology in this study.

The parallel interpretation has a higher sensitivity than either method used alone, and 80% of seropositive herds had at least 1 positive fecal qPCR or BTM sample. The improvement mainly relates to detection of low- (> 3% to 6%) and medium- (> 6% to 9%) seropositive herds [fecal qPCR alone versus combined with BTM ELISA: 76% (95% CI: 62% to 85%) versus 86% (95% CI: 73% to 93%), and 77% (95% CI: 60% to 89%) versus 93% (95% CI: 79% to 98%) for low- and medium-apparent prevalence herds, respectively].

Similarly, Serraino et al (31) conducted a study to evaluate the sensitivity and specificity of the repetitive analysis of BTM ELISA and in-line milk filter (ILMF) PCR to detect MAP-positive dairy herds. A highly significant association was shown between the median apparent prevalence herd status (> 5%) and positivity to at least 1 ILMF or BTM sample.

In conclusion, ELISA of BTM samples had a limited sensitivity in determining the status of MAP in herds. In the context of dairy farming in western France, the study confirmed the improvement of sensitivity at lower cut-off values than those defined by the manufacturer without marked lowering of specificity. However, study design did not precisely assess the specificity due to the absence of an unbiased seronegative control group. Repeated BTM testing of the same herd could also improve the diagnostic performance, although this approach requires further evaluation. The use of sensitive qPCR for 1 composite fecal sample after a concentration step appears to be an effective, inexpensive, and non-invasive approach to detect MAP non-seronegative dairy herds, especially when coupled with BTM ELISA. However, the strategy is more time-consuming due to the sampling regime used for environmental areas, which may limit its use as a first screening approach.

Losses due to paratuberculosis were estimated between 32 € and 95 € per cow per year in positive herds (3,22,33). On this basis, study results could be used to evaluate the economic benefit of a regional control program using BTM ELISA and/or composite fecal qPCR as screening tools. This requires further evaluation using realistic assumptions about herd prevalence, motivation for farmers’ participation in a voluntary control program, and costs.

Acknowledgments

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References


Tissue residue depletion of fenbendazole after oral administration in turkeys

Saad S. Enouri, Michele T. Guerin, Innes G. Wilson, Patricia M. Dowling, Ron J. Johnson

Abstract — The objectives of this study were to determine tissue depletion of fenbendazole in turkeys and estimate a withdrawal interval (WDI). Forty-eight 9-week-old turkeys were fed fenbendazole at 30 mg/kg of feed for 7 consecutive days. Three hens and 3 toms were sacrificed every 2 days from 2 to 16 days post-treatment, and tissues were collected to determine fenbendazole sulfone (FBZ-SO₂) concentrations using mass spectrometry. At all timepoints, FBZ-SO₂ concentrations in liver and skin-adherent fat were above the limit of quantification (1 ppb), with higher concentrations than those in kidney and muscle. Two turkeys had detectable FBZ-SO₂ concentrations in kidney at 16 days. No detectable FBZ-SO₂ concentrations were found in muscle at 14 and 16 days. Fenbendazole residues depleted very slowly from the liver and a WDI of at least 39 days should be observed under the conditions of this study, in order to comply with Canadian regulatory agencies.

Résumé — Déplétion du fenbendazole pour les résidus tissulaires après l’administration orale chez les dindons. Les objectifs de cette étude consistaient à déterminer la déplétion du fenbendazole dans les tissus chez les dindons et d’estimer un délai d’attente (DA). Du fenbendazole a été administré à quarante-huit dindons âgés de 9 semaines, à raison de 30 mg/kg d’aliments pendant 7 jours consécutifs. Trois dindes et 3 dindons ont été sacrifiés tous les deux jours pendant les jours 2 à 16 après le traitement et les tissus ont été prélevés pour déterminer les concentrations de fenbendazole sulfone (FBZ-SO₂) en utilisant la spectrométrie de masse. À tous les moments de prélèvement, les concentrations de FBZ-SO₂ dans le foie et le gras adhèrent à la peau étaient supérieures à la limite de quantification (1 ppm), avec des concentrations supérieures à celles présentes dans les reins et les muscles. Deux dindes avaient des concentrations de FBZ-SO₂ détectables dans les reins à 16 jours. Aucune concentration détectable de FBZ-SO₂ n’a été trouvées dans les muscles à 14 et à 16 jours. Les résidus de fenbendazole se résorbaient très lentement du foie et un DA d’au moins 39 jours devrait être observé conformément aux conditions de cette étude afin de satisfaire aux exigences des agences réglementaires canadiennes.

Introduction

Ascarids cause significant economic losses to poultry producers due to reduced feed intake, lower body weights, reduced egg production, and increased mortality following heavy infection (1–4). A number of anthelminthic compounds are available for the control of parasitic nematodes in food-producing animals; however, the options are limited in avian species including turkeys. Fenbendazole [FBZ; methyl-5-(phenylthio)-2-benzimidazole-carbamate], a benzimidazole, is a broad-spectrum veterinary anthelminthic that is widely used for treatment of gastrointestinal nematode infection in food-producing animals and has proven efficacy in poultry and game bird feeds (5–9). Fenbendazole exerts its effect by binding with greater affinity to parasite tubulin compared to that of mammalian and avian species and causing a disruption of the parasite tubulin-microtubule dynamic equilibrium, thus giving fenbendazole a wide margin of safety for use in food-producing animals (10,11). Because of this mechanism of action, the efficacy of benzimidazoles, including fenbendazole, correlates best with duration of therapy rather than dose. Therefore, the in-feed administration of this class of anthelminthic is preferable. Following its absorption, fenbendazole is predominantly metabolized in the liver through oxidation to oxfendazole (fenbendazole sulfoxide, FBZ-SO₂), a main active metabolite, and is subsequently metabolized to fenbendazole sulfone (FBZ-SO₂), which is considered the marker residue for monitoring by North

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American regulatory agencies including the Canadian Food Inspection Agency (CFIA) (9,12).

Fenbendazole medicated premix is approved for the control of nematodes in turkeys in the United States (US) with a zero-withdrawal time when it is fed at 16 ppm in complete feed for 6 d, with a tolerance limit of 6 ppm in the liver (target tissue), and 2 ppm in the muscle (9). The tolerance limit is the maximum allowable drug residue level in edible products of food-producing animals in the US and is equivalent to the maximum residue limit (MRL) used in Canada and the European Union. In Canada, although fenbendazole is approved for use in cattle and swine, it is not approved for use in turkeys, despite the fact that its use has proven effective when added to the feed. Additionally, while water additive fenbendazole products have been registered for use in chickens in Canada, Europe, and the US, none are currently approved for turkeys. The use of fenbendazole in turkeys in Canada therefore constitutes extra-label drug use (ELDU) and consequently, the Canadian Global Food Animal Residue Avoidance Databank (CgFARAD) has received numerous inquiries for the use of fenbendazole in growing turkeys for the prevention and treatment of ascarids.

Avoiding drug residue violations in edible tissues from treated animals is of importance for public health and consumer food safety. Maximum residue limits and average daily intakes are important regulatory parameters on which consumer food safety is based. Currently, there are no MRLs or withdrawal times established by the Veterinary Drugs Directorate (VDD) of Heath Canada for fenbendazole in the edible tissues of turkeys; thus, the detection of any fenbendazole residues in the edible tissues of turkeys by the CFIA is considered to be a regulatory violation. As a result, there is a need for a depletion study that will provide veterinarians with an evidence-based withdrawal interval (WDI) for fenbendazole in turkeys destined for human consumption, thereby ensuring food safety while also assisting producers and the industry with maintaining their productivity and animal welfare. The objectives of this depletion study were to assess residue depletion of fenbendazole in the edible tissues of growing turkeys and estimate a WDI following in-feed administration of fenbendazole using the most common dosing regimen according to historical CgFARAD requests from licensed Canadian veterinarians, which is 30 ppm (0.15 kg/metric ton) for 7 d.

Materials and methods

Forty-eight 2-day-old turkey poult (24 females and 24 males) were obtained from a commercial flock (Cuddy Farms, Strathroy, Ontario) and used in this study. Birds were raised at the Arkell Poultry Research Station at the University of Guelph, Guelph, Ontario, for the duration of the study according to standard handling protocols. Following euthanasia, no other drugs were administered to the birds during the study. To be eligible for inclusion in the study, birds had to be healthy and free of disease; thus, the birds were monitored daily for general health. All birds were considered to be healthy at the start of the study based on physical examination. The experimental protocol was approved by the Institutional Animal Care and Use Committee of the University of Guelph, and conformed to standards set forth by the Canadian Council on Animal Care.

The experimental design, including the number of birds per sacrifice timepoint, was chosen based on current recommendations of the Veterinary International Conference on Harmonisation (VICH) guideline No. 48 for marker residue depletion studies to establish compound withdrawal periods (13). The guideline stipulates that the marker residue is the parent molecule, or metabolite, determined from total residue and metabolism studies in the target species to deplete in known relation to depletion of total residues. This guideline is currently used by the VDD of Health Canada and the US Food and Drug Administration-Center for Veterinary Medicine for regulatory approval of drugs in food-producing animals that require a withdrawal time. However, this depletion study was not conducted under good laboratory practices guidelines as would be required by Health Canada for pharmaceutical companies seeking veterinary drug approvals in Canada. All birds were reared on standard, commercial complete feeds containing no drugs, and provided water ad libitum. At 8 wk of age, birds were identified individually by wing tags. At 9 wk of age, all birds were switched to the test diet consisting of a commercial complete grower ration containing fenbendazole (Safe-Guard Premix 20%, 200 mg/g; Merck Animal Health, Intervet Canada, Kirkland, Quebec) at 30 mg of fenbendazole/kg of complete feed (0.15 kg/metric ton of feed) as the sole ration for 7 consecutive days. The diet was then switched to a commercial complete grower ration containing no fenbendazole, and birds were randomized to 1 of 8 sacrifice timepoints (2, 4, 6, 8, 10, 12, 14, or 16 d after the end of treatment with the test diet) with 6 birds (3 hens, 3 toms) allocated per sacrifice timepoint. All birds were sacrificed by carbon dioxide inhalation followed by exsanguination at the research station’s processing plant according to standard handling protocols. Following euthanasia, tissue samples, including skin-adherent fat (entire skin covering the breast muscle and underlying fat), breast muscle (minimum 100 g), liver (entire liver), and kidney (both kidneys) were collected in this order at each sacrifice timepoint for each bird. All samples were identified and stored individually at −80°C until they were analyzed.

Liquid chromatography-tandem mass spectrometry analysis

Determination of FBZ-SO₂ residues in edible tissues of turkeys was conducted by the University of Guelph Laboratory Services Division, Guelph, Ontario. Tissue extracts were assayed for FBZ-SO₂ concentrations in each tissue matrix type using a liquid chromatography-tandem mass spectrometry system consisting of an Agilent 1200 series pump, column heater, and autosampler (Agilent Technologies Canada, Mississauga, Ontario) coupled to a triple quadrupole mass spectrometer (QTRAP 5500; AB SCIEX, Concord, Ontario). Tissue samples were extracted and analyzed following the addition of a deuterated internal standard. Tissues were homogenized and extracted into acetonitrile using a Geno/Grinder with salting out. Sample
extracts were further refined prior to analysis using centrifugation (5 min at 4000 x g at 15°C) followed by dispersive solid phase extraction (C18) to remove potential interferences from co-extractive compounds. Isocratic chromatographic separation was carried out using a Poroshell 120EC-C18 column (50 mm x 4.6 mm I.D., 2.7 μm; Agilent Technologies, Santa Clara, California, USA) and a mobile phase of methanol-water-formic acid (60:40:0.1, v/v/v), which was delivered at a flow rate of 0.5 mL/min. The column temperature was maintained at 35°C. The sample injection volume was 2 μL and the run time was 6 min. The target ion transitions for FBZ-SO2 and deuterated FBZ-SO2 (d3) were 332.0 to 299.9 and 335.0 to 299.9, respectively. The qualifying ion transitions for FBZ-SO2 and deuterated FBZ-SO2 were 332.0 to 159.0 and 335.0 to 158.8, respectively. Analysis was performed in positive ion mode (MRM) with a declustering potential of 31 V, collision energy of 30 V and ion spray voltage of 4500 V. Quantitation was conducted using a matrix matched standard curve and deuterated FBZ-SO2. The validated limit of quantification (LOQ) and limit of detection (LOD) for FBZ-SO2, calibration curves were 1 part per billion (ppb) and 0.3 ppb, respectively, for the edible tissues skin-adherent fat, muscle, liver, and kidney. The calibration curves (1 to 600 ppb) were evenly distributed with a coefficient of determination (r²) > 0.99 for each curve. Calibration curves were run at the beginning and end of each day’s sample testing runs with additional standards interspersed throughout the run. The highly specific nature of LC-MS/MS detection was verified by including the injection of both solvent and matrix blanks following the highest calibration standards (600 ppb) analyzed. Results demonstrated no residue carry over between injections and no interfering co-extractives were present in any of the tissues tested. Intra-day accuracy and precision (percent recovery, n = 3) for the 5 ppb fortified quality control samples for FBZ-SO2 for skin/fat, kidney, liver, and muscle were 92% ± 2.5, 101% ± 2.0, 95% ± 6.7, and 100% ± 3.0, respectively, and for the 50 ppb fortified quality control samples for FBZ-SO2 for skin/fat, kidney, liver, and muscle were 91% ± 0.7, 95% ± 1.0, 94% ± 0.4, and 86% ± 1.2, respectively. Inter-day accuracy and precision (percent recovery, n = 3) for the 5 ppb fortified quality control samples for FBZ-SO2 for skin/fat, kidney, liver, and muscle were 96% ± 3.0, 92% ± 5.3, 92% ± 3.5, and 80% ± 4.2, respectively, and for the 50 ppb fortified quality control samples for FBZ-SO2 for skin/fat, kidney, liver, and muscle were 92% ± 1.3, 82% ± 3.2, 82% ± 3.2, and 82% ± 3.5, respectively. The percent coefficient of variation for reference curve FBZ-SO2 concentrations in all matrices, including the LOQ, was < 15%. Quality control samples (5 ppb and 50 ppb) were included in all test sample runs and were within a tolerance of ± 15% of the nominal value.

Table 1. Fenbendazole sulfone concentrations (ng/g) in 48 turkeys following in feed administration at 30 mg/kg of feed for 7 consecutive days.

<table>
<thead>
<tr>
<th>Days post-treatment</th>
<th>Liver</th>
<th>Skin-adherent fat</th>
<th>Kidney</th>
<th>Muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>252.67 ± 342.76</td>
<td>56.17 ± 56.42</td>
<td>70.33 ± 98.13</td>
<td>24.73 ± 36.98</td>
</tr>
<tr>
<td>4</td>
<td>10.82 ± 7.66</td>
<td>9.08 ± 2.88</td>
<td>3.25 ± 2.35</td>
<td>1.22 ± 1.06 (4/6)</td>
</tr>
<tr>
<td>6</td>
<td>3.15 ± 2.38</td>
<td>3.92 ± 1.34</td>
<td>&lt; LOQ (1/6)</td>
<td>&lt; LOQ (1/6)</td>
</tr>
<tr>
<td>8</td>
<td>3.0 ± 1.38</td>
<td>2.13 ± 0.27</td>
<td>&lt; LOQ (3/6)</td>
<td>&lt; LOQ (1/6)</td>
</tr>
<tr>
<td>10</td>
<td>2.97 ± 2.03</td>
<td>2.18 ± 0.58</td>
<td>&lt; LOQ (2/6)</td>
<td>&lt; LOQ (2/6)</td>
</tr>
<tr>
<td>12</td>
<td>3.78 ± 2.97</td>
<td>2.17 ± 0.86</td>
<td>1.23 ± 1.35</td>
<td>&lt; LOQ (2/6)</td>
</tr>
<tr>
<td>14</td>
<td>2.1 ± 0.48</td>
<td>2.10 ± 0.46</td>
<td>&lt; LOQ (1/6)</td>
<td>ND (0/6)</td>
</tr>
<tr>
<td>16</td>
<td>2.27 ± 1.19</td>
<td>1.8 ± 0.63</td>
<td>&lt; LOQ (2/6)</td>
<td>ND (0/6)</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD.

a vs. kidney and muscle.

b vs. skin-adherent fat within a timeframe (P < 0.05).

Numbers in parentheses denote number of individual birds with FBZ sulfone concentrations above LOQ. LOQ — limit of quantification = 1 ng/g; ND — not detected; n = 6, number of birds per sacrifice timepoint.

Statistical analysis

Data analyses were conducted with the assistance of biostatisticians (Steven Radecki, Petoskey, Michigan, USA; William Sears, Department of Population Medicine, University of Guelph, Guelph, Ontario). The FBZ-SO2 concentrations in tissues at each sacrifice timepoint were compared by analysis of variance (ANOVA) for repeated measures (Version 9.1.3; SAS Institute, Cary, North Carolina, USA). Prior to analysis of data for the WDI estimation, FBZ-SO2 concentrations were transformed using the natural logarithm (Ln). Least square means and 95% confidence intervals were reported along with back-transformed values. The statistical significance level was set at P = 0.05. Statistical analyses were begun with a full factorial model that included all interactions (i.e., gender, tissue, and time) with terms being removed if P-values were > 0.05. Regression analyses were performed on tissue FBZ-SO2 concentrations to determine the time required for FBZ-SO2 levels to reach a predetermined tissue concentration, i.e., the LOQ for the analyte in each matrix. As there is no approved MRL for fenbendazole in edible tissues of turkeys in Canada, the allowable levels are 0 ppb of the analyte, which was set at the current CFIA-validated LOD for FBZ-SO2 of 1 ppb (Dr. Joseph Boisson, Adjunct Professor of Chemistry, Chemistry Department, University of Saskatchewan, Saskatoon, Saskatchewan, personal communication, 2016). Initial regression analysis including all sacrifice timepoints was influenced by extreme values on the first sacrifice timepoint (day 2). Removal of the first sacrifice timepoint (day 2) in its entirety yielded a better statistical fit of the data. Additionally, due to the fact that most, if not all, values at the final sacrifice timepoint were above the CFIA’s LOD, analyses of FBZ-SO2 tissue residue data for WDI determination by a statistical method that determined the statistical tolerance limit for the central 99% of the population, as used by Health Canada and the FDA for regulatory submissions, was not possible in the current study. Instead, regression
The FBZ-SO₂ concentration in the breast muscle in all birds in some individual birds at each sacrifice timepoint (Table 1). While at 6 d post-treatment and thereafter it was above the LOQ in all birds was above the LOQ at 2 and 4 d post-treatment, no observable adverse effects were noted in any birds while all study sacrifice timepoints, with residues being higher than those in the kidneys and breast muscle tissues at each respective study sacrifice timepoint (P < 0.0001, Table 1), with the exception of kidney tissues at 2 d post-treatment, where mean FBZ-SO₂ concentrations were higher than that obtained in skin-fat (P = 0.0189). The FBZ-SO₂ concentration in kidneys in all birds was above the LOQ at 2 and 4 d post-treatment, while at 6 d post-treatment and thereafter it was above the LOQ in some individual birds at each sacrifice timepoint (Table 1). The FBZ-SO₂ concentration in the breast muscle in all birds was above the LOQ at 2 d post-treatment, while at 4 to 12 d post-treatment it was above the LOQ in some individual birds at each sacrifice timepoint, and at 14 d and 16 d post-treatment it was not detectable in any of the birds (Table 1). Regression of the depletion data, excluding the day 2 sacrifice timepoints, to the CFIA-validated LOD of FBZ-SO₂ of 1 ppb with 95% CI, was possible in the liver and skin-adherent fat matrices only. The upper 95% CI from the analyses was below 1 ppb at 39 d and 23 d in the liver and skin-adherent fat, respectively, suggesting that these would be the minimum WDI s for each of these tissues (Figures 1 and 2, respectively) using the current data set.

Discussion

No mortality or signs of morbidity were noted in this study, supporting the safety of fenbendazole fed to turkeys at 30 mg/kg of feed for 7 d. Anthelmintic compounds are used extensively for the prevention and treatment of parasitic nematodes in poultry, and fenbendazole has been found to be effective against this type of infection (5–9). There are currently no fenbendazole products approved by Health Canada for use in turkeys. The use of fenbendazole in this species, therefore, is considered extra-label, with no (zero) allowable levels of fenbendazole in edible tissues. Edible tissues containing drug residues can pose health hazards to the consumer including increased drug resistance, allergic reactions, and possible direct toxic effects. Thus, a safe withdrawal interval must be provided by the prescribing veterinarian, such that the drug will not represent a public health concern, or be out of regulatory compliance, when fenbendazole is used in turkeys. The CgFARAD is frequently contacted for fenbendazole withdrawal guidance after in-feed administration to turkeys to control parasitic nematodes. Given the lack of tissue residue profiles following in-feed administration of fenbendazole to turkeys, to estimate an appropriate WDI that assures consumer safety, the study reported here was conducted by the CgFARAD.

The results of this study showed that concentrations of the marker residue FBZ-SO₂ were above the assay LOQ, and therefore violative in all birds, in the breast muscle at 2 d and in the kidneys at 2 d and 4 d post-treatment. Furthermore, some birds had FBZ-SO₂ concentrations above the LOQ for up to 12 d post-treatment in the breast muscle, and across all sacrifice timepoints in the kidneys. Considering that the same dose of fenbendazole was administered in-feed to birds of the

**Figure 1.** Liver concentration-time profile across sacrifice timepoints (2, 4, 6, 8, 10, 12, 14, and 16 d post-treatment) for fenbendazole sulfone following in-feed administration at 30 mg/kg for 7 consecutive days in 42 turkeys (n = 6 birds per sacrifice timepoint). Values are plotted on a log scale. The horizontal line at 1 ng/g, the limit of assay quantification (LOQ). Dotted lines, upper and lower 95% CI.

**Figure 2.** Skin-adherent fat concentration-time profile across sacrifice timepoints (2, 4, 6, 8, 10, 12, 14, and 16 d post-treatment) for fenbendazole sulfone following in-feed administration at 30 mg/kg for 7 consecutive days in 42 turkeys (n = 6 birds per sacrifice timepoint). Values are plotted on a log scale. The horizontal line at 1 ng/g, the limit of assay quantification (LOQ). Dotted lines, upper and lower 95% CI.
same age and being kept under the same environmental conditions (e.g., lighting, temperature), these findings may indicate individual variation in FBZ-SO₂ depletion from the muscle and kidneys of turkeys (14). The FBZ-SO₂ concentrations in the liver and skin-adherent fat remained above the LOQ in all birds, at all sacrifice timepoints, with concentrations being significantly higher in these tissues than in corresponding kidney and breast muscle. The liver is the slowest depleting organ for many veterinary drugs undergoing hepatic metabolism. The degree of metabolism for a drug is affected by the drugs lipophilicity. In this study, fenbendazole also accumulated in the skin-adherent fat. Previous residue depletion and metabolism studies with fenbendazole in turkeys showed that most of the fenbendazole was eliminated in the feces by 24 h post-dosing (9). In this study, FBZ-SO₂ concentrations were detected in all edible tissues studied beginning at 2 d post-treatment, with mean FBZ-SO₂ concentrations at the day 2 and day 4 sacrifice timepoints following the rank order: liver > skin-adherent fat > kidneys and breast muscle. This trend in the accumulation of FBZ-SO₂ in turkey tissues is similar to that reported after fenbendazole administration to pheasants at 100 ppm for 7 d without feed withdrawal (15). Additionally, beginning at 6 d post-treatment and thereafter, the mean FBZ-SO₂ concentrations in the edible tissues followed the rank order: liver and skin-adherent fat > kidneys and breast muscle.

In the US, fenbendazole is currently approved for use in complete turkey feeds at 16 ppm to be fed for 6 consecutive days with no withdrawal time required and FDA approved tolerances of 6 ppm and 2 ppm in liver and muscle, respectively (9). In Canada, the target tissue for fenbendazole that is monitored by the CFIA is the liver and the marker residue that is monitored is FBZ-SO₂. In Canada, as there are no MRLs approved for fenbendazole in edible tissues of turkeys, the detection of any amount by the CFIA at processing constitutes a residue violation and a regulatory compliance concern. Unfortunately, the depletion data set obtained from this study did not allow us to calculate the WDIs for fenbendazole in the collected tissues using a statistical tolerance limit of 99%, as is required with sponsor submissions for regulatory approval of veterinary drugs for use in food-producing animals. Although our study design was based on the VICH guidelines, a pilot study was not feasible to establish a range of sacrifice days that would have provided raw data points to the LOQ for the assay (i.e., 1 ppb). Our choice of sacrifice timepoints was based on limited data obtained from a New Animal Drug Application (NADA) 131-675–July 3, 2000 for Fenbendazole for grower turkeys that was designed to evaluate fenbendazole depletion to a tolerance level of 6 ppm in the liver and 2 ppm in the muscle (9). As such, analysis of the data and determination of a WDI for liver and skin-adherent fat relied on extrapolation of the data from the last sacrifice timepoint to the LOQ of the assay and did not include raw data points at the assay LOQ of 1 ppb. Initial regression analysis including all sacrifice timepoints was influenced by extreme values on the first sacrifice time point (day 2). A pilot study would have allowed us to re-design the sacrifice timepoints to focus on later timepoints closer to the assay LOQ, while removing earlier ones. Modeling fenbendazole depletion data to the current CFIA LOD for FBZ-SO₂ of 1 ppb resulted in estimations of WDIs of at least 39 and 23 d for the liver and skin-adherent fat, respectively. Given that the liver is considered the target tissue for fenbendazole residues testing by the CFIA following its extra-label use in food-producing animals, a WDI estimation of at least 39 d following the last treatment with fenbendazole should be observed under the conditions of this study. It is important to note that the estimation of a WDI for FBZ in this study does not represent an official WDI, which may only be issued by Health Canada.

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References

Adoption of technology and management practices by Canadian cow-calf producers

Murray Jelinski, Reynold Bergen, Brenna Grant, Cheryl Waldner

Abstract — Statistics Canada’s 2016 census data were analyzed to determine the proportion of Canadian cow-calf producers who had adopted the use of 7 different technologies and 2 different grazing/feeding management practices, collectively referred to as “management tools.” The 4 most commonly used management tools were rotational grazing, in-field winter grazing/feeding, smartphones/tablets, and computers/laptops. Differences in the adoption of these technologies by geographical region, number of producers/operations, herd size, operator gender, and operator age were examined using logistic regression. Estimates of the mean proportion of producers in eastern (65%) and western (60%) Canada using rotational grazing were similar (P = 0.24). However, a greater proportion of producers in western Canada versus eastern Canada were using in-field winter grazing/feeding (P < 0.001), smartphones/tablets (P < 0.001), and computers/laptops (P = 0.002). Adoption of all 4 tools was higher on farm operations with ≥ 2 operators versus those with 1 operator (P < 0.001). Larger herd size was associated with higher adoption rates across all 4 management tools. The effect of gender on adoption rates was equivocal.

Résumé — Adoption de la technologie et des pratiques de gestion par les éleveurs-naisseurs canadiens. Les données du recensement 2016 de Statistique Canada ont été analysées afin de déterminer la proportion d’éleveurs-naisseurs bovins canadiens qui avait adopté l’usage de 7 différentes technologies et de 2 différentes pratiques de gestion pour le pâturage et l’alimentation, collectivement appelées « outils de gestion ». Les quatre outils de gestion les plus communément utilisés étaient la rotation du pâturage, le pâturage et l’alimentation dans les champs en hiver, les téléphones intelligents et les tablettes et les ordinateurs/ordinateurs portables. Les différences au niveau de l’adoption de ces technologies selon la région géographique, le nombre de producteurs/exploitations, la taille du troupeau, le sexe de l’exploitant et l’âge de l’exploitant ont été examinées à l’aide d’une régression logistique. Les estimations de la proportion médiane de producteurs dans l’Est (65 %) et dans l’Ouest (60 %) du Canada qui avaient recours à la rotation de pâturage étaient semblables (P = 0,24). Cependant, une proportion supérieure de producteurs dans l’Ouest canadien avait recours au pâturage et à l’alimentation dans les champs en hiver (P < 0,001), aux téléphones intelligents/tablettes (P < 0,001) et aux ordinateurs/ordinateurs portables (P = 0,002). L’adoption des quatre outils était supérieure dans les exploitations agricoles de ≥ 2 exploitants par rapport à celles ayant 1 exploitant (P < 0,001). Un troupeau de taille supérieure était associé à des taux d’adoption supérieurs pour les quatre outils de gestion. L’effet du sexe sur les taux d’adoption était équivoque.

Introduction

Research in the early 1960s led to the development of the “diffusion model” to help explain the adoption of technologies by agricultural producers (1). The premise was that the dissemination of information is a critical driver for the adoption of innovative technologies and practices. Subsequent research in the early 1980s concluded that even though producers might be well-informed and eager to adopt new technologies, economic constraints may preclude their adoption (2). A more contemporary study of cattle producers found that unfamiliarity and perceived non-applicability were the main reasons why they chose not to adopt various best management practices (3). Insufficient labor and profitability were also identified in a study that examined factors associated with the adoption of different grazing strategies for beef cattle production in the southern US (4). In general, producers must anticipate a positive net return...
(economically, environmentally, or socially) in order to adopt a new innovation.

One of the few sources of data relating to the adoption of technologies by Canadian agricultural producers comes from Statistics Canada’s (StatsCan) Census of Agriculture. The Census of Agriculture is mandatory under the Statistics Act; therefore, all individuals who produce agricultural products intended for sale must complete the census (5). The data represent all commodities, geographical locations, and varying sizes of farming operations (6). While agricultural data have been generated from censuses spanning many decades, changing agricultural practices have resulted in the survey questions evolving over time, which is problematic when it comes to comparing data across time. For example, the use of computers for farm management increased from 2.7% to 59.6% from 1986 to 2011 (7). The earliest census data, however, provide no information as to how the computers were being used for farm management. It was not until the 2001 census did StatsCan begin to ask whether computers were being used for specific activities such as bookkeeping, payroll, livestock record-keeping, word processing, Internet, and e-mail (8). Then, in 2011, the census reverted to only asking whether the farm operator had a high-speed Internet connection (9). More recently, the 2016 census included a new section titled “technologies,” which included the use of smartphones/tablets for farm management, computers/laptops for farm management, GPS technology, and GIS mapping, among other technologies (10). Thus, this latest census provides the first opportunity to gain insight into the uptake of a broad array of technologies by Canadian cow-calf producers.

The objectives of this study were to i) determine what proportion of Canadian cow-calf beef producers had adopted the technologies described in the 2016 census as well as 2 feeding/grazing management practices (rotational grazing and in-field winter grazing/feeding); and ii) identify operator (producer) and operation (farm) characteristics associated with the adoption of these technologies and feeding/grazing management practices.

**Materials and methods**

All data used in the analyses were obtained from Statistics Canada’s 2016 Census of Agriculture using a customized data extraction, with producer and herd parameters determined by the authors. The analyses were restricted to farm operators with cow-calf beef operations; operators (producers) were defined by Statistics Canada (StatsCan) as any person responsible for the management decisions for an agricultural operation as of May 10, 2016 (10). Cow-calf operations were defined as farms, ranches, or other operations that returned a census indicating that they had cows or heifers (1 y or older) for beef purposes. The census survey also inquired about how many hours/weeks each operator worked, if the operator earned off-farm income, and if the farm remunerated family and non-family employees; however, these parameters were not included in the current analyses. Additional information on how the census was administered, analyzed, and reported can be found elsewhere (11).

The initial analysis examined 7 technologies: i) the use of computers/laptops for farm management; ii) use of smartphones/tablets for farm management; iii) GPS technology; iv) GIS mapping; v) auto-steer; vi) auto-feeding; and vii) automated environmental controls for animal housing (Step 23 of the Census of Agriculture). Two feeding/grazing management practices from a separate section of the census (Step 13) were also examined: rotational grazing and in-field winter grazing/feeding.

The respondents were asked if they had used these technologies or grazing/feeding practices in 2015. These 7 technologies and
2 management practices are herein collectively referred to as "management tools" and the proportion of producers using each tool was considered the adoption rate.

The number of producers using each management tool was stratified by gender (female and male); number of beef cattle operators per farm (1 and ≥ 2); producer age (< 26 y, 26 to 30 y, 31 to 35 y, 36 to 40 y, 41 to 45 y, 46 to 50 y, 51 to 55 y, 56 to 60 y, and > 60 y); and herd size (< 51, 51 to 100, 101 to 200, 201 to 300, 301 to 500, and > 500 breeding female cattle). Herd size data were determined by summing the number of beef cows and replacement heifers (> 1 y of age) per operation. StatsCan provided the extracted data at the provincial level with the Atlantic provinces being reported as 1 region. These data were then collated into 3 regions: Canada, eastern Canada (Atlantic provinces, Quebec, and Ontario), and western Canada (Manitoba, Saskatchewan, Alberta, and British Columbia). Eastern and western Canada are herein referred to as "East" and "West," respectively.

The extracted data were provided in a commercial spreadsheet (Microsoft Excel v. 12; Microsoft Corporation, Redmond, Washington, USA) and then exported to a statistical program for analyses (IBM SPSS Statistics ver 24; IBM Corporation, Armonk, New York, USA). Descriptive statistics were generated to gain an understanding of the relative adoption of each management tool. Generalized estimating equations (GEE) with a logit link function and binomial distribution were then used to examine factors associated with the adoption of each management tool, correcting for clustering associated with herds within each geographical code (6 provinces and Atlantic Canada). The following factors were used in each of the final multivariable models: region (East or West), number of operators/farm (1 or ≥ 2), gender, producer age, and herd size. The total number of producers using the management tool in each category was the numerator for the model, and the total number of producers reporting to the census in each category was the denominator. Because complete census data were used for the analysis, the model could be used to generate predicted probabilities of adopting the management tool for each category with 95% confidence intervals (CI). The absolute differences in the probabilities of those adopting and those not adopting each management tool were then determined for each factor with 95% CI. Residuals were examined for outliers. As this was intended as an exploratory analysis of factors associated with all of the most common management tools no interactions are reported.

### Results

In 2016, Canada had 72,820 cow-calf producers, 19,315 (26.5%) in the East and 53,505 (73.5%) in the West. Of these, 30,065 (41.3%) were sole operators: 27,245 (90.6%) males and 2,820 (9.4%) females. The age distribution of all producers was: < 26 y (1.8%), 26 to 30 y (3.1%), 31 to 35 y (4.8%), 36 to 40 y (6.3%), 41 to 45 y (7.3%), 46 to 50 y (9.7%), 51 to 55 y (15.1%), 56 to 60 y (16.5%), and > 60 y (35.5%). The distribution of herds based on size (number of cows and
replacement heifers) was: <51 (60.4%), 51 to 100 (16.8%), 101 to 200 (13.4%), 201 to 300 (4.9%), 301 to 500 (3.1%), and >500 (1.3%). In summary, 35.5% of producers were >60 y of age and most herds (60.4%) had <51 breeding female cattle. Herds with 1 reported operator were 1.12 (95% CI: 1.10 to 1.13; $P<0.0001$) times more likely to have <51 breeding females than herds with ≥2 operators. To put the producer data in context with the number of farm operations, there were 53,837 farms reporting beef cows in 2016 (12), or an average of 1.4 operators/cow-calf operation.

The initial analysis involved graphing the proportion of producers who had adopted the use of the 7 technologies and 2 grazing/feeding management practices (Figure 1). Management tools such as GIS, environmental controls for animal housing, and auto-feeders had low adoption rates (<6.0%) in all provinces and the GPS and auto-steer technologies were primarily adopted by operators in the West. Therefore, these lesser used technologies were not examined further. Multivariable models were then developed for each of the 4 most commonly used management tools: rotational grazing, in-field winter grazing/feeding, smartphones/tablets, and computers/laptops. Tables 1 to 4 summarize the associations between herd attributes and the reported use of each management tool.

There was no difference ($P=0.24$) in the adoption rate of rotational grazing between the East and West (Table 1). However, a greater proportion of producers in the West were using in-field winter grazing/feeding (Table 2), smartphones/tablets (Table 3), and computers/laptops (Table 4). The adoption of all 4 management tools was higher on farms having ≥2 operators (Tables 1 to 4). Operations that listed a female as being involved in the operation, as opposed to farms managed solely by males, had higher adoption rates for rotational grazing, in-field winter feeding/grazing, and computers/laptops. While gender-associated differences were significant, the measure of effect was marginal (1% to 2%).

The largest herds (>500 head) had the highest adoption rate for rotational grazing (Table 1), while the next largest herds (301 to 500 head) had the highest adoption rates for the remaining 3 management tools. In general, increasing herd size was associated with an increase in the adoption of all 4 management tools. There was a consistent trend for the youngest (<26 y) and oldest (>60 y) cohorts to have the lowest rates of adoption of the 4 management tools (Tables 1 to 4). Overall, herd size accounted for the largest differences (measure of effect) in rotational grazing and in-field winter grazing/feeding, while producer age was associated with the largest differences in smartphone/tablet and computer/laptop use (Tables 1 to 4).

Discussion

There were no appreciable differences in the adoption of rotational grazing amongst producers in the East versus the West; however, producers in western Canada were more likely to incorporate the use of in-field winter grazing/feeding practices, smartphones/tablets, and computers/laptops in their cow-calf

<p>| Table 2. Estimates of the mean (95% CI) proportion of producers who were using in-field winter grazing/feeding, stratified by region, number of producers/herds, gender, age, and herd size (breeding heifers and cows) and absolute differences in proportions among groups. |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Region</th>
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<th>Lower</th>
<th>Upper</th>
<th>Difference from reference group</th>
<th>Lower</th>
<th>Upper</th>
<th>$P$-value</th>
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<td>−0.26</td>
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<td>0.63</td>
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<td>−0.03</td>
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<td>26 to 30</td>
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<td>0.08</td>
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</tr>
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<td>31 to 35</td>
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<td>0.43</td>
<td>0.58</td>
<td>0.09</td>
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<td>0.13</td>
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<td>36 to 40</td>
<td>0.52</td>
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<td>0.57</td>
<td>0.11</td>
<td>0.07</td>
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<td>41 to 45</td>
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<td>0.57</td>
<td>0.10</td>
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<td>46 to 50</td>
<td>0.49</td>
<td>0.44</td>
<td>0.53</td>
<td>0.07</td>
<td>0.05</td>
<td>0.09</td>
<td>&lt;0.001</td>
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<tr>
<td>51 to 55</td>
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<td>0.42</td>
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<td>0.04</td>
<td>0.03</td>
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</tr>
<tr>
<td>56 to 60</td>
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<td>&gt;60 y</td>
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<td>0.38</td>
<td>0.45</td>
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<td>&lt;0.001</td>
</tr>
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<td>Herd size</td>
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</tr>
<tr>
<td>&lt;51</td>
<td>0.29</td>
<td>0.26</td>
<td>0.32</td>
<td>Reference</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>51 to 100</td>
<td>0.39</td>
<td>0.35</td>
<td>0.43</td>
<td>0.11</td>
<td>0.007</td>
<td>0.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>101 to 200</td>
<td>0.49</td>
<td>0.43</td>
<td>0.55</td>
<td>0.21</td>
<td>0.14</td>
<td>0.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>201 to 300</td>
<td>0.58</td>
<td>0.52</td>
<td>0.64</td>
<td>0.29</td>
<td>0.23</td>
<td>0.36</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>301 to 500</td>
<td>0.59</td>
<td>0.49</td>
<td>0.68</td>
<td>0.31</td>
<td>0.19</td>
<td>0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;500</td>
<td>0.56</td>
<td>0.45</td>
<td>0.66</td>
<td>0.27</td>
<td>0.17</td>
<td>0.38</td>
<td>&lt;0.001</td>
</tr>
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operations. After controlling for the other factors, operations with ≥ 2 operators/farm had higher adoption rates for all 4 management tools compared to single-operator farms. While no single age cohort had the highest adoption rates across all 4 management tools, the youngest and oldest cohorts were consistently the lowest adopters. The impact of gender on adoption of the management tools was significant, but the measure of effect was marginal. The models estimated that operations with a female operator(s) would increase the adoption of rotational grazing, in-field winter grazing/feeding practices, and computers/laptops use by 1% to 2% over the farms managed solely by male operators.

While there were no differences in the uptake of rotational grazing between eastern and western Canada, there were differences at the provincial level. Approximately 60% of producers in Quebec (QC) and British Columbia (BC) used rotational grazing, while < 50% of Saskatchewan (SK) and Ontario (ON) producers had adopted this practice (Figure 1). These findings suggest that unique factors (i.e., environmental, geographical, regulatory, herd size) may be influencing the use of rotational grazing at the provincial level.

There were clear differences in the adoption of in-field winter grazing/feeding strategies in the West (57%) compared to the East (39%). This may be related in part to climatic conditions and regulatory constraints. Eastern Canada tends to have warmer and wetter winters, resulting in more trampling, muddy field conditions, and the potential for damage to the forage stand. Deeper snow also precludes swath grazing and stockpiling, although bale grazing and bale unrolling could still occur in the deeper snow. Furthermore, Quebec has environmental legislation that precludes extensive winter grazing, hence stockpiling as well as swath and bale grazing are not allowed (13). A more detailed analysis is needed to determine where, and by whom, in-field winter grazing/feeding strategies are being practiced.

The marginal effect of having women involved in the management of the farm needs to be interpreted with caution. The effect may have been greater had single operator farms managed by males been compared to single operator farms managed by females. In the current analysis, farms with a combination of male and female operators were compared to male-only managed operations. The male versus female-only analysis could not be conducted due to the limited numbers of sole female operators when considered across all of the factors examined in this analysis. This is unfortunate since there is a paucity of contemporary data relating to women’s influence on agriculture, particularly in industrialized countries.

It has been suggested that women’s contributions to agriculture may be higher than reported. Specifically, the lack of visibility of wives and daughters working in agriculture has resulted in the under-reporting of their contributions to agriculture (14). An American study conducted in the 1980’s concluded that women’s contribution or participation in agriculture may be systematically under-reported and that their involvement with farming remains obscure because their contributions are ill-defined (15).

### Table 3. Estimates of the mean (95% CI) proportion of producers who were using smartphones/tablets for farm management, stratified by region, number of producers/herds, gender, age, and herd size (breeding heifers and cows) and absolute differences in proportions among groups.

<table>
<thead>
<tr>
<th>Region</th>
<th>Mean</th>
<th>Lower</th>
<th>Upper</th>
<th>95% CI Difference from reference group</th>
<th>Lower</th>
<th>Upper</th>
<th>P-value</th>
</tr>
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<tr>
<td>East</td>
<td>0.47</td>
<td>0.41</td>
<td>0.53</td>
<td>-0.14</td>
<td>-0.20</td>
<td>-0.08</td>
<td>&lt; 0.001</td>
</tr>
<tr>
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<td>0.67</td>
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<th>Female</th>
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<th>Difference from reference group</th>
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<th>Upper</th>
<th>P-value</th>
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<td>0.44</td>
<td>0.56</td>
<td>-0.08</td>
<td>-0.11</td>
<td>-0.06</td>
<td>&lt; 0.001</td>
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<td>≥ 2 Operators</td>
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<table>
<thead>
<tr>
<th>Producer age</th>
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<td>46 to 50</td>
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<td>0.50</td>
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<tr>
<td>56 to 60</td>
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<td>0.37</td>
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<td>&gt; 60</td>
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<td>0.57</td>
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Furthermore, women’s off-farm employment was more likely to be captured in greater detail by surveys than was on-farm work. While only 2% to 4% of females had the final authority when it came to decision-making, ~45% were involved in making major decisions such as purchasing land, equipment, and the timing of when to sell farm products. Whether this American study from the 1980s informs the current discussion remains unclear, and as such, is an area requiring additional research.

The potential effect of age on the adoption of management tools is of particular interest because the Canadian cow-sector is currently undergoing a major generational shift in farm ownership (16). Canada’s cow-calf sector had 12.4% fewer operations and 12.4% fewer producers in 2016 than in 2011. Furthermore, at the time of the last census, 35% of all cow-calf producers were > 60 y and for every 1 producer < 31 y of age there were ~7 producers > 60 y of age. The demographic profile of the Canadian cow-calf sector is such that over the coming decade the current cohort of cow-calf producers who comprise the baby boom generation (born between 1946 and 1964) will have retired, leaving a generation of millennials (Generation-Y) to manage the farm operations.

The millennial generation is defined by those persons born between the early 1980s and mid-1990s and is frequently referred to as “echo of the baby boom.” They are also considered to be technologically savvy, being referred to as the “digital generation” (17), “digital natives,” or “digital immigrants” (18). They are stereotyped as having a lower tolerance for delays and therefore seek readily accessible information, preferring graphics before text and having the opportunity to network and multi-task. Many veterinarians can attest to millennials having researched their disease or production problem before coming to seek advice. The exponential growth of information through social media and the internet could have significant implications with respect to how veterinarians charge for consulting services.

While a relatively recent survey of Saskatchewan beef producers ranked veterinarians as the main source of information, 13.5% of respondents considered the internet in the top 3 sources for information (19). Veterinarians need to be cognizant that the next generation of operators may require different means of communication.

Age had a relatively small effect on the use of rotational grazing and in-field winter grazing/feeding but was a major factor when it came to use of smartphones/tablets for farm management. The estimate of the mean proportion of producers aged 31 to 35 using smartphones/tablets for farm management was 67% compared to 31% of producers > 60 y. The smartphone/tablet data, however, were difficult to reconcile with smartphone usage by the general population. While 58% of producers < 26 y of age used a smartphone/tablet in the operation of the farm, 94% of all Canadians 15 to 34 y of age own a smartphone (20). StatsCan has acknowledged that the respondents’ interpretation of what constitutes “use” may have led to under-reporting (21). The same may apply to the proportion of younger people using computers/laptops. Only

The millennial generation, also referred to as “echo of the baby boom,” is considered technologically savvy, being referred to as the “digital generation,” “digital natives,” or “digital immigrants.” They are stereotyped as having a lower tolerance for delays and therefore seek readily accessible information, preferring graphics before text and having the opportunity to network and multi-task. Many veterinarians can attest to millennials having researched their disease or production problem before coming to seek advice. The exponential growth of information through social media and the internet could have significant implications with respect to how veterinarians charge for consulting services.

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<table>
<thead>
<tr>
<th>Region</th>
<th>Mean</th>
<th>Lower</th>
<th>Upper</th>
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<td>0.66</td>
<td>0.70</td>
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<td>&gt; 500</td>
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</table>

Table 4. Estimates of the mean (95% CI) proportion of producers who were using computers/laptops for farm management, stratified by region, number of producers per herd, gender, age, and herd size (breeding heifers and cows) and absolute differences in proportions among groups.
61% of producers < 26 y of age indicated that they were using computers/laptops to assist in farm management, whereas 71% of Canadians > 15 y of age own a laptop and 50% own a desktop computer (20). It will be of interest to see how adoption rates of these digital-based technologies increase over the coming decade as more millennials become the sole managers of the farming operation. The increased use of these technologies will also be aided by improvements in hardware, software, and new and more novel agricultural applications.

There was a consistent trend with respect to the effect of herd size. Generally, producers with larger herds had greater adoption rates, while the lowest adoption rates were in herds of < 51 breeding females. This relationship may be related, in part, to constraints on labor and profitability (4). In the current study, operations with ≥ 2 operators consistently had higher adoption rates for all 4 management tools compared to the farms operated by 1 person. Presumably the additional amount of available labor allowed or facilitated a higher adoption rate of all 4 management tools. However, profitability has also been shown to influence the adoption of newer technologies and larger operations tend to capture the economies of scale and therefore are potentially more profitable. Therefore, profitability may have confounded the effect of farm size on the adoption of the new technologies.

The 2016 Census of Agriculture was the first to include questions relating to a host of technologies. Of interest was the use of electronic devices such as smartphones/tablets and computers/laptops. Conceivably, the adoption of technology and innovative management practices will increase as the cow-calf sector continues to consolidate, resulting in fewer farms, fewer producers, but larger herds. Technology holds the potential to assist producers in managing more efficiently, allowing fewer producers to manage more animals. Veterinarians should anticipate that the next generation of producers, who are more technology savvy, will be more informed and also more willing to accelerate the adoption of technologies such as drones for surveilling land and livestock, GPS tracking of individual animals, enhanced hardware and software for data acquisition and reporting, to name a few. While a constantly evolving census questionnaire makes it difficult to compare data across time, it is equally important that the questions remain relevant to the changing technologies.

References
Pharmacokinetics of regional limb perfusion using a combination of amikacin and penicillin in standing horses

Roee Dahan, Gil L. Oreff, Amos J. Tatz, Tal Raz, Malka Britzi, Gal Kelmer

Abstract — The objectives of this study were to evaluate the compatibility and the pharmacokinetic properties of combined amikacin and penicillin administration by intravenous regional limb perfusion (IVRLP) in horses. A tourniquet was applied proximal to the carpus of 7 clinically healthy adult horses and 2 g of amikacin and $10^3$ IU of penicillin (100 mL total volume) were sequentially injected into the cephalic vein just distal to the tourniquet. Synovial samples were collected from the joint at several times after injection. All samples were analyzed for amikacin and penicillin concentration. The mean maximum concentration ($C_{\text{max}}$) of both amikacin and penicillin was over 10-fold the relevant minimal inhibitory concentration (MIC) for all horses and remained above those MICs for at least 24 hours. The results of this study indicate that combining amikacin with penicillin during IVRLP in normal horses delivers high therapeutic synovial concentrations of both drugs.

Résumé — Pharmacocinétique de la perfusion régionale des membres en utilisant une combinaison d’amikacine et de pénicilline chez des chevaux debout. Les objectifs de cette étude consistaient à évaluer la compatibilité et les propriétés pharmacocinétiques de l’administration combinée d’amikacine et de pénicilline par perfusion intraveineuse régionale des membres (PIRM) chez les chevaux. Un tourniquet a été appliqué proximalement au carpe de sept chevaux adultes en bonne santé clinique et 2 g d’amikacine et $10^3$ UI de pénicilline (total de 100 mL) ont été injectés en séquence dans la veine céphalique légèrement distale au tourniquet. Des échantillons synoviaux ont été prélevés à plusieurs fois après l’injection. Tous les échantillons ont été analysés pour la concentration d’amikacine et de pénicilline. La concentration maximale moyenne ($C_{\text{max}}$) de l’amikacine et de la pénicilline était plus de 10 fois supérieure à la concentration inhibitrice minimale (CIM) pertinente pour tous les chevaux et est demeurée au-dessus de ces CIM pendant au moins 24 heures. Les résultats de cette étude indiquent que la combinaison de l’amikacine avec la pénicilline durant la PIRM chez des chevaux en santé offre des concentrations synoviales thérapeutiques élevées des deux médicaments.

Can Vet J 2019;60:294–299

Introduction

Intravenous regional limb perfusion (IVRLP) is a well-established method for delivering high antimicrobial concentrations to the equine distal limb for preventing and treating equine orthopedic and soft tissue infections (1,2). The IVRLP antimicrobial drug selection should ideally be based on culture and sensitivity results. It is, however, common practice to use an empirical broad-spectrum antibiotic for infection prevention early in the course of therapy, when microbial culture and susceptibility data are not available or when there is no positive bacterial culture (3). Broadening the antimicrobial spectrum by systemic administration of combined antimicrobial drugs was shown to improve treatment efficacy. Antibiotic combinations may be used to broaden the antimicrobial spectrum when mixed
bacterial infections are known or suspected to be present, to help prevent or overcome resistance, or to improve efficacy through synergistic effects (4,5). Since similar antimicrobial drugs are used in IVRLP, and similar bacterial populations are targeted, it is reasonable to extrapolate from these data and predict that use of antimicrobial drug combinations in IVRLP will lead to similar advantages.

Penicillin belongs to the beta-lactam class of antimicrobials; it is effective mainly against Gram-positive bacteria and anaerobe bacteria by exerting a bactericidal effect. Penicillin has been the backbone of equine antibacterial drug therapy for many years and is still one of the most commonly used prophylactic antibiotic drugs (6). Although it is used clinically in IVRLP (1), a single IVRLP pharmacokinetic study using penicillin was only recently reported (7).

Amikacin belongs to the aminoglycoside class of antimicrobials; it has a broad spectrum of activity and is the most effective drug against commonly isolated bacteria causing orthopedic infections in horses (8). Moreover, amikacin is the most commonly used and studied antibiotic in IVRLP (1–3,7,9–14).

The beta-lactam-aminoglycoside combination is one of the most frequently used antimicrobial drug combination therapy, commonly used systemically (1,15). Clinically, this combination was used effectively as a local therapy both by IVRLP and by intra-synovial lavage (1,16). The beta-lactam-aminoglycoside combination has a synergistic effect that is exerted via bacterial cell wall destruction by beta-lactam antibiotics, facilitating the aminoglycoside transport into the bacterial cell, exerting its bactericidal effect by interfering with ribosomal protein synthesis (17). Although there is supportive evidence of synergism, the beta-lactam-aminoglycoside combination also proved to have a negative drug interaction in confined compartments in an in vitro study (18). Moreover, a recent equine study showed that the combination of amikacin and ticarcillin/clavulanate, used for IVRLP, resulted in reduced amikacin concentrations and antimicrobial activity in the synovial fluid (11).

Our goal was to evaluate the PK properties of the combination of penicillin G and amikacin sulfate delivered by IVRLP through the cephalic vein to standing horses and sampling the metacarpophalangeal (MCP) joint.

We hypothesized that the amikacin-penicillin combination delivered by IVRLP would yield maximal MCP synovial penicillin and amikacin concentrations ($C_{\text{max}}$) well above the relevant minimal inhibitory concentration (MIC$_{90}$) and that these concentrations would remain high for at least 24 h following the perfusion.

### Materials and methods

#### Animals

Seven adult mixed breed horses participated in the study, including 5 geldings and 2 mares. The average age was 8 y (range: 4 to 15 y) and the average weight was 408 kg (range: 320 to 500 kg). Horses were clinically healthy according to physical evaluation, and all were sound when trotted. Horses were housed in separate stalls, had continuous access to fresh water, and were fed grass hay. The study design was approved by the University Animal Care and Use Committee.

#### Antimicrobial perfusion

Catheter application, horse sedation, and limb IVRLP treatments followed by tourniquet removal were performed as previously described (19). The antibiotic solutions were prepared just prior to performing the perfusion. Two grams of amikacin sulfate were diluted with isotonic saline in three 20-mL syringes (Amikacin–fresenius; Boden, Port Elizabeth, South Africa) and $10 \times 10^6$ IU benzylpenicillin sodium (Penicillin G Sodium; Sandoz GmbH, Kundl, Austria) were diluted with isotonic saline solution in two 20-mL syringes, to a total volume of 100 mL. The prepared solutions were administered sequentially, through the cephalic catheter, in five 20-mL syringes, over approximately 2 min.

#### Sample collection

Blood samples from the jugular catheter and synovial fluid samples from the metacarpophalangeal (MCP) joint of the treated limb were taken before IVRLP as described (19). Sedation with xylazine 0.5 mg/kg body weight (BW), IV was used as needed to prevent discomfort and movement during the sampling procedure.

Following aseptic preparation of the centesis site, aspiration of synovial fluid from the MCP joint was carried out using an approach described by Bassage et al (20). Blood sampling and treatment, acquisition of synovial fluid followed by phenylbutazone administration, amikacin sulfate instillation into each MCP

### Table 1. Pharmacokinetic values, mean, median (50th), 25th and 75th percentiles for amikacin and penicillin in serum and in synovial fluid in the MCP joint after regional limb perfusion. $C_{\text{max}}$ = maximal concentration ($\mu$g/mL), AUC$_{0-36}$ = area under the concentration time curve from 0 to 36 h ($\mu$g-h/mL).
Antibiotic analysis

Antibiotic analysis was based on established methodology in a previously reported PK study (14). Concentrations of amikacin and penicillin G in serum and in synovial fluid at each time point were determined by mass spectrometry (liquid chromatography/tandem mass spectrometry (LC/MS/MS)) and preparation of serum samples was as described (14). Concentrations above the upper limit of quantification were determined by diluting the samples with extracted drug-free serum/synovial fluid.

Liquid chromatography parameters for analysis of amikacin: A mixed-mode SiELC, Obelisc R column (5 μm, 100 × 2.1 mm, SiELC Technologies, Wheeling, Illinois, USA) was used for separation as previously described (19) except that the mobile phase consisted of 0.5% formic acid and acetonitrile at a flow rate of 0.6 mL/min. A gradient was applied by decreasing the acetonitrile concentration from 65% at 1 min to 5% at 3 min. This ratio was maintained for 0.5 min and then brought back to the initial conditions. The column compartment was kept at 30°C, and the injection volume was 10 μL.

Liquid chromatography parameters for analysis of penicillin-G: A C18 Symmetry column (3.5 μm, 100 × 2.1 mm, Waters, Ireland) was used for separation. The mobile phase consisted of 0.2% formic acid (Sigma-Aldrich, Israel) and acetonitrile at a flow rate of 0.35 mL/min. A gradient was applied by increasing the acetonitrile concentration from 5% at 0 min to 50% at 5 min. This ratio was maintained for 11 min and then brought back to the initial conditions. The column compartment was kept at 25°C, and the injection volume was 20 μL.

Turbo ion spray ESI/MS/MS in positive ion mode was operated at a temperature of 550°C and 450°C for amikacin and penicillin-G, respectively. Multiple reactions monitoring (MRM) was applied. The precursor ion was 586.3 m/z for amikacin and 357 for penicillin G. The product quantifier ions were 163.3 and 197.9 m/z for amikacin and penicillin G, respectively. The qualifier ions were 425.3 and 181.9 m/z for amikacin and penicillin G, respectively. Drug-free serum/synovial fluids were fortified with amikacin and penicillin G to obtain calibration curves in the range of 0.5 to 250 μg/mL in synovial fluid and 0.25 to 25 μg/mL in serum. Three replicates of calibration samples were prepared on 3 different days. The accuracy and intra-day and inter-day precision were calculated for 0.25 μg/mL, 2.5 μg/mL, 25 μg/mL in serum and 0.5 μg/mL, 25 μg/mL, 250 μg/mL in synovial fluid. These concentrations represented the lower level of quantification, the mid-level of quantification, and the high level of quantification.

The calibration curves for each of the antibiotics in both serum and in synovial fluid were linear over the tested range with a correlation coefficient of 0.991 (serum) and 0.963 (synovial) for penicillin-G and 0.981 (serum) and 0.978 (synovial) for amikacin. Accuracy was 95% to 120% (serum) and 90% to 113% (synovial) for penicillin-G and 98% to 112% (serum), 96% to 109% (synovial) for amikacin. Precision was 8% to 27% (serum) and 9% to 14% (synovial) for penicillin-G and 18% to 20% (serum), 14% to 18% (synovial) for amikacin.

Pharmacokinetic analysis

Amikacin and penicillin in the serum and the synovial fluid were assessed using a pharmacokinetic program (PK solutions 2.0; Summit Research Services Montrose, Colorado, USA), which computed (area under the curve) AUC_{0–36} using the trapezoidal rule. Serum and synovial fluid maximum synovial fluid concentration (C_{max}) of both drugs and the time of maximum synovial fluid concentration of both drugs (T_{max}) were determined by viewing graphs of the time course of each drug in synovial fluid. To evaluate the predicted efficacy of penicillin, we recorded the duration of time that the drug remained above the MIC_{90}.
(T > MIC\textsubscript{90}) and calculated the AUC\textsubscript{0–36}/MIC\textsubscript{90} ratio. To evaluate the predicted efficacy of amikacin C\textsubscript{max}/MIC\textsubscript{90} ratio and AUC\textsubscript{0–36}/MIC\textsubscript{90} ratio were calculated. Amikacin and penicillin MIC\textsubscript{90} for common susceptible equine bacterial pathogens were defined as 16 μg/mL and 1 μg/mL respectively, (21,22).

**Statistical analysis**

Statistical analyses were performed with computerized software (Statistix 8 Student edition, Analytical Software, Tallahassee, Florida, USA). A repeated measures analysis of variance (ANOVA) test followed by Tukey’s HSD all-pairwise comparisons test were used to compare the differences in penicillin or amikacin concentrations in the different time points after regional limb perfusion. These tests were also used to compare concentrations in the plasma and synovial fluid. Comparisons of C\textsubscript{max}, T\textsubscript{max}, and AUC between the plasma and the synovial fluid were made with Wilcoxon signed-rank test. Differences were considered significant at P ≤ 0.05. Unless otherwise noted, results are presented as median (1st quartile, 25%; 3rd quartile, 75%), or as mean ± standard error of the mean (SEM).

**Results**

Other than 1 horse with local edema at the cephalic catheter site and temporary lameness, none of the horses showed clinically noticeable adverse effects during the study. That 1 horse moved following injection of the entire perfusate, dislodging the cephalic catheter which resulted in immediate swelling at the site of venipuncture. In spite of this incident, the tourniquet remained in place and all synovial and blood samples were taken from this horse according to the protocol. The horse was mildly lame at a walk and had significant edema of the affected leg. After the last sample, the horse was treated with phenylbutazone, 2.2 mg/kg BW, q12h, PO for 5 d and application of 1% diclofenac sodium liposomal cream to the venipuncture site (Voltaren Emulgel 1%; Novartis Consumer Health SA, Nyon, Switzerland), q12h for 5 d and the limb was bandaged. Both lameness and edema resolved after 1 wk. One horse was excluded from the study because of aggressive behavior during the injection, which led to tourniquet release resulting in low synovial antibiotic concentrations.

Synovial fluid was successfully obtained from the MCP joint of all horses at all time points.

**Pharmacokinetic analyses**

Amikacin and penicillin were not detected in the serum or in the synovial fluid before perfusion. Median and percentiles of AUC and mean, median, and percentiles of C\textsubscript{max} of amikacin and penicillin measured in the serum and synovial fluid of the MCP joint are summarized in Table 1. The concentrations of amikacin and penicillin over time in the synovial fluid and in the serum are presented in Figures 1 and 2, respectively. The concentration of penicillin in the synovial fluid of the MCP joint was initially greater than the minimal inhibitory concentration (MIC) of most susceptible pathogens and the time greater than the MIC (T > MIC) was at least 24 h. The AUC\textsubscript{0–36}/MIC\textsubscript{90} ratios for penicillin in the synovial fluid were > 125 for all horses.

**Discussion**

We demonstrated that amikacin and penicillin administered sequentially by IVRLP resulted in a high synovial fluid concentration of both drugs. Although we did not administer amikacin alone in this study, our amikacin C\textsubscript{max} concentrations in the synovial fluid, using a combination of amikacin-penicillin, were higher than in a recent similar study (7). In that study identical doses of the amikacin-penicillin combination were used but the synovial amikacin concentration turned out to be an order of magnitude lower than in the current study. In addition, 12 h after perfusion, penicillin was detectable in only 1 horse, compared to all horses in the current study. These differences may be partially related to the fact that in our study a higher volume of perfusate was used (100 mL compared to 60 mL). Two recent studies, using significantly different experimental setups, have both shown that using a higher volume in IVRLP is associated with significantly higher antibiotic concentrations than with lower volumes (13,14). However, 2 other studies found no significant effect of perfusate volume on synovial antibiotic concentrations and the lower volumes had a trend towards higher concentrations (12,23). Another potential explanation for the discrepancy between the 2 studies, is that in Nieto at al (7) the tourniquet may have failed to completely prevent blood flow and thus some of the perfusate may have leaked into the systemic circulation while the tourniquet was still on. This is consistent with the fact that not only the penicillin but also the amikacin concentration appeared markedly lower in that study compared to the current one. Also, the absence of systemic antibiotic concentration measurements that prevented assessment of tourniquet failure was stated by these authors as a limitation (7). Finally, Nieto et al (7) mixed both antibiotics together in the same syringe while in vitro studies have demonstrated that aminoglycosides and penicillin can have mutual antagonist effects (18,24). All the above may explain our significantly higher antibiotic concentrations.

The amikacin-penicillin combination in the present study also yielded seemingly markedly higher amikacin synovial PK variables compared with previously reported synovial fluid amikacin IVRLP PK studies in which amikacin was used as the sole drug (10,12–14). For example, current results include a mean C\textsubscript{max} of 1391 (95% CI: 192 to 2590) versus 277 and 579 μg/mL and a mean AUC of 2127 (95% CI: 381 to 3874) versus 499 and 1042 μg·h/mL in 2 of these previous PK studies (10,14). Moreover, the synovial amikacin PK/PD most critical parameter, C\textsubscript{max}/MIC\textsubscript{90} ratio, was > 10 not just on an average but in each individual horse, and that is associated with an optimal bactericidal effect and with a reduced selection for resistance (25).

A comparison to other independent studies may have limitations. Variables such as the strength of the applied tourniquet
by different persons, the different breeds, and thus different volumes of the distal limbs, different temperaments of the horses, and different environmental conditions, could all potentially reduce the reliability of the comparison. Nevertheless, due to the markedly positive PK results demonstrated in this study, it may be concluded that the sequential delivery of the combination therapy: amikacin and penicillin, during IVRLP, has a potential therapeutic advantage. Adding penicillin to the amikacin IVRLP does not seem to have a negative effect on amikacin concentrations in the MCP joint and may even be associated with an increase in synovial fluid amikacin concentrations in the MCP joint after cephalic IVRLP.

One horse in this study developed regional swelling around the perfusion site accompanied by lameness. According to our clinical and research experience, this reaction is very unusual in IVRLP with amikacin alone and is likely associated with the use of penicillin. Thus, when using IVRLP with penicillin, this potential of local adverse reaction should be taken into consideration. In our clinical use, edema continued to be observed when penicillin was diluted with 40 mL; however, after increasing the dilution volume to 60 mL for penicillin in over 20 additional cases, no edema was observed.

Although systemic antimicrobial combinations have been used for many years in equine medicine (15), very few studies evaluated antimicrobial drugs combinations in IVRLP (7,11,19). While one IVRLP PK study found reduced antimicrobial concentration of amikacin when combined with ticarcillin/clavulanate (11), another IVRLP PK study reported a higher imipenem concentration when it was combined with marbofloxacin (19). In both of these studies, the two antibiotic drugs were injected sequentially, each antibiotic drug in separate syringes. Thus, each antimicrobial combination should be tested in its relevant setting (e.g., IVRLP) and the PK achieved by systemic combined drug administration cannot be automatically assumed to be similar when IVRLP is used.

Traditionally, concentration-dependent antimicrobials are considered more suitable for use in IVRLP. The reason is that the PK of this group, with the emphasis being on a high peak concentration as opposed to a sustained concentration of drugs, best matches the technique. For the sake of the animal’s welfare the technique involves sedation of the horse to ameliorate the pain elicited from the tourniquet. Thus, when considering the potential risk of frequent sedation (26), IVRLP is typically used once a day in a clinical setting (1,9). However, rather than systemic administration, the results presented here suggest that the use of time-dependent penicillin antimicrobials for IVRLP may be justified because this technique delivers much higher therapeutic concentrations of the antimicrobial in infected ischemic tissues for a longer period (27). In addition, after the tourniquet is released the high antimicrobial concentrations diffuse from the surrounding tissues which serve as a depot (3). The reason is that the pharmacokinetic/pharmacodynamic (PK/PD) relations of this group correlate well with the therapeutic efficacy of the various beta-lactam antibiotics including penicillin, especially the duration of time that the drug concentration is greater than the relevant MIC (T > MIC) (28). Our high synovial penicillin concentrations were greater than the 1 µg/mL MIC break point for its susceptible pathogens (22) and remained greater for 24 h. The other critical PK/PD parameter for beta-lactam antibiotics is AUC0–36/MIC90 and in certain situations, such as osteomyelitis or other isolated infections, the Cmax/MIC90 is also a valuable predictor of efficacy (29). The penicillin AUC0–36/MIC90 ratio was > 125, and the Cmax/MIC90 ratio was > 10; these values are indicative of highly effective bacterial killing that leads to minimal development of bacterial resistance (29). These results justify the once-a-day use of penicillin by IVRLP in the clinical setting. Although previous studies also enabled the goal of Cmax/MIC90 > 10 to be reached, we believe the higher amikacin concentration in the synovial fluid achieved in the current study, along with the combination of amikacin-penicillin, may possess a clinical advantage. It was recently shown in vitro, that some isolates of methicillin-resistant Staphylococcus aureus (MRSA) have greater MIC values for amikacin, some of them exceeding the upper limit of the E-test strips (256 µg/mL) (30). As MRSA is a common and problematic pathogen in equine practice (31), reaching greater concentrations (> 256 µg/mL) in the joint during IVRLP may be helpful, and even crucial in some clinical cases. Also, according to a thorough recent in vitro study on septicemic human neonatal blood (32), the combination of aminoglycosides-beta-lactams resulted in marked synergism against resistant coagulase negative Staphylococci and can be used effectively to treat neonatal sepsis. Thus, using the combination reported herein has the potential to effectively combat MRSA and other resistant bacteria in horses as well.

Our results contradict the Zantingh et al (11) recommendation that the combination of aminoglycoside-beta-lactams should not be used in IVRLP. This contradiction indicates that each different drug combination should be evaluated for its own PK properties. The PK data acquired in the present study support our working hypothesis that the amikacin-penicillin combination delivered through IVRLP is potentially efficacious for horses with bacterial infection in the distal portion of the limb. One major drawback in this study design is the lack of IVRLP with amikacin and IVRLP with penicillin separate groups. This would have enabled a direct comparison between the IVRLP with each antibiotic compared to the other and to both combined. The small study group is another limitation of this study, one that is common to most equine research studies. However, in this case the most important PK/PD values (Cmax/MIC and AUC/MIC) of amikacin and penicillin were uniformly above the ideal threshold in all tested horses. Thus, due to these unequivocal consistent results, the small study group was not an obstacle to the power of statistics.

Another limitation is the use of healthy horses and the lack of a biological assay to assess the activity of the antimicrobial drugs and not only their synovial concentrations. In addition, the lack of published PK data regarding penicillin use in IVRLP did not enable us to compare our penicillin PK values with another study in which penicillin was used as a sole IVRLP antibiotic. Nevertheless, in a similar study setting we did perform a preliminary study (unpublished), conducted on 2 healthy adult horses, using solely 10 × 106 MU benzylpenicillin sodium. In these 2 horses we found lower penicillin concentrations in the MCP joint (mean: Cmax 67 µg/mL) than in the current combination.
study (mean: $C_{\text{max}}$ 556 µg/mL). Thus, the amikacin in the combined perfusion did not seem to inhibit the accumulation of penicillin in the joint, it may have facilitated penicillin accumulation, but that is yet to be elucidated in future studies.

In summary, our results indicate that properly combining penicillin and amikacin during IV-IVRLP in healthy horses delivered high therapeutic concentrations of both drugs. Therefore, this drug combination should be considered for use in IVRLP in order to broaden the antimicrobial coverage when dealing with treatment or prevention of distal limb infections in horses.

References

Case Report Rapport de cas

An atypical presentation of multi-systemic B-cell lymphoma in a horse

Albert Torrent, Isabelle Kilcoyne, Amanda Johnson, Verena K. Affolter, Emily Berryhill, Monica Aleman

Abstract — This report describes an unusual presentation of multicentric B-cell lymphoma with central and peripheral nerve involvement in a horse that was presented with acute onset, severe, multiple limb lameness, and muscle atrophy. This case highlights the importance of including neoplasia in the differential list in horses presenting for severe limb lameness associated with muscle atrophy, muscle fasciculations, and weakness.

Résumé — Présentation atypique d’un lymphome à cellules B multisystémique chez un cheval. Ce rapport décrit la présentation inhabituelle d’un lymphome à cellules B multicentrique avec une implication du nerf central et périphérique chez un cheval qui avait été présenté avec une boiterie aiguë et grave de plusieurs membres et de l’atrophie musculaire. Ce cas souligne l’importance d’inclure la néoplasie dans la liste des diagnostics différentiels des chevaux présentés pour une boiterie grave d’un membre associée à l’atrophie musculaire, aux fasciculations musculaires et à la faiblesse.

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Lameness is one of the most prevalent veterinary complaints in the horse and is caused by trauma, congenital or acquired disorders, infections, metabolic disorders, or nervous and circulatory system disease. This report describes clinical and pathologic findings in a horse with acute onset left front and left hind limb lameness, an atypical gait, and mild muscle atrophy over the quadriceps region caused by a multicentric B-cell lymphoma. Upon treatment with corticosteroids and antibiotics, the attitude of the horse improved initially, but it continued to be severely lame. The horse developed pneumonia and died 1 mo after treatment. At necropsy the severe lameness was attributed to the neoplastic B-cell infiltrates of the dorsal nerve roots of the left sciatic nerve and to a lesser extent the ventral nerve roots at the level of the 7th cervical vertebral body forming a poorly demarcated extradural mass.

Case description

A 20-year-old, 455-kg Quarter Horse gelding was presented to the William R. Pritchard Veterinary Medical Teaching Hospital of the University of California–Davis with a history of severe acute onset left hind limb lameness, suggestive of a long bone/appendicular fracture. The owner noticed a left-sided trembling during a barrel racing competition a week before presentation as well as left-sided muscle fasciculations and left hind lameness following moderate exercise 3 d before presentation. The horse also had mild obtundation. Due to progression of the lameness over the next 3 d, the attending veterinarian referred the horse for possible left hind limb fracture. There was no recent history of trauma or injury, the horse was up-to-date on vaccinations and had been de-wormed 3 mo previously.

On admission, the horse was bright and alert, with an adequate body condition score of 4/9 and no evidence of external trauma. The initial physical examination showed mild tachycardia (52 beats/min) and tachypnea (24 breaths/min), but the remainder of the examination was unremarkable. On the lateral aspect of the left front hoof there was a hoof crack extending 3 cm distally from the coronary band. Muscle atrophy was noticed in the cervical region, more pronounced on the left side of the neck, together with mild atrophy of the left quadriceps musculature. The horse was grade 4/5 lame on the left front limb and left hind limb. Although he was able to bear weight on both limbs, he had an unstable left carpus — characterized by knuckling. In addition, he collapsed in his left stifle and hock (Video Clip S1 available on request from the corresponding author).

An orthopedic examination revealed no response to hoof testers in the left front limb or pain elicited on palpation of the quarter crack. An abaxial sesamoid nerve block did not significantly change the lameness. No pain was elicited on palpation of the soft tissue and boney structures. Radiographs of the left elbow and left stifle showed no evidence of boney abnormalities. No lesions were identified on ultrasound examination of the left pelvis, and a rectal examination was unremarkable. On standing cervical spine radiographs a mild osteoarthritis of the C6–7 cervical facet joint was noted.
A complete blood (cell) count (CBC) revealed a normal white blood cell count [6.4 × 10^3 cells/μL; reference range (RR): 5 to 11.6 × 10^3 cells/μL] with a mild lymphopenia (1.5 × 10^3 cells/μL; RR: 1.6 to 5.8 × 10^3 cells/μL). Biochemistry analysis identified a mild hyperglycemia (6.6 mmol/L; RR: 2.8 to 5.9 mmol/L), hyperproteinemia (81 g/L; RR: 58 to 77 g/L) characterized by a hyperglobulinemia (51 g/L; RR: 16 to 50 g/L), mildly elevated creatine kinase (CK, 495 IU/L; RR: 119 to 287 IU/L), mild hypertriglyceridemia (0.46 mmol/L; RR: 0.02 to 0.50 mmol/L), and mild hyperbilirubinemia (77.0 μmol/L; RR: 8.6 to 39.3 μmol/L).

Based on the aforementioned findings, with presence of significant gait abnormalities despite normal radiographic and ultrasound images, the list of differential diagnoses consisted of neurologic diseases rather than orthopedic, and included multifocal spinal cord trauma, myelitis with predominance of lower motor neuron involvement (infectious and non-infectious), equine motor neuron disease (EMND), equine protozoal myeloencephalitis, West Nile virus, and neoplasia.

The patient was medicated with flunixin meglumine (Intervet, Madison, New Jersey, USA), 0.5 mg/kg body weight (BW) IV, q12h, and morphine sulfate (Westward, Cherry Hill, New Jersey, USA), 0.1 mg/kg BW, IM, q12h, to reduce possible inflammation and pain, and was placed on stall rest. The horse remained recumbent frequently for prolonged periods of time. It was able to rise without assistance, but with some difficulty such as prolonged time to rise and increased fasciculations. The gelding maintained a good appetite, adequate gastrointestinal borborygmi in all 4 quadrants, and urination and defecation appeared normal during hospitalization.

A neurologic examination was performed by a Board-certified neurologist (MA) 2 d later during hospitalization; the findings included mild obtundation and normal cranial nerve responses, reactions, and reflexes. Segmental spinal reflexes, including cervicofacial, cutaneous trunci, anal and perineal, were within normal limits. Flexor (withdrawal) reflexes were reduced in all limbs especially in the left hind limb. Cutaneous sensation, tail and anal tone were normal. Proprioceptive deficits were observed in all limbs. Upon gait evaluation, tetraparesis, and weakness of all limbs were noticed, with hind limbs being more affected than front limbs; the left hind limb was most severely affected and had a drooped stifle and hock in the walk as a reduced toe extension (Video Clip S1). The horse had mild to moderate multifocal to diffuse asymmetrical muscle atrophy of cervical, thoraco-lumbar, gluteal, and limb muscles; the latter were most prominent on the left hind limb. Generalized muscle fasciculations predominately in the left triceps muscle, were apparent standing at rest. The findings indicated multifocal processes in the central and peripheral nervous systems, with predominant lower motor neuron involvement, and left femoral and sciatic nerve deficits.

An equine protozoal myeloencephalopathy (EPM) indirect immunofluorescent antibody (IFA) blood test for Sarcocystis neurona had a titer of 80 and was negative for Neospora hughesi. An IgM antibody capture enzyme-linked immunosorbent assay (ELISA) blood test for West Nile virus (WNV) was negative. Although not suspected based on neuroanatomical localization (unlikely distribution and clinical signs), a nasal swab was tested by polymerase chain reaction (PCR) for EHV-1; the result was negative.

Cytology of cerebrospinal fluid (CSF) obtained from the lumbosacral space revealed xanthochromic fluid with a total nucleated cell count of 28 cells/μL, which included 2% neutrophils, 60% small mononuclear cells, and 38% large mononuclear cells based on a 100-cell count. Protein in the CSF was elevated at 3.7 g/L (RR: 0.2 to 0.8 g/L). An IFA on CSF was negative for both S. neurona and N. hughesi. Although muscle atrophy was presumed to be of neurogenic origin, presenting clinical signs made EMND less likely, and muscle biopsies to further explore this assumption were offered, but declined due to financial constraints.

In the absence of a specific diagnosis, the horse was started on broad-spectrum oral antibiotics (trimethoprim-sulfamethoxazole; Aurobindo Pharma, Dayton, New Jersey, USA), 30 mg/kg BW, PO, q12h, and supportive neuroprotective and anti-inflammatory treatments, which included α-tocopherol (Stuart Products, Bedford, Texas, USA), 10 IU/kg BW, PO, q24h, dimethyl sulfoxide (DMSO; Valhoma Corporation, Tulsa, Oklahoma, USA), 1 mg/kg BW, IV, q12h for 2 d, and phenylbutazone (MWI, Boise, Idaho, USA), 2.2 mg/kg BW, IV, q12h. Based on the negative EPM result, a single high dose of dexamethasone (MWI, Boise, Idaho, USA), 0.088 mg/kg BW, IM was administered, followed by a tapering dose in order to reduce nervous system inflammatory response. After initiation of therapy the attitude of the horse improved substantially over a period of 4 d, but he continued to display a markedly altered gait.

The horse was discharged from the hospital 4 d after presentation due to financial constraints of the owner and the owner's preference to continue the treatment at home. Discharge instructions included: administration of phenylbutazone (MWI), 2.2 mg/kg BW, PO, q24h for 7 d, trimethoprim-sulfamethoxazole (Aurobindo Pharma), 30 mg/kg BW, PO, q12h for 7 d, and dexamethasone (MWI), 0.06 mg/kg BW, IM q24h for 3 d, followed by 0.04 mg/kg BW, IM, q24h for 4 more days.

At the follow-up examination 1 wk after discharge, the horse showed significant improvement of his demeanor and gait. Although muscle atrophy was still apparent, the horse was walking much more comfortably. At this stage the treatment with dexamethasone (MWI) was discontinued and the phenylbutazone (MWI) and trimethoprim sulfamethoxazole (Aurobindo Pharma) were continued for 5 more days.

Three weeks later the horse was referred to the VMTH again because of worsening of his condition. He had been found down in the stall by his owner that afternoon with difficulty breathing. Upon arrival at the clinic the horse was found dead in the trailer.

Gross and histopathologic examination revealed multicentric B-cell lymphoma in numerous organs and body systems, including the intestinal tract, the central and peripheral nervous system, and the heart. Grossly, the duodenum, jejunum, and less severely the cecum and colonic mucosa were disrupted by numerous black to purple variably ulcerated nodules, overlain with small amounts of yellow fibrinous material. Mesenteric lymph nodes were variably enlarged. Two raised, dark red

**Discussion**

This case report describes an unusual presentation of multicentric B-cell lymphoma with central and peripheral nerve involvement in a horse that was presented with acute onset of severe unilateral multiple limb lameness consistent with a fractured limb and muscle atrophy that have not been previously described in the horse. The horse was referred for assessment of acute onset left hind limb lameness with suspicion of bone fracture and required an exhaustive examination to diagnose neoplasia as the primary cause. On evaluation, a multiple limb gait abnormality was confirmed, together with mild atrophy of the left quadriceps musculature. No bony abnormalities were observed in radiographs or on ultrasound examinations. Thorough anamnesis and physical examination, combined with full hematological and serum biochemistry, and an abaxial sesamoid nerve block were pursued to eliminate possible systemic disease or pain as the cause of the tremors observed in the left front limb. Once these causes were deemed unlikely, neurologic diseases were considered. The presence of an altered mental status (mild obtundation) in the absence of other systemic pathologic findings (such as EPM or EHV-1) and lack of significant improvement despite administration of analgesic drugs, suggested a possible multifocal neurologic component (central and peripheral) with predominant lower motor neuron involvement, and left femoral and sciatic deficits. The abnormal gait, tetraparesis, weakness (knuckling/collapse) upon weight-bearing, muscle fasciculations/tremor and muscle atrophy were all consistent with lower motor neuron (LMN) paresis. Most common causes of lameness such as trauma, compressive injury, EPM, EMND, and vertebral disease were already discarded, but neoplasia was still a possibility. Neoplasia can cause nerve damage through compression or infiltration (1). Although uncommonly reported, lymphoma is the most common neoplasia that can affect nerves in horses. In 1970, Bruere et al (2) described a subtle “shifting lameness” with no obvious external pathological changes caused by lymphoma involving the bone marrow. Neurolymphomatosis is a rare manifestation of lymphoma characterized by neoplastic infiltration of cranial and spinal nerves, and nerve roots (3–4). Lymphoma is the most common hematopoietic neoplasm encountered in horses (5) and can occur at any age (6). The lymphoma can be classified into multicentric, generalized, alimentary or intestinal, splenic, mediastinal, thymic, and cutaneous (6). Lymphoma arises from lymphoid tissue that includes lymph nodes, spleen, and GI tract-associated lymphoid tissue (5,7,8). Multicentric lymphoma is the most common form and consists of widespread involvement of lymph nodes, most likely through distribution of neoplastic lymphocytes via lymphatic circulation (5). Other locations include the liver, kidney, bone marrow (leukemic lymphoma), the upper airway and lungs, heart, adrenal glands, retro-orbital, skeletal muscle, and central nervous system (brain, meninges, spinal cord) (9–17). Metastasis can occur to other organs (6). When lymphoid tissue other than lymph nodes is involved, the lymphoma is classified as generalized, and is
considered end-stage (6). Current literature describes lymphoma as a cause of neurologic alterations, lameness, osteolysis, and pathologic fractures (18–25). On 2 surveys of postmortem examinations, prevalence of lymphoma in the horse was estimated to be 2% to 5% (26,27). Zeman et al (25) described a case of multicentric lymphoma with involvement of vertebral bone that resulted in hind limb paresis. A recent report found that lymphoma was amongst the most common malignant neoplasms in older horses, with none of the 19 affected animals having secondary nervous system disease (28). In another study, only 2% of 203 horses with lymphoma examined at necropsy had dissemination to the central nervous system, and none were presented with signs of primary peripheral nerve involvement (29). However, peripheral nerve involvement was documented in multicentric and central nervous system lymphoma in the horse (30–31). Infiltration of peripheral nerves with neoplastic lymphoid cells (neurolymphomatosis) causing chronic unilateral hind limb lameness was described in another 2 horses by Lehmbecker (3), and primary peripheral nerve lymphoma was also described recently in another horse (23). In a case report by Adolf et al (30), the clinical signs included severe unilateral thoracic limb lameness with marked muscle atrophy and severe pain. In another case report a horse was also presented with unilateral hind limb gait abnormality at the walk, with normal cranial nerve responses, weakness in all 4 limbs, intermittent muscle fasciculations, and increased recumbency times (23). The degree of pain observed in 1 of these horses prompted euthanasia, but pain was not observed in our horse. Histologic examination in those 2 horses revealed lymphocytic infiltration of thoracic nerves (proximal radial nerve and ventral branch of the 8th cervical spinal nerve in one horse, and both brachial plexi in the second one). The latter also had dense perineural and endoneural infiltrates with different size lymphocytes in both sciatic nerves. It is unknown whether painless neuropathy may reflect an earlier stage in the disease course (23) and potentially, infiltrating cells dissecting into and around nerve fibers and bundles could explain the initiation of neuropathic pain.

Unfortunately, clinical signs of lymphoma for most affected horses are typically nonspecific, and diagnosis is made late in the course of the disease, after it has progressed to end-stage, at which time clinical signs reflect the organ(s) involved (5). As observed in this case, results of CBC and serum biochemistry are often not helpful with diagnosis of lymphoma (5). The typical leukogram of horses with lymphoma includes mild to moderate leukocytosis due to mature neutrophilia (25). Anemia, hyperfibrinogenemia, hyperproteinemia, and hypoalbuminemia were not observed, but a normal CBC with only mild hyperproteinemia (81 g/L secondary to hyperglobulinemia (51 g/L) occurred. Results of the cerebrospinal fluid (CSF) analysis showed xanthochromia with a dramatically increased protein of 3.7 g/L. The cytologic examination of the fluid showed a moderate lymphocytic inflammation.

Gross and microscopic examination demonstrated neoplastic lymphocytes scattered throughout numerous organs, including the central and peripheral nervous system, and could explain the altered mentation in this case (32). Histopathology revealed neoplastic lymphocytes infiltrating the central and peripheral nervous system. Neoplastic infiltrates were most concentrated within the extradural space, nerve roots, and meninges at the level of the 7th cervical vertebral body. Additionally, high numbers of neoplastic lymphocytes were identified within the left sciatic nerve. Lower numbers of neoplastic cells were scattered throughout the cerebral and cerebellar meninges, as well as the perivascular spaces with mild infiltration of the adjacent neuropil. The widespread infiltration of central and peripheral nervous system by neoplastic B-lymphocytes explains the altered mentation and gait abnormalities.

Medical management of the patient did result in an initial improvement of demeanour although the lameness persisted. Finally, the horse died due to a complication with severe bronchoalveolar pneumonia, with intralesional bacteria, likely an opportunistic infection attributable to his compromised immune system secondary to the lymphoma and treatment with steroids. Recently, 1 case of EHV-5 infection was associated with lymphoma in the horse (33); however, analysis for EHV-5 was not performed in the present case. No respiratory signs were apparent on physical examination in previous visits. Lymphoma has been associated with reduced immune capacity by causing T-cell deficiency not evaluated here (34). This could have been further compromised by possible immune-suppressive effects of steroidal drugs.

Antemortem confirmation of lymphoma could not be made in this horse. Lack of definitive clinical signs has hampered antemortem diagnosis of lymphoma in the past (25). In retrospect, a full abdominal and thoracic ultrasound could have been performed on this horse and potentially would have helped identify the presence of masses to be sampled (5,35). However, no abnormal lung sounds were auscultated while the horse was hospitalized and there were no clinical signs referable to the thoracic and gastrointestinal systems such as weight loss, diarrhea, colic, or coughing.

Based on this case report, lymphoma should be included in the differential diagnosis for adult horses presenting for severe single or multiple limb lameness with associated signs such as muscle atrophy, muscle fasciculations, and weakness.

References
Case Report  
Rapport de cas

Sex-hormone producing adrenal tumors causing behavioral changes as the sole clinical sign in 3 cats

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Abstract — Three neutered cats with adrenocortical tumors that were presented with behavioral changes but no evidence of hyperaldosteronism or hypercortisolism are described. All 3 cats had resolution of their clinical signs following adrenalectomy. For neutered cats presenting with behavior changes, a sex-hormone secreting adrenal tumor should be considered as a differential diagnosis.

Résumé — Tumeurs surrénaliennes produisant des hormones sexuelles causant des changements de comportement comme seul signe clinique chez 3 chats. Les cas de trois chats stérilisés ayant des tumeurs surrénaliennes qui ont été présentés avec des changements comportementaux mais aucun signe d’hyperaldostéronisme ou hypercortisolisme sont décrits. Les trois chats ont eu une résorption de leurs signes cliniques après une surrénalectomie. Pour les chats stérilisés présentant des changements comportementaux, une tumeur surrénalienne sécrétant des hormones sexuelles devrait être considérée comme un diagnostic différentiel.

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Adrenal tumors are rarely reported in cats, with the most common presenting complaints being due to hyperaldosteronism or hypercortisolism (1,2). Common clinical signs in cats with adrenal tumors include hypokalemic polymyopathy and hypertension-induced blindness associated with hyperaldosteronism and less commonly, alopecia, skin fragility, and a pot-bellied appearance associated with hypercortisolism (1,2). Rarely, cats with adrenal tumors may be presented with behavioral changes secondary to excessive sex-hormone production, without concurrent hyperaldosteronism or hypercortisolism (3–5). There are several case reports in the literature describing sex hormone production in cats with adrenal tumors (3–11); however, only 2 of these cases had behavioral changes as the only clinical sign (3,4). A third case reported behavioral changes in concert with mammary hyperplasia without hyperaldosteronism or hypercortisolism (5). Differential diagnoses in these patients include retained gonadal tissue such as an ovarian remnant or retained testicle, estrogen or testosterone-producing tumors, or administration of exogenous sources of these hormones (3). Presenting with behavioral changes as the only clinical sign is atypical for cats with adrenal tumors and should be considered as a differential diagnosis in these cases.

Case descriptions

Case 1
An 11-year-old castrated male domestic shorthair (DSH) cat (Case 1) was evaluated for behavioral changes. Six months before presentation, the cat had begun to display behavior typical of an intact male cat (mounting, urine spraying, and increased aggression toward his owners). The cat had been castrated at 4 mo of age and had never exhibited these male behaviors. Testosterone concentrations provided by the referring veterinarian before presentation at our facility were elevated at 0.37 nmol/L (reference value for a castrated male cat: ≤ 0.02 nmol/L).

On physical examination, the cat was bright, alert, and responsive but vocal, hyperactive, and difficult to handle. Spines were noted on examination of the penis (Figure 1), analogous with an intact male cat. There were no significant abnormalities on complete blood (cell) count (CBC), serum biochemistry, serum thyroxine, or urinalysis. Baseline cortisol [29.8 nmol/L; reference range (RR): 27.6 to 82.8 nmol/L] and aldosterone (382 pmol/L; RR: 194 to 388 pmol/L) concentrations were established before pursuing adrenalectomy and were within reference ranges. An anti-Müllerian hormone assay was negative for a retained cryptorchid testicle. During abdominal ultrasound, a hypoechoic left adrenal gland mass (2.5 cm × 2.4 cm × 2.2 cm) was noted with no invasion into the caudal...
The right adrenal gland appeared normal in size and architecture and no other abnormalities within the abdomen were identified. Thoracic radiographs were unremarkable. An abdominal computed tomography (CT) scan confirmed the presence of a left-sided adrenal mass with no other significant findings (Figure 2).

The left adrenal gland and mass were removed during a standard midline laparotomy (Figure 3). The cat was administered dexamethasone (Dexamethasone sodium phosphate; Bimeda-MTC Animal Health, Cambridge, Ontario), 0.05 mg/kg body weight (BW), IV, during surgery due to the concern of a sex-hormone producing tumor potentially suppressing endogenous glucocorticoid production. Twenty-four hours after surgery the cat was hypocortisolemic (9.7 nmol/L; RR: 138 to 276 nmol/L) 1 h following administration of cosyntropin (Cortosyn; Amphastar Pharmaceuticals, Rancho Cucamonga, California, USA), 5 µg/kg BW, IV. Prednisolone (PrednisTab; Lloyd Pharmaceuticals, Shenandoa, Iowa, USA) was given for 1 mo (0.5 mg/kg BW, PO, q24h for 1 wk then 0.25 mg/kg BW, PO, q24h for 3 wk), at which point another ACTH stimulation test was performed with a baseline cortisol of 120.8 nmol/L (RR: 55 to 166 nmol/L) and post-ACTH stimulation value of 176.0 nmol/L. Prednisolone was slowly tapered with a plan to recheck in 1 mo. At recheck examination with the referring veterinarian, the baseline cortisol was 226.2 nmol/L and the post-ACTH cortisol was 268.7 nmol/L. Glucocorticoids were discontinued at that time. The cat’s aggressive behavior, mounting, and urine spraying had resolved within that timeframe, 2 mo following adrenalectomy. Histopathology of the mass confirmed an adrenocortical carcinoma.

Fifteen months after surgery, the cat was presented with recurrence of virilizing behavioral signs. An abdominal computed tomography (CT) scan demonstrated apparent regrowth of the adrenal tumor with 2 closely associated, contrast-enhancing abdominal masses presumed to be metastases (Figure 4). In addition, the previously normal right adrenal gland was now a mass with extension into the caudal vena cava (Figure 4). No signs of metastasis were identified on thoracic CT. The cat was euthanized after further treatment was declined. A necropsy was not conducted.

Case 2

Case 2 was a 6-year-old neutered male cat that was presented with a 2-month history of increased aggression toward the other cat in the household, urine spraying, and weight loss. Although the cat had been neutered at 6 mo of age, spines were noted on the penis on physical examination. Testosterone concentrations were elevated at 14 nmol/L (reference value: 0.5 nmol/L for a castrated male). An abdominal CT scan revealed a contrast-enhancing nodule on the cranial pole of the right adrenal gland measuring 9 mm × 9 mm × 7 mm; the left adrenal gland appeared normal in shape, size, and architecture. Laparoscopic surgery was performed to remove the right adrenal gland and mass. Histopathology was consistent with an adrenocortical carcinoma. Immunohistochemistry for Factor VIII-related antigen highlighted a segment of discontinuous vascular endothelium, interpreted as early vascular invasion. Testosterone concentrations taken immediately after surgery were 6 nmol/L and had fallen to 2.6 nmol/L by 2 wk post-adrenalectomy. There was resolution of behavioral signs within 5 d of surgery.

Fifteen months after surgery, the cat was seen by the referring veterinarian for weight loss and vomiting. A cranial abdominal mass was suspected on physical examination and the cat was euthanized. There had been no recurrence of behavioral signs at the time of euthanasia. A necropsy was not conducted.

Case 3

Case 3 was a 4-year-old spayed female DSH cat with a 2-month history of overt estrous behavior (pacing, vocalizing, lordosis). The cat was spayed at approximately 6 mo of age. Estradiol levels were 121 pmol/L (reference value: 92 pmol/L for a spayed female). Abdominal ultrasound revealed a well-circumscribed 8-mm diameter mass on the right adrenal gland. The left adrenal gland appeared normal. Thoracic radiographs were normal. Under the working diagnosis of an ovarian remnant, an abdominal exploratory surgery was performed. Normal
spay scarring and adhesions were found in the region of both ovarian pedicles and a normal appearing left adrenal gland was found. The right adrenal gland and mass were removed, and histopathology of the mass was consistent with an adrenocortical adenoma. Clinical signs resolved within 14 d of adrenalectomy.

At 16 mo after surgery, the cat was presented for recurrence of feminizing behavioral signs. An area of irregular tissue was seen on abdominal ultrasound at the area of the previously excised right adrenal gland. Estradiol levels were once again elevated at 119 pmol/L. The cat was euthanized for presumed recurrence of the right adrenal tumor. A necropsy was not carried out.

Discussion

The clinical presentation of cats with overt sexualized behavior as the sole clinical sign secondary to an adrenal tumor is rare. Table 1 summarizes the pertinent clinical findings from the 3 cats reported here along with those cats previously reported in the literature (3–5).

Due to the few cases reported, it is difficult to draw any strong conclusions on the prognosis for cats with functional adrenal tumors causing an increase in sexually dimorphic behaviors. However, clients are particularly concerned as to whether behavioral changes are likely to resolve following adrenalectomy. All cats reported here had clinical resolution of behavioral signs within 2 mo of adrenalectomy suggesting that the prognosis is good for complete resolution of the undesirable sexual behavior following tumor removal until recurrence of the tumor.

All cats herein were euthanized within 16 mo of surgery because of recurrence of clinical signs and/or likely tumor regrowth, even though in 1 of the cats the tumor was identified as an adrenocortical adenoma. Historically, cats have been described to have a poor outcome following adrenalectomy with commonly cited reports of 4/10 cases not surviving more than 14 d after surgery and 5/8 cats dying within 5 wk (12,13). These poor outcomes appear to contrast with our findings and a more recent retrospective study of 33 cats with adrenal neoplasia (2). That study reported a median survival time following surgery of 50 wk and a 2-week survival of 77% (2). In another recent report of 11 cats undergoing laparoscopic adrenalectomy, of the 10 cats that survived to discharge, the median survival time was 114 wk (14). It appears, therefore, that the prognosis following adrenalectomy in cats may be better than previously thought. Survival times did not appear to be affected by histopathologic diagnosis of adrenocortical carcinoma or adenoma in these studies (2,12–14).

In cats with adrenal neoplasia, cortical tumors are reportedly more common than medullary tumors (91% versus 9%, respectively) (2). The adrenal cortex has 3 distinct layers. The outer zona glomerulosa is responsible for aldosterone secretion, the middle zona fasciculata largely secretes glucocorticoids but can secrete small amounts of adrenal androgens and estrogens, and the inner zona reticularis secretes adrenal androgens, with small amounts of estrogens, progesterone, and glucocorticoids (15,16).

Tumors that originate from the zona fasciculata or reticularis could, therefore, secrete estrogen, progesterone, or testosterone resulting in behavior changes. Although the exact cortical location of the tumors reported here could not be determined by histopathology, Case 1 had plasma aldosterone and cortisol concentrations determined before surgery. The aldosterone level was within the reference range ruling out an aldosterone secreting tumor. The baseline cortisol was at the low end of the reference range, but this alone does not exclude a functional cortisol secreting tumor.

Hyperadrenocorticism in cats can be diagnostically challenging but is generally ruled out with a normal high dose dexamethasone suppression test (0.1 mg/kg BW dexamethasone IV).
Table 1. Summary of cats with adrenal tumors without hyperaldosteronism or hypercortisolaemia presenting with sexual behavior changes.

<table>
<thead>
<tr>
<th>Case</th>
<th>Signalment</th>
<th>Presenting complaint</th>
<th>Duration of signs</th>
<th>Preoperative sex hormone levels</th>
<th>Tumor type</th>
<th>Postoperative sex hormone levels</th>
<th>Postoperative behavioral signs</th>
<th>Outcome</th>
<th>Survival time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11 y MN DSH</td>
<td>Urine spraying, mounting</td>
<td>6 mo</td>
<td>Testosterone 0.37 nmol/L (≤ 0.02 nmol/L castrated male). Anti-Müllerian hormone negative</td>
<td>Left adrenocortical carcinoma</td>
<td>2 mo post-surgery: testosterone 0.03 nmol/L (≤ 0.02 nmol/L castrated male)</td>
<td>Complete resolution of clinical signs at 2 mo</td>
<td>Euthanized due to recurrence of clinical signs and presumed tumor regrowth with local metastasis</td>
<td>15 mo</td>
</tr>
<tr>
<td>2</td>
<td>6 y MN DSH</td>
<td>Mounting, howling, aggression, urine spraying, weight loss</td>
<td>2 mo</td>
<td>Testosterone 14 nmol/L (&lt; 0.5 nmol/L castrated male)</td>
<td>Right adrenocortical carcinoma</td>
<td>Immediately post-surgery testosterone 6 nmol/L (&lt; 0.5 nmol/L castrated male); 2 wk post-surgery testosterone 2.6 nmol/L</td>
<td>Resolution in 5 d following surgery</td>
<td>Euthanized due to presumptive cranial abdominal mass</td>
<td>15 mo</td>
</tr>
<tr>
<td>3</td>
<td>4 y FS DSH</td>
<td>Pacing, howling, decreased appetite, agitation and rolling</td>
<td>2 mo</td>
<td>Estradiol 121 pmo/L (&lt; 92 pmo/L spayed female)</td>
<td>Right adrenocortical adenoma</td>
<td>N/A</td>
<td>Resolved within 14 d</td>
<td>Euthanized due to recurrence of clinical signs, elevated estradiol, irregular tissue at surgery site</td>
<td>16 mo</td>
</tr>
<tr>
<td>Millard et al (4)</td>
<td>13 y MN DSH</td>
<td>Urine spraying, malodorous urine, round face, weight loss</td>
<td>2 y</td>
<td>Testosterone 25 nmol/L (&lt; 1.25 nmol/L castrated male)</td>
<td>Right adrenocortical adenoma</td>
<td>2 wk post-surgery: testosterone 0.12 nmol/L (&lt; 1.25 nmol/L castrated male)</td>
<td>Resolved by 8 wk</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Meler et al (3)</td>
<td>15 y FS DSH</td>
<td>Cyclic intermittent estrous behavior (every 2 wk), posturing, licking the vulva, vocalizing, rolling on the ground and head rubbing, weight loss, aggression</td>
<td>1 y</td>
<td>Estradiol 357 pmo/L (206 to 272 pmol/L)</td>
<td>Right adrenocortical carcinoma</td>
<td>1 mo post-surgery: estradiol 345 pmo/L (206 to 272pmol/L); 2 mo: 225 pmol/L</td>
<td>Resolved 24 h after surgery</td>
<td>Euthanized due to chronic renal failure. No evidence of tumor regrowth at that time</td>
<td>10 mo</td>
</tr>
<tr>
<td>Nadolksi et al (5)</td>
<td>14 y MN DSH</td>
<td>Mounting, howling, mammary hyperplasia</td>
<td>1 mo</td>
<td>Estradiol 343 pmo/L (1.44 to 328 pmol/L)</td>
<td>Right adrenocortical carcinoma</td>
<td>18 mo post-surgery: estradiol 210.3 pmo/L (143.5 to 327.8 pmol/L)</td>
<td>Resolved</td>
<td>600 d; no recurrence of mammary development or behavioral signs</td>
<td>N/A</td>
</tr>
</tbody>
</table>

* Gonadal remnants were not found in any of the cases. MN — male, neutered; FS — female, spayed; DSH — domestic shorthair; N/A — not available.
Although that test was not performed in any of the cases herein, a cortisol secreting adrenal tumor was considered unlikely as all 3 cats had normal skin and hair coats, no history of concurrent infections, and normal blood glucose levels, ruling out concurrent diabetes mellitus. Given these results, and clinical resolution of behavioral changes in all cats after surgery, it can be assumed that these tumors secreted sex hormones.

Due to the proximity of the adrenocortical layers responsible for sex hormone production and cortisol, it is important to recognize the risk of potential contralateral adrenal suppression and postoperative hypoadrenocorticism (1,2,17). In a retrospective study of cats with adrenal neoplasia, biochemical, and/or clinical hypoadrenocorticism was only identified in 3 of 26 cats after tumor removal; however, most cats were not tested for this potential postoperative complication (2). In dogs with adrenal tumors, postoperative hypoadrenocorticism is a well-recognized complication following adrenalectomy (17). It is often recommended that dogs receive dexamethasone or another glucocorticoid intravenously upon tumor removal followed by oral prednisone after surgery, tapered over approximately 3 mo (17). Similarly, electrolytes are monitored after surgery as it is possible for some abnormalities to arise within 72 h of surgery (17).

Case 1 was identified to be cortisol deficient following the administration of ACTH within 24 h of adrenalectomy. In hindsight, it would have been interesting to test glucocorticoid reserve with an ACTH stimulation test before adrenalectomy in this case, given the low normal baseline cortisol. The glucocorticoid deficiency resolved over 2 mo with glucocorticoid supplementation; however, it is important to raise awareness of this significant complication before adrenalectomy in cats. In this case, subsequent ACTH stimulation tests at 1 and 2 mo allowed initiation and completion of glucocorticoid tapering. The electrolytes remained normal throughout the peri- and post-operative periods, thus mineralocorticoid supplementation was not necessary.

In the 3 cats reported here, retained gonadal tissue was a differential diagnosis. In Case 1 this was ruled out with a negative anti-Müllerian hormone (AMH) assay. This test was recently validated in dogs and cats (18,19). In dogs, this test has a high specificity (100%) and good sensitivity (90% in females, 76% in males) for determination of remaining gonadal tissue (18). In cats, the use of an AMH assay had a 100% specificity and sensitivity in the ability to detect neuter status (19). The use of this assay is helpful in ruling out this common differential in dogs and cats. Castration status was confirmed at surgery in Cases 1 and 2, and in Case 3, visual inspection and histopathology ruled out an ovarian remnant. These findings, along with the fact that sex hormone concentrations declined and behavioral issues resolved following adrenalectomy, suggest that the behavioral changes were the result of functional adrenal tumors.

Two out of 3 cats reported here had standard midline laparotomy approaches to remove their tumors. Only 1 adrenal tumor was removed laparoscopically. A study in 48 dogs undergoing laparoscopic or open adrenalectomies found that laparoscopic procedures were associated with a low complication rate, a low conversion rate (4%), and shorter hospitalization and surgical times compared with open procedures (20). This makes laparoscopic adrenalectomy an attractive procedure for cats; however, in a previous report of 11 cats with non-invasive adrenocortical tumors removed laparoscopically, the conversion rate was 36% (14). Reasons for conversion included excessive fat, adherence to surrounding vascular structures, and inability to maintain body cavity inflation due to connective tissue fragility (14). Although minimally invasive procedures are typically associated with less postoperative pain and morbidity and increased visualization, the high conversion rate in this species needs to be recognized.

A paucity of information exists on cats presenting with an increase in sexually dimorphic behavior typically seen in sexually intact cats, as the only clinical sign secondary to an adrenal tumor. Clients are particularly interested whether behavioral changes will resolve following surgery. It appears that the prognosis for resolution of behavioral signs is good, until the mass recurs based on these 3 cats. The prognosis for survival is similar to what has been reported in recent studies. In addition, the commonly recognized complication in dogs of postoperative hypoadrenocorticism should be considered in cats and tested for and treated as necessary. For neutered cats presenting with either feminizing or virilizing behavior changes, a sex-hormone secreting adrenal tumor should be a differential diagnosis.

Acknowledgments

The authors thank Dr. John Randolph for his clinical expertise in the management of these cases and Dr. Edward Feldman for review of the manuscript.


New Products
Nouveaux produits

Elanco announced Onsior (robenacoxib) 6 mg tablets for cats are now approved in Canada for the treatment of pain and inflammation associated with chronic musculoskeletal disorders (CMSD), such as osteoarthritis (OA).

Kristin Butler, DVM, veterinary technical consultant with Elanco, says, “This new indication for Onsior tablets for cats is very exciting. Onsior is the 1st labelled nonsteroidal anti-inflammatory drug (NSAID) in Canada that veterinarians can use to help treat chronic painful conditions like osteoarthritis in feline patients. Veterinarians and cat owners now have an effective, safe and convenient solution when treating chronic pain, allowing cats to enjoy more active lives.”

Dr. Butler says Onsior is proven to be effective in providing relief of acute pain and inflammation associated with cat bites and scratches with and without abscesses, as well as for musculoskeletal injuries, such as sprains and strains in cats. She adds that it’s also effective as an adjunctive medication in the control of postoperative surgical pain and inflammation.

That same effectiveness can be applied to the treatment of cats suffering from CMSD. “Chronic pain negatively affects the performance of a cat’s daily activities, as well as its demeanor,” Dr. Butler says. “Studies have proven that when treated with Onsior, cats with CMSD become more active, have an improved temperament, appear happier, and are better able to perform their daily activities. And, Onsior tablets are not only easy to administer but also have a tasty flavoring that cats love.”

Studies also demonstrate long-term safety when cats receive Onsior, as it was well tolerated when administered orally for up to 12 weeks at the recommended therapeutic dose of 1 mg/kg bw/day.

Onsior is easy for cat owners to administer. It is available in small, 6-mg, yeast-flavored tablets that can be given with or without a small amount of food. The majority of cats can be treated with just one tablet per day.

Chronic pain caused by feline degenerative joint disease (DJD), a term often used interchangeably with OA, is a common problem in cats. Although studies vary, on average ~90% of household cats show signs of arthritis on x-ray, but only ~40% of cats showed detectable pain during clinical examination. And when signs of pain are detected, many cats still go untreated. In a study conducted that polled veterinarians, it found that even after being diagnosed with OA, 41% of cats did not receive treatment after diagnosis.

Despite its prevalence, CMSD is difficult to detect for several reasons: behavioral changes in the home are not obvious because they happen gradually; in-clinic assessment can be challenging; cats hide pain and restrict their own activity; and, there is a misconception that changes in behavior are due to cats simply getting older and certain changes are inevitable.

“Osteoarthritis is a common disease in middle-aged and senior cats but it can be challenging to detect, especially for owners,” says Susan Little, DVM, DABVP (Feline), Bytown Cat Hospital, Ottawa. “Changes are gradual and subtle and there is a tendency to think a cat is ‘just getting older’ when actually the cat is in pain from osteoarthritis.” References available upon request.

Contact: Elanco Canada Limited, Research Park Centre, 150 Research Lane, Suite 120, Guelph, Ontario N1G 4T2; phone: 1-800-265-5475; fax: 519-821-7831.
Pemphigus foliaceous

Elizabeth Goodale

**Introduction**

The epidermis consists of multiple layers of keratinocytes and makes up the outer layers of the skin (1). The keratinocytes in the epidermis are held together by desmosomes, which are cell-cell adhesion molecules made of several different proteins, such as desmocolin and desmoglein (1). These adhesion molecules are frequent targets for autoimmune diseases and their destruction results in superficial blistering or acantholysis (1). Pemphigus foliaceous is the most common autoimmune disease in dogs and is most often caused by autoantibodies targeting desmocollin-1 (2,3).

**Clinical presentation**

The classical lesions of pemphigus foliaceous are large pustules that span multiple hair follicles (1,4). The pustules often begin as papules and rapidly progress to crusts and erosions (1,4). Lesions occur most commonly on the trunk, inner pinnae, face, and footpads and are generally symmetrical (4,5). Mucosal lesions are extremely rare and are not considered a feature of pemphigus foliaceous (4). Pruritus is common and dogs with severe generalized disease can have anorexia, depression, fever, and weight loss (1,3,4).

Several breeds are reported as predisposed, but the Akita and chow chow are consistently reported as being overrepresented (3). Other breeds that have been reported as overrepresented include cocker spaniel, dachshund, doberman, collie, and Shar-pei (3). Secondary bacterial infections are common and can make the diagnosis more challenging (1,4). Involvement of the pinnae, nasal planum, and paw pads is more suggestive of pemphigus foliaceous than bacterial pyoderma which more commonly affects the ventrum (1).

Most cases of pemphigus foliaceous are idiopathic, but drug-induced cases have been reported, although the evidence is often weak (1,3,4). A history of atopic dermatitis and flea allergy dermatitis is common, but since these are often found in the general canine population it is unclear if there is truly an increased incidence (5,6). Disease progression can vary widely with some patients showing a rapid progression and other cases having a more gradual course (1,4).

**Diagnostics**

Cytology is a useful tool when initially examining a dog suspected to be suffering from pemphigus foliaceous. It is important to rule out bacterial pyoderma, which is the main...
A definitive diagnosis should be obtained using histopathology before instituting treatment. Dogs with secondary bacterial pyoderma should be treated with antibiotics for 2 to 4 wk before obtaining biopsies whenever possible. Biopsies should be taken from intact pustules or tightly adherent crusts. Care should be taken to avoid rupturing the pustules or removing the crusts while obtaining samples. This typically means that the skin should not be scrubbed. If a crust falls off the sample, it should be included in the formalin jar. Multiple punch or wedge biopsy samples should be taken and submitted to a dermatohistopathologist.

The classical histopathological findings for pemphigus foliaceous are subcorneal pustules containing rafts of acantholytic keratinocytes (7). These pustules are often layered and span multiple hair follicles (7). Nondegenerate neutrophils, and less commonly eosinophils, are typically present within the pustules (4,7). Special stains to rule out dermatophytosis should be considered (7).

Routine hematology and biochemistry should be performed before instituting therapy for pemphigus foliaceous (1). A severe neutrophilia is common (1).

**Treatment**

Treatment of pemphigus foliaceous requires the use of immunosuppressive medications. Corticosteroids are the most commonly used medications either as a single agent or concurrently with a second immunosuppressive medication (1,4). Prednisone or prednisolone at a dose of 2 mg/kg body weight (BW) per day either given once daily or divided into twice daily dosing is the most common medication used (3). Some clinicians prefer to use methylprednisolone because it has less mineralocorticoid activity and may cause less polyuria and polydipsia (8). Refractory cases may respond to more potent glucocorticoids such as triamcinolone (0.2 to 0.6 mg/kg BW per day) or dexamethasone (0.2 to 0.4 mg/kg BW per day) (8). Short- and long-term side effects are common with corticosteroid usage and include polyuria, polyphagia, panting, increased risk of infections (urinary tract infections, pyoderma, demodecticis, dermatophytosis), alopecia, cutaneous atrophy, calcinosis cutis, and steroid hepatopathy (1,8,9).

One retrospective study did not find a significant difference in treatment outcomes for cases treated with corticosteroid monotherapy compared with prednisone and azathioprine used in combination (4). Regardless of these findings, many clinicians (including the author) typically begin with a combination of a corticosteroid and a second immunosuppressive medication for cases of generalized pemphigus foliaceous and reserve single agent corticosteroids for mild cases (1).

If there is secondary bacterial infection it should be treated. Antibiotic use at the beginning of treatment was associated with a better outcome in 1 study, but other studies have not found a significant difference between cases treated with and without antibiotics (4,6).

Azathioprine is the most frequently reported secondary immunosuppressive medication used to treat pemphigus foliaceous (1,4). Azathioprine is a purine antagonist that is less expensive than many of the other immunosuppressive medications (1). Side effects include pancreatitis, bone marrow suppression, and hepatotoxicity, so a baseline complete blood count and serum biochemistry profile should be obtained prior to initiating therapy (1,10). This should be repeated after 2 wk, 4 wk, and monthly for the first 3 mo (10). Hepatotoxicity is most likely to occur within the first 2 to 4 wk and bone marrow suppression typically occurs with prolonged usage (10). It is typically dosed at 2.2 mg/kg BW once daily and clinical response can take 3 to 6 wk (1,9).

Cyclosporine has been reported to have variable success in managing pemphigus foliaceous (11–13). Cyclosporine is a calcineurin inhibitor that is commonly used to treat atopic dermatitis in dogs (1,13). Transient vomiting and diarrhea are the most common side effects and the maximal effect is typically seen after 4 wk (9,13). Anecdotally, freezing the capsules and administering them frozen reduces the incidence of vomiting and does not appear to impact the bioavailability (13,14). The use of the brand name microemulsified product is preferred, but this medication is unfortunately very expensive and can be cost-prohibitive in large dogs. Doses between 5 to 10 mg/kg BW per day are typically recommended for pemphigus foliaceous (8,13).

Mycophenolate mofetil is a purine antagonist that has not been used as extensively as azathioprine, but is gaining popularity in the treatment of pemphigus foliaceous (1,15). Mycophenolate mofetil has fewer side effects than azathioprine, so intensive monitoring of blood is not required (1,9). Diarrhea is the most common side effect reported and clinical response can take 3 to 8 wk (1,9,15). Doses of 20 to 40 mg/kg BW per day divided into 2 to 3 doses daily are recommended for pemphigus foliaceous (9,15).

Typically treatment with corticosteroids, with or without a secondary immunosuppressive agent, is instituted and continued until complete remission is achieved (1). The corticosteroids are then tapered by 25% every 2 to 4 wk until doses less than 0.5 mg/kg BW every other day for prednisone, 0.05 to 0.1 mg/kg BW every 2 to 3 d for dexamethasone, or 0.1 to 0.2 mg/kg BW every 2 to 3 d for triamcinolone are achieved (1). The secondary agent is then tapered with the ultimate goal of giving the corticosteroid and secondary agent every other day or on alternating days (1,8).

For milder cases, the use of a combination of tetracycline (or doxycycline) and niacinamide has been reported (16). This combination of an antibiotic and a B vitamin has immunomodulatory effects, although the exact mechanisms are not fully understood (1). Hepatotoxicity has been rarely reported with doxycycline, and generally this combination is well-tolerated (9).
This drug combination has a very slow onset of action, which limits its utility in cases of pemphigus foliaceus that are generalized or severely pruritic (1). This can be combined with corticosteroids to try to hasten the onset of action (8). Tetracycline and niacinamide are dosed at 500 mg of each 3 times daily for dogs weighing > 10 kg and 250 mg of each 3 times daily for dogs weighing < 10 kg (8,16). Topical glucocorticoids or tacrolimus 0.1% could also be considered for localized lesions (1,8).

Prognosis

Retrospective studies have found variable treatment success rates, but generally most cases have a positive response to treatment (1,3). An older retrospective study reported a 1-year survival of 53% and another had a case fatality rate of 60.5% (5,6). Newer retrospective studies have had more positive outcomes with 52% and another had a case fatality rate of 60.5% (5,6). Survival beyond 10 mo is associated with a positive long-term outcome (6). There does not appear to be any difference in treatment outcomes for dogs with localized versus generalized disease or rapid onset versus slow onset (4). Most patients with pemphigus foliaceus will require lifelong treatment with medication although they are tapered to the lowest effective dose (1). A few patients may have prolonged periods of remission after their treatments have been withdrawn (4,17).

In conclusion, pemphigus foliaceus is the most common autoimmune disease affecting dogs (1). It is most commonly associated with bilaterally symmetrical crusting affecting the head, trunk, and footpads (4,5). A definitive diagnosis is made with histopathology, but cytology should be used to help differentiate cases from superficial pyoderma (1,4). Treatment typically requires immunosuppressive doses of glucocorticoids with or without a secondary immunosuppressive medication (1,4,5,8). Many clinicians initiate treatment with a combination of glucocorticoids and a secondary immunosuppressive medication but there is no clear evidence that this improves outcomes over glucocorticoid monotherapy (4). Most patients will require lifelong treatment, but the doses should be tapered to the lowest effective dose (1). A few patients may be euthanized due to treatment failure, treatment side effects, or poor quality of life, which most commonly occurs during the early phase of treatment (6).

References

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EXPERIENCE TORONTO: DISCOVER THE WORLD
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Saskatchewan and Newfoundland & Labrador had increases in revenue and net income well above the national weighted average growth rate. On the other side of the coin, Alberta, Nova Scotia, Prince Edward Island, and British Columbia saw their net incomes decline year-over-year.

Typically, when revenues are expanding, the dollar amount of expenses will grow as well. This stands to reason, as a hospital that is seeing more clients and pets, providing more services, performing more surgeries, selling more medications and pet foods, will incur a greater cost in the generation of this revenue. It is for this reason that expenses are expressed as a percentage of gross revenue, allowing for a meaningful comparison across both provinces and years, while the amount of gross revenue may fluctuate widely.

After hitting a high of 69.6% in 2016, Canadian companion animal hospitals have been able to significantly decrease their non-DVM expenses as a percentage of gross revenue, falling to 68% in 2018 (Figure 2). On a revenue of $591 757, this equates to expenses falling by almost $9500 per FTE DVM.

This would seem to indicate a shifting focus among Canadian companion animal hospitals. In previous years, much emphasis was placed on boosting revenues, sometimes to the detriment of prudent expense control. As a result, both revenues and expenses expanded, resulting in slower growth in net incomes. Today, companion animal hospitals continue to strive to grow their revenue, yet also appear to be taking budgeting seriously, as evidenced by the decline in expenses. This is great news for net incomes.

While the financial metrics were all positive, client metrics were less encouraging. Both current clients per FTE DVM and new clients per FTE DVM declined in 2018, by 3.2% and 4.1%, respectively (Figure 3). While these figures remain above the lows of 2015, the decline does raise some cause for concern.

Combining the financial metrics with the client metrics paints a picture of the average Canadian companion animal veterinarian doing more with fewer clients. Certainly, some of the revenue growth has been a result of fee increases, yet another portion has been through increased compliance and greater spending by each client.

Increasing revenues aside, a shrinking client base will eventually limit this growth. Retaining current clients, attracting new clients, raising fees, and improving compliance, all in tandem, would seem to indicate a shifting focus among Canadian companion animal hospitals. In previous years, much emphasis was placed on boosting revenues, sometimes to the detriment of prudent expense control. As a result, both revenues and expenses expanded, resulting in slower growth in net incomes. Today, companion animal hospitals continue to strive to grow their revenue, yet also appear to be taking budgeting seriously, as evidenced by the decline in expenses. This is great news for net incomes.

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Increasing revenues aside, a shrinking client base will eventually limit this growth. Retaining current clients, attracting new clients, raising fees, and improving compliance, all in tandem,
will allow veterinary hospitals to expand at a faster rate. To retain current clients and boost compliance, pre-booking routine appointments and implementing Wellness Plans are 2 strategies that have been shown to be impactful. For attracting new clients, providing great service to current clients and encouraging recommendations, as well as ensuring a positive online presence, are a hospital’s best bets to endear themselves to those pet owners seeking a veterinarian.

**Mixed and large animal hospitals**

Mixed and large animal hospitals across Canada also had an exceptionally positive year, with revenues and net incomes surging. The national weighted average revenue climbed by 13.2%, to $535 851 per FTE DVM, far surpassing the previous record high set in 2017. While expenses also increased by a substantial 15.6%, this was not enough to stop the jump in profitability; net incomes grew by 8.7%, to a national weighted average of $178 987 per FTE DVM (Figure 4).

Unlike companion animal hospitals, the headline positive news in mixed and large animal hospitals extended almost universally to the constituent provinces. Revenues expanded in all provinces measured, with above-average growth in Manitoba, British Columbia, and Saskatchewan. The only mild hiccup was in Alberta; revenues increased, but were outpaced by growing expenses, resulting in a slight decline in net incomes.

**Cliniques mixtes et pour grands animaux**

Les cliniques mixtes et pour grands animaux du Canada ont aussi connu une année exceptionnellement positive et ont observé un bond du revenu et du bénéfice net. Le revenu moyen pondéré à l’échelle nationale a grimpé de 13.2%, pour se situer à 535 851 $ par vétérinaire ETP, dépassant largement l’ancien record établi en 2017. Tandis que les dépenses ont aussi augmenté d’un pourcentage substantiel de 15,6 %, ce chiffre n’a pas été suffisant pour freiner la hausse de la profitabilité, et le bénéfice net a augmenté de 8,7%, pour une moyenne pondérée nationale de 178 987 $ par vétérinaire ETP (Figure 4).

Contrairement aux cliniques pour animaux de compagnie, les nouvelles positives pour les cliniques mixtes et pour grands animaux s’étendaient presque universellement à toutes les provinces. Les revenus ont augmenté dans toutes les provinces...
After a few years of declining expenses, mixed and large animal hospitals saw a slight tick upwards in 2018, with non-DVM expenses as a percentage of gross revenue rising to 66.5%. This remains below the companion animal figure of 68%, and well below the recent high of 69.4% in 2015 (Figure 5).

While companion animal veterinarians appeared to focus on expense control in 2018, their mixed and large animal colleagues seemingly directed their attention to expanding revenues. Fortunately, the escalation of expenses remained modest in mixed and large animal hospitals. Moving forward, it will be important to continue controlling expenses through budgeting and monitoring of expenditures, to ensure that revenue growth translates into greater net income.

As in previous years, positive results can breed complacency. A veterinary hospital that is busy and growing may not see the need to implement strategies such as Wellness Plans or budgeting. However, the cyclical nature of economic expansions dictates that the next downturn or recession will eventually arrive. Make hay while the sun is shining to better prepare for any storm clouds on the horizon.

Notes: Data for the CVMA Practice Owners Economic Survey are derived from the 2018 Provincial Practice Owner’s Economic Surveys. Provincial averages are weighted based on relative population size to calculate a national weighted average for all metrics. For the purposes of this research, a full-time equivalent veterinarian is assumed to work 1750 hours annually. Note that, due to data gaps in 2014 and 2015, Quebec is omitted from the calculation of the national averages for all years presented.
A 14-year-old spayed female Yorkshire terrier dog was examined at the ophthalmology service at the Western College of Veterinary Medicine for evaluation of bilateral corneal opacity and ocular discharge. The menace responses, palpebral, oculocephalic, and direct and consensual pupillary light reflexes were present bilaterally. Schirmer tear test (Schirmer Tear Test Strips; Alcon Canada, Mississauga, Ontario) values were 10 and 7 mm/min in the right and left eyes, respectively. The intraocular pressures were estimated with a rebound tonometer (Tonvet; Tiolat, Helsinki, Finland) and were 22 and 23 mmHg in the right and left eyes, respectively. Fluorescein staining (Fluorets; Bausch & Lomb Canada, Markham, Ontario) was negative bilaterally. On direct examination there was bilateral mucoid ocular discharge, conjunctival hyperemia, superficial pigmentation extending from the limbus toward the central cornea, and diffuse corneal opacity which was denser on the lateral aspect of the corneas of both eyes. Biomicroscopic examination (Osram 64222; Carl Zeiss Canada, Don Mills, Ontario) revealed the opacity to be associated with thickened corneal stroma consistent with corneal edema. Following application of 0.5% tropicamide (Mydriacyl; Alcon Canada, Mississauga, Ontario) indirect ophthalmoscopic (Heine Omega 200; Heine Instruments Canada, Kitchener, Ontario) examinations were completed bilaterally and abnormalities were not detected. Photographs of the right and left eyes at presentation are provided for your assessment (Figure 1).

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

Discussion

Our clinical diagnoses were bilateral corneal edema due to corneal endothelial dysfunction and keratoconjunctivitis sicca (KCS). Corneal edema due to endothelial dysfunction is associated with a variety of causes, including age-related endothelial degeneration, inherited corneal endothelial dystrophy, which is most common in the Boston terrier, as well as endothelial damage associated with persistent pupillary membranes, mechanical trauma (e.g., anterior lens luxation, intraocular surgery), toxic reactions, anterior uveitis, endothelial inflammation, and glaucoma (1). In this case, the signalment and clinical findings were most consistent with age-related corneal endothelial degeneration.

Keratoconjunctivitis sicca in dogs is most commonly due to immune-mediated destruction of the lacrimal gland. In this case, the KCS was coincident rather than related to the corneal endothelial degeneration. The main clinical manifestations of
KCS noted in this dog included conjunctival hyperemia, mucoid ocular discharge, and corneal pigmentation.

The corneal endothelium is a single layer of cells lining the inner cornea and is both a physical and physiological barrier to corneal stromal absorption of aqueous humor. The endothelium normally maintains relative dehydration of the cornea by an energy-dependent, sodium-potassium transport pump that actively transports aqueous humor into the anterior chamber (1). As animals age, the endothelial cell density gradually decreases. In many species, including the dog, corneal endothelial cells do not regenerate following loss or injury. To maintain a functional monolayer, endothelial cells enlarge and migrate rather than divide (2,3). If cell numbers become too diminished there are insufficient pumps present to remove aqueous humor from the stroma. Corneal decompensation and development of edema usually occur when the cell density falls below 500 to 800 cells/mm² (1).

The diagnosis of corneal endothelial degeneration is based on signalment and clinical manifestations. The main clinical manifestation of corneal endothelial degeneration is loss of corneal clarity due to corneal edema. The corneal opacity has a bluish-white appearance with a lack of corneal vascularization or conjunctival hyperemia. In this case, the conjunctival hyperemia and corneal pigmentation were due to KCS rather than endothelial disease. Initially, corneal edema is often located temporally and progresses slowly to involve the entire cornea. With progression of endothelial degeneration the severity of edema increases. This leads to compromised vision as well as formation of multifocal fluid-filled bullae in the corneal stroma and epithelium. These bullae can rupture causing painful ulcerative keratitis (2,4).

Therapy for corneal edema due to endothelial degeneration is usually palliative and aimed at managing clinical signs. Application of hyperosmotics may decrease the extent of bullae formation by drawing fluid out of the cornea; however, significant corneal clearing does not occur. The most commonly used agents are 5% NaCl ointment or solution. The frequent necessary application and occasional local irritation can limit usefulness of hypertonic saline treatment and while it may be effective in mild cases, it eventually fails to maintain corneal dehydration as the condition progresses. Corneal ulcerations are managed using topical broad-spectrum antibiotics in addition to the hyperosmotics. Persistent or recurrent corneal ulceration can necessitate surgical intervention to relieve ocular pain. Surgical options for treatment of severe corneal edema due to endothelial dysfunction include penetrating keratoplasty, thermokeratoplasty, and permanent conjunctival grafts (1,4). Penetrating keratoplasty or corneal transplantation is the only definitive treatment for endothelial cell dysfunction. This surgery is infrequently performed in dogs, however, due to difficulty in obtaining fresh corneal tissue for transplantation. Additionally, rejection of transplanted cornea and subsequent loss of corneal clarity is a potential complication. Thermokeratoplasty uses cautery to induce fibrosis of the anterior stroma, forming a barrier against uptake of fluid. The subepithelial scar tissue acts as a partial barrier to the flow of fluid through the cornea and helps reduce build-up of fluid that results in epithelial bullae (4). Because the primary complication is corneal scarring, this is only indicated when prognosis for vision is poor.

Superficial keratectomy and conjunctival advancement hood flap (SKCAHF) has been reported for the management of bullous keratopathy secondary to progressive corneal edema (5,6). In a case series of 9 dogs, authors noted improvement in corneal edema that lasted for at least 1 year with resolution of corneal bullae and reduction in frequency of topical NaCl. Improvement in vision and corneal clarity following hood flap placement was also noted (5). The precise mechanism by which corneal edema is improved with SKCAHF is unknown. It is speculated that stromal fluid takes the path of least resistance through the keratectomized area (6). The conjunctival flap may help maintain corneal detergescence by providing an alternate route for fluid drainage via conjunctival vessels. While corneal clarity adjacent to the graft may be improved, it is impaired in the region of the graft itself (6).

Corneal collagen cross-linking (CXL) was recently reported as a potential treatment for corneal edema and bullous keratopathy. This treatment is based on the exposure of the photosensitizer riboflavin (Vitamin B2) to UV-A light with a wavelength at the riboflavin absorption peak. The result is an increase in the biomechanical and biochemical stability of the cornea. In dogs in which CXL has been used for bullous keratopathy, resolution in corneal ulceration and ocular pain has been reported for up to 6 months. Current protocols for CXL have been shown to improve patient comfort but not achieve resolution of corneal edema (7,8).

In this dog, symptomatic treatment for corneal edema was initiated with topical 5% NaCl ophthalmic solution (Muro 128; Bausch & Lomb Canada, Vaughan, Ontario) 3 to 4 times daily. Treatment for KCS was initiated with a topical immunomodulating lacrimostimulant, 0.2% cyclosporine ointment twice daily (Optimmune; Merck Animal Health, Madison, New Jersey, USA). Superficial keratectomy with conjunctival hood graft placement was recommended as an option for future therapy to address the progressive corneal edema.

The prognosis for corneal endothelial dysfunction is guarded. Progressive loss of corneal endothelial cells with time leads to progressive corneal edema, which causes vision loss as well as persistent or recurrent painful corneal ulcerations. Symptomatic therapy with hypertonic saline is often inadequate and surgical interventions may eventually be required to maintain comfort.

References
5. Horikawa T, Thomasy SM, Stanley AA, et al. Superficial keratectomy and conjunctival advancement hood flap (SKCAHF) for the management of


Answers to Quiz Corner
Les réponses du test éclair

1. B) Mucus and hematochezia are common with large bowel diarrhea. All other statements are correct.

2. D) Most cases of megacolon in cats are idiopathic.

3. E) Borrelia burgdorferi is NOT transmitted from pets to humans.

4. B) Pregnancy is not palpable until approximately 35 days gestation. Pregnancy occurs on the ipsilateral side to the corpus luteum. Also, it is not recommended to breed cows until approximately 60 days after calving, so that the intercalving interval approximates a year. Mucometra is associated with ovaries containing thin-walled, follicular cysts and no corpora lutea. Neoplasia does occur in the uterus, but does not distend the uterus with fluid. The most common types of neoplasia are leiomyomas, fibromyomas, fibromas, adenocarcinomas, and lymphosarcomas. Likewise, the palpable characteristics of mummies are pathognomonic, and not fluid in nature.

5. A) Chinchillas are very susceptible to Listeria monocytogenes.

B) La présence d’un fœtus n’est pas palpable jusqu’à environ 35 jours de gestation. La gestation a lieu du côté ipsilatéral au corps jaune. Aussi, il n’est pas recommandé d’accoupler les vaches jusqu’à environ 60 jours après le vêlage, de sorte que l’intervalle entre les vêlages soit d’environ 1 an. Le mucomètre est associé aux ovaires possédant des kystes folliculaires à parois minces sans corps jaune. Les néoplasies peuvent affecter l’utérus, mais ne causent pas de distension de l’utérus par du liquide. Les néoplasies les plus fréquentes sont les léiomyomes, les fibromyomes, les fibromes, les adénocarcinomes et les lymphosarcomes. Les caractéristiques palpables des fœtus momifiés sont pathognomoniques et ne sont pas liquides de nature.

A) Les chinchillas sont très sensibles à Listeria monocytogenes.
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