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La Revue vétérinaire canadienne

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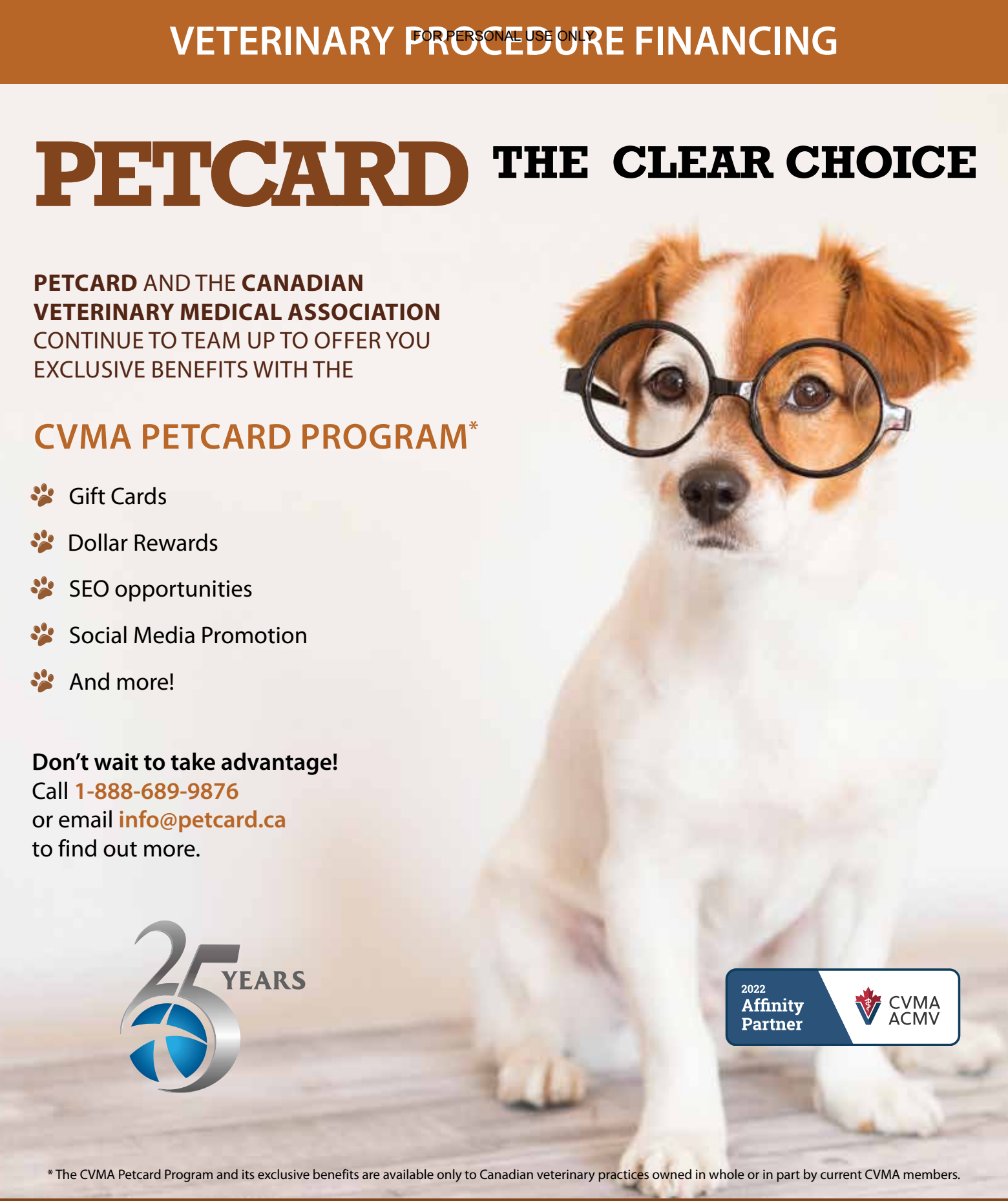

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"Instructions for authors" are available online (www.canadianveterinarians.net).

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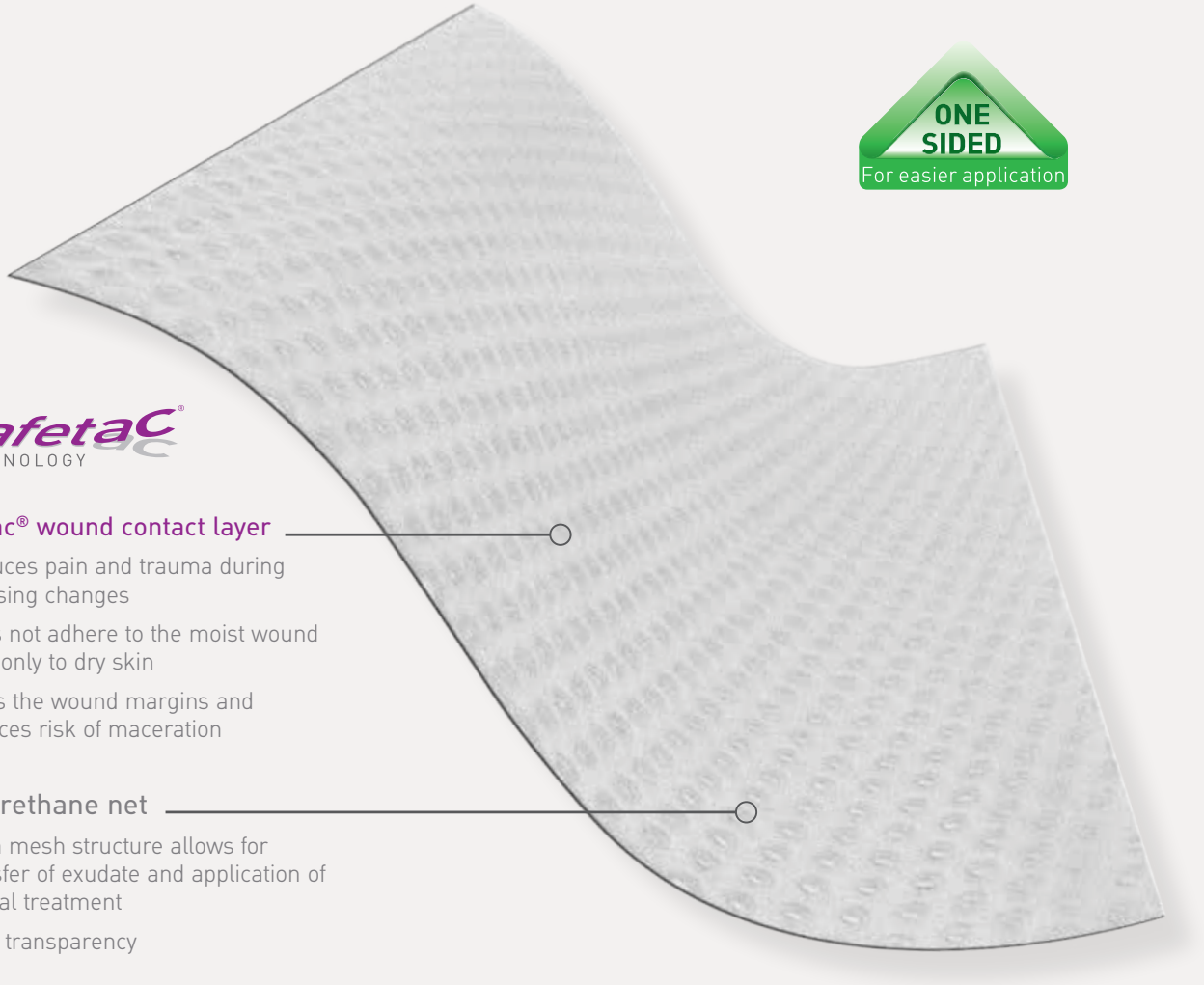

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Editorial Éditorial

Moving Quiz Corner forward!

Un nouveau format pour le test éclair!

Dr./Dr John Kastelic

Dr./Dr Tim Ogilvie

We are thrilled to announce that, with this issue, our Quiz Corner feature has been substantially updated.

Surveys of our readership have consistently indicated that this feature is popular and greatly appreciated. It has been a long-standing source of practice questions for students and graduate veterinarians preparing for the North American Veterinary Licensing Examination (NAVLE). Furthermore, there are also clear indications that it is frequently read by practitioners who use it as a personal challenge and source of informal Continuing Professional Education.

Despite its success and popularity, after nearly 3 decades, it was abundantly clear that it was time to refresh Quiz Corner and make substantial upgrades to question content, format, style, and presentation. Through these changes, we will strive to conform to current learning, teaching and testing methodologies, to adopt current NAVLE-style questions, and embrace contemporary pedagogy regarding learning and testing. For more insights into contemporary learning and pedagogy, we recommend the website for the Centre for Teaching Excellence at the University of Waterloo (1).

The first Quiz Corner appeared in *The Canadian Veterinary Journal* in October, 1993 (2). Although this feature began as a series of 10 questions and answers, it was modified to 5 questions and answers in 2014. Regardless, it has always appeared monthly.

From the outset, the questions and answers for Quiz Corner were derived from *Review Questions and Answers for Veterinary Boards* used by kind permission of the publisher, Mosby–Year Book, Inc., St. Louis, Missouri. For several years, our source was the 1st edition and more recently, it has been the 2nd edition of a 5-volume series including: Basic Sciences; Clinical Sciences; Small Animal Medicine and Surgery; Large Animal Medicine and Surgery; and Ancillary Topics.

Nous sommes fiers de vous présenter dès ce mois-ci le nouveau format revu et amélioré du test éclair!

Les sondages auprès de nos lecteurs indiquent que cette rubrique demeure toujours aussi populaire et appréciée. Elle est depuis longtemps une source de questions pratiques pour les étudiants et les vétérinaires diplômés qui se préparent en vue de l'examen nord-américain d'agrément vétérinaire (NAVLE), et elle est aussi souvent consultée par les praticiens qui l'utilisent comme un défi personnel et de la formation continue informelle.

Malgré son succès, après près de trois décennies, le temps était venu de revamper le test éclair et d'apporter des changements importants au contenu, au format, au style et à la présentation des questions. Avec ces modifications nous souhaitons nous conformer aux méthodes actuelles d'apprentissage, d'enseignement et d'évaluation, adopter le style actuel des questions du NAVLE, et observer la pédagogie contemporaine en matière de transmission des connaissances et d'examens. Si vous souhaitez en savoir plus sur ces méthodes et la pédagogie contemporaine, nous vous invitons à consulter le site du Centre for Teaching Excellence de l'Université de Waterloo (1).

Le premier test éclair est paru dans *La Revue vétérinaire canadienne* en octobre 1993 (2). Il a paru tous les mois depuis – avec 10 questions initialement, et 5 questions depuis 2014.

Dès le début, les questions et réponses du test éclair étaient tirées de *Review Questions and Answers for Veterinary Boards* et utilisées avec l'aimable permission de l'éditeur, Mosby–Year Book, Inc., de Saint-Louis, au Missouri. Pendant plusieurs années, nous avons utilisé la première édition, puis la deuxième depuis plus récemment, de ce manuel en cinq volumes consacrés aux sciences fondamentales, aux sciences cliniques, à la médecine et à la chirurgie des petits animaux, à la médecine et à la chirurgie des grands animaux, et à divers sujets connexes.

These sources have served us well and we have greatly appreciated the privilege of using them. However, over the years, there have been many changes in both the form and content of NAVLE-style questions, recommended approaches to studying and test-taking, and delivery of Continuing Professional Education. In particular, there have been shifts away from stand-alone multiple choice questions. The current approach encourages learning in context by using multiple choice questions based on case scenarios augmented with photographs, diagnostic images, laboratory findings, and other supplemental materials, and with detailed explanations in answer keys.

For a source of these new-style questions, we are working with a team from Zuku Review (4) who have graciously agreed to provide 2 multiple choice questions/month accompanied by images and other supplemental material. Answers will appear on a separate page (similar to present Quiz Corner configuration), accompanied by more complete explanations and references. We are confident that limiting this feature to 2 questions monthly will facilitate inclusion of valuable ancillary material (photos, etc.), as well as more comprehensive explanations, and still respect space considerations. Also, given the broad perspectives of our readership, we intend to provide a balanced set of questions, taking into account species, discipline, speciality, etc.

We encourage you to share with us your assessment of the new version of Quiz Corner. Finally, we remind you that we are always pleased to receive your comments and input regarding the *CVJ,* as that helps us to further refine and improve **your** journal.

References

1. https://uwaterloo.ca/centre-for-teaching-excellence/ Last accessed March 28, 2022.
2. Quiz Corner. Can Vet J 1993;34:598–599, 629.
3. Review Questions and Answers for Veterinary Boards for several years the 1st and then for most of its existence, 2nd ed., a 5-volume series including Basic Sciences, Clinical Sciences, Small Animal Medicine and Surgery, Large Animal Medicine and Surgery, and Ancillary Topics, by kind permission of the publisher, Mosby–Year Book, Inc., St. Louis, Missouri.
4. https://zukureview.com/ Last accessed March 28, 2022. ■

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John Kastelic (jpkastel@ucalgary.ca)

Cet ouvrage nous a bien servi et nous sommes reconnaissants d'avoir eu le privilège de pouvoir l'utiliser. Cependant, au fil des ans, il y a eu de nombreux changements dans la forme et le contenu des questions du NAVLE, les approches recommandées pour étudier et pour passer les tests, et la prestation de la formation professionnelle continue. Par exemple, on voit de moins en moins de questions simples à choix multiples. L'approche actuelle encourage l'apprentissage en contexte en utilisant des questions à choix multiples basées sur des scénarios de cas complétés par des photographies, des images diagnostiques, des résultats de laboratoire et d'autres éléments, et préconise de fournir des explications détaillées dans le corrigé.

Pour offrir ce nouveau style de questions, nous travaillons avec une équipe de Zuku Review (4) qui a gracieusement accepté de nous transmettre deux questions d'autres éléments à choix multiples par mois accompagnées d'images et de matériel à l'appui. Les réponses apparaîtront sur une page distincte (comme c'est le cas actuellement), et seront étayées par des explications et des références plus complètes. Nous sommes convaincus que nous limiter à deux questions par mois facilitera l'inclusion d'éléments connexes importants (photos, etc.) et d'explications plus approfondies, tout en respectant l'espace dont on dispose. De plus, compte tenu du vaste éventail d'intérêts de notre lectorat, nous avons l'intention de proposer des questions sur divers sujets touchant différentes espèces, disciplines, spécialités, etc.

Nous vous encourageons à nous faire part de vos commentaires sur le nouveau format du test éclair, et nous vous rappelons que nous sommes toujours heureux de recevoir vos avis et suggestions concernant *La RVC*, car vous nous aidez à peaufiner et à améliorer **votre** revue.

Références

1. https://uwaterloo.ca/centre-for-teaching-excellence/ (dernière consultation le 28 mars 2022).
2. Test éclair. *Can Vet J* 1993;34:598-599, 629.
3. Les questions et les réponses du test éclair ont été tirées de *Review Questions and Answers for Veterinary Boards* (de la première édition pendant plusieurs années puis de la deuxième édition pour la majeure partie de son existence), un manuel comprenant cinq volumes intitulés *Basic Sciences*, *Clinical Sciences*, *Small Animal Medicine and Surgery*, *Large Animal Medicine and Surgery* et *Ancillary Topics*, avec l'aimable permission de l'éditeur, Mosby–Year Book, Inc., de Saint-Louis, au Missouri.
4. https://zukureview.com/ (dernière consultation le 28 mars 2022). ■

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Ethical question of the month — March 2022

The Canadian Veterinary Medical Association (CVMA) position statement on the Care of Neonatal Calves on Dairy Farms states that euthanasia/humane killing of surplus calves is the preferable option to the suffering endured by calves without a ready place to care for them. This practice of euthanasia/humane killing of newborn calves may put the dairy industry, and the veterinarians that provide care, at risk of losing public trust — specifically the public statement indicating that the CVMA condones euthanasia of healthy calves if there is no other avenue for marketing these calves. It must be considered that many veterinarians ethically object to killing healthy companion animals for the convenience of the owners. In Europe, euthanasia of healthy calves is already outlawed in some countries (e.g., Denmark) and in others there is a commitment to ending this practice (Ireland, Great Britain). There is a clear expectation by society that farmers accept the role that they are experts in animal care, and with this comes responsibilities regarding duty of care for all animals, including low-value surplus offspring that are born to sustain the farmer's business. **Are veterinarians at risk of losing public trust if they condone euthanasia/humane killing of these animals in a position statement?**

Question de déontologie du mois — Mars 2022

L'énoncé de position de l'Association canadienne des médecins vétérinaires (ACMV) sur les soins aux veaux nouveau-nés dans les fermes laitières indique que l'euthanasie ou l'abattage sans cruauté des veaux excédentaires est préférable aux souffrances endurées par les veaux s'il n'est pas possible de leur fournir des soins adéquats. Cette pratique d'euthanasie ou d'abattage sans cruauté des veaux nouveau-nés peut ébranler la confiance du public envers l'industrie laitière, et envers les médecins vétérinaires qui prodiguent les soins puisque l'ACMV déclare publiquement qu'elle tolère l'euthanasie de veaux en bonne santé s'il n'y a pas de possibilité de les vendre. Or, beaucoup de médecins vétérinaires s'opposent éthiquement à l'euthanasie « de convenance » d'animaux de compagnie en santé. En Europe, l'euthanasie des veaux en santé est déjà interdite dans certains pays (le Danemark, par exemple) et on s'est engagé à mettre fin à cette pratique dans d'autres (Irlande, Grande-Bretagne). La société s'attend à ce que les agriculteurs acceptent leur rôle d'experts en matière de soins aux animaux, et ce rôle vient avec la responsabilité de s'occuper de tous les animaux, y compris les veaux excédentaires ayant peu de valeur économique qui sont nés pour soutenir les activités des producteurs. **Les médecins vétérinaires risquent-ils de perdre la confiance du public s'ils tolèrent l'euthanasie ou l'abattage sans cruauté de ces animaux dans un énoncé de position?**

Ethicists' commentary on humane killing of healthy surplus animals

This month's question concerns a CVMA position statement allowing for the humane killing of healthy new-born bull calves considered surplus. In fact, there are really 2 questions: an explicit one about public trust, and an implicit one about the ethical position reflected in the statement.

The question about public trust implies that if veterinarians act in ways that do not fit neatly with public values, public trust in the profession will be undermined. In our view, whereas disconnects between policy and public intuitions should be taken seriously, the veterinary profession should always take an honest stance when making policy and should avoid making commitments merely to please a potentially critical public. In the long term, this approach should build trust rather than diminish it.

This leads us to the second question: can the CVMA statement on the humane killing of surplus calves stand up to ethical scrutiny? At first blush the answer seems obvious; offering a humane death to avoid the prospect of severe suffering has long been a central service of the veterinary profession. Indeed, shirking the responsibility to diminish animal suffering can be seen as serious breach of veterinary ethics, as we have discussed in previous answers. In this sense, euthanizing a surplus calf to save it from certain suffering (for example, on a farm ill-equipped to care for it) can be seen as fulfilling a central commitment of the veterinary oath.

However, the issue of killing newborn calves of little economic value to the dairy industry reflects a systemic issue that has been with us for generations: many more calves (especially male calves) are typically born than can be used on dairy farms. In this context, we argue that although a veterinarian may, in the short term, help a client with the 'least-bad' option

of humane killing, such a veterinarian should also, possibly in collaboration with other advisors, work with the client to implement other options now available to the dairy industry to proactively address the underlying issue in the medium to long term. These options include the use of sexed semen and beef genetics as detailed in the June 2021 CVMA Position Statement. This balance is arguably implied in the current wording of the Statement: "Veterinarians should support their clients by providing advice on how to meet appropriate health and welfare standards, and if necessary, how to provide appropriate methods of euthanasia/humane killing."

Now, given this context, let us return to the question of public trust. Enabling a humane death for animals, such that they avoid suffering, is a core service of the profession — provided that there is no better alternative. But this action needs to be seen in its larger context. If veterinarians are seen to be complicit in a system that doesn't actively try to prevent the problem of producing surplus animals (that must then be killed as part of routine practice), their reputation is indeed likely to be tarnished.

Drs. Clare Palmer, Peter Sandøe, and Dan Weary

Ethical question of the month — June 2022

You are an equine veterinarian who relies on firocoxib as your "go to" for chronic arthritis pain. There was no equine-labelled product in Canada until recently, so you were dispensing a divided dose of the canine product. An equine product has recently come available but is almost 2.5 times the cost. When you raise this issue with the pharmaceutical manufacturer, their response is that you should lower your markup on the medication. You comply, despite it being a less than ideal practice management decision, as you are concerned some of your clients cannot or will not afford the price increase and their horses will go without pain control.

You see a horse that you have prescribed firocoxib and your client tells you she has found a small animal veterinarian that will prescribe the less expensive canine version of the drug to use for her horse. She is unwilling to provide the name of the prescriber. **What do you do?**

Question de déontologie du mois — Juin 2022

Vous êtes en pratique équine et le firocoxib est votre agent de prédilection pour soulager la douleur chronique associée à l'arthrose. Il n'y avait pas de produit homologué chez les chevaux au Canada jusqu'à récemment, donc vous utilisiez les comprimés pour chiens. Un produit conçu pour les chevaux est maintenant disponible, mais il coûte presque 2,5 fois plus cher. Lorsque vous mentionnez ce constat au fabricant pharmaceutique, on vous répond que vous devriez réduire votre marge de profit sur le médicament. Vous suivez ce conseil même s'il s'agit d'une décision de gestion de la pratique qui est loin d'être idéale, car vous craignez que certains de vos clients refusent le produit plus coûteux ou n'aient pas les moyens de se le procurer, ce qui privera leurs chevaux du soulagement de la douleur dont ils ont besoin.

Vous voyez un cheval à qui vous avez prescrit du firocoxib, et votre cliente vous dit qu'elle a trouvé un médecin vétérinaire en pratique des petits animaux qui lui prescrira la version canine moins chère du médicament à utiliser pour son cheval. Elle refuse de vous dévoiler son nom. **Que faites-vous?**

Responses to the case presented are welcome. Please limit your reply to approximately 50 words and forward along with your name and address to: **Ethical Choices, c/o Dr. Bettina Bobsien, 4353 Yellowpoint Road, Ladysmith, British Columbia V9G 1G5; email: bettinadvm@gmail.com**

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

Les réponses au cas présenté sont les bienvenues. Veuillez limiter votre réponse à environ 50 mots et nous la faire parvenir avec vos nom et adresse à l'adresse suivante : **Choix déontologiques, a/s de la Dre Bettina Bobsien, 4353 rue Yellowpoint, Ladysmith (Colombie-Britannique) V9G 1G5; courriel : bettinadvm@gmail.com**

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

Quiz Corner
Test éclair

1. A 7-year-old female spayed cocker spaniel is presented with a 2-day history of progressively worsening lethargy, inappetence, and occasional vomiting. Physical examination showed mild icterus and tachycardia. A blood smear displayed agglutination of red blood cells visible to the naked eye. Stained microscopy, hematology, and urinalysis results are shown in Figure 1. Blood chemistry results showed marked bilirubinemia (Tables 1, 2).

What is the presumptive diagnosis?

A. Idiopathic thrombocytopenia (ITP).
B. Immune-mediated hemolytic anemia.
C. Anticoagulant rodenticide toxicity.
D. Disseminated intravascular coagulation (DIC).
E. Myelodysplastic syndrome.

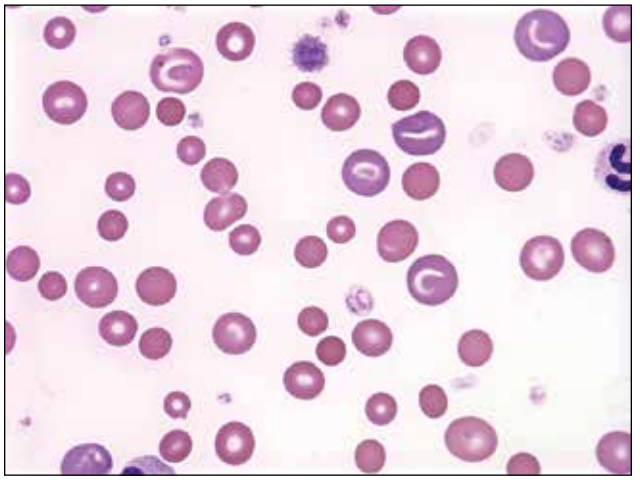

Figure 1. Stained microscopy, hematology, and urinalysis (image courtesy of Seth Chapman DVM, MS, DACVP)./Microscopie colorée, hématologie et examen de l'urine (image courtoisie de Seth Chapman, D.V.M., M.Sc., DACVP).

1. Une chienne épagneul cocker stérilisée, âgée de 7 ans, présente de la léthargie qui se détériore progressivement, de l'inappétence et du vomissement occasionnel, depuis 2 jours. L'examen physique révèle un ictère modéré et de la tachycardie. Un frottis sanguin montre une agglutination de globules rouges visible à l'œil nu. Une microscopie colorée, l'hématologie et les résultats de l'examen de l'urine sont présentés dans la figure 1. Les résultats de la biochimie sanguine présentent une bilirubinémie marquée (tableaux 1 et 2).

Quel est le diagnostic de présomption?

A. Thrombocytopénie idiopathique
B. Anémie hémolytique à médiation immunitaire
C. Empoisonnement aux rodenticides anticoagulants
D. Coagulation intravasculaire disséminée
E. Syndrome myélodysplasique

Table 1/Tableau 1. Canine hematology./Hématologie canine.

Test	Value Valeur	Normal Normale
RBC/Globules rouges	4.05	5.39 to/à 8.70 M/μL
Hematocrit/Hématocrite	25.4	38.3 to/à 56.5%
Hemoglobin/Hémoglobine	10.1	13.4 to/à 20.7 g/dL
MCV/ Volume globulaire moyen	68	59 to/à 76 fL
MCH/TCMH	24	21.9 to/à 26.1 pg
MCHC/CCMH	35.9	32.6 to/à 39.2 g/dL
Reticulocytes/Réticulocytes	160	10 to/à 110 K/μL
WBC/Globules blancs	15.3	4.9 to/à 17.6 K/μL
Neutrophils/Neutrophiles	11.80	2.94 to/à 12.67 K/μL
Lymphocytes	2.01	1.06 to/à 4.95 K/μL
Monocytes	0.94	0.13 to/à 1.15 K/μL
Eosinophils/Éosinophiles	0.08	0.07 to/à 1.49 K/μL
Basophils/Basophiles	0.2	0 to/à 0.1 K/μL
Nucleated RBC/ Globules rouges nucléés	1	0 to/à 2 per/par 100 WBC/globules blancs
Platelets/Plaquettes	145	143 to/à 448 K/μL
Polychromasia/Polychromasie	Moderate Modérée	
Spherocytes/Sphérocytes	Moderate Modérée	

Table 2/Tableau 2. Canine urinalysis./Examen de l'urine du chien.

Test	Value/Résultat
Collection/Prélèvement	Voided/Miction
Color/Couleur	Orange
Clarity/Transparence	Clear/Claire
Specific Gravity (N = 1.016 to 1.060)/Densité (N = 1,016 à 1,060)	1.049
pH	7.0
Urine protein/Protéines	3+
Glucose	Negative/Négatif
Ketones/Corps cétoniques	Negative/Négatif
Blood/Hemoglobin/Sang/hémoglobine	2+
Bilirubin/Bilirubine	4+
Urobilinogen/Urobilinogène	Normal
Mucus	None seen/Aucun observé
Casts/Cylindres	None seen/Aucun observé
Crystals/Cristaux	None seen/Aucun observé

2. A 12-year-old Quarter Horse gelding was presented with a complaint of hematuria after exercise. His appetite, attitude, and performance were normal. Physical examination did not reveal any abnormalities.

The horse was sedated with an α-2 agonist (detomidine) and butorphanol to facilitate cleaning the sheath and passage of a urinary catheter.

The urine was grossly normal. Urinalysis revealed 2+ blood.

Transrectal palpation revealed a hard, golf-ball sized mass in the urinary bladder. Transrectal ultrasound of the urinary bladder revealed the following image shown in Figure 1.

What is the recommended treatment?

A. Lavage the bladder to remove the sabulous debris.
B. Urinary acidification to dissolve the concretion.
C. Endoscopic-guided injection of the mass with cisplatin.
D. Euthanasia is recommended due to poor prognosis in horses.
E. Surgical removal.

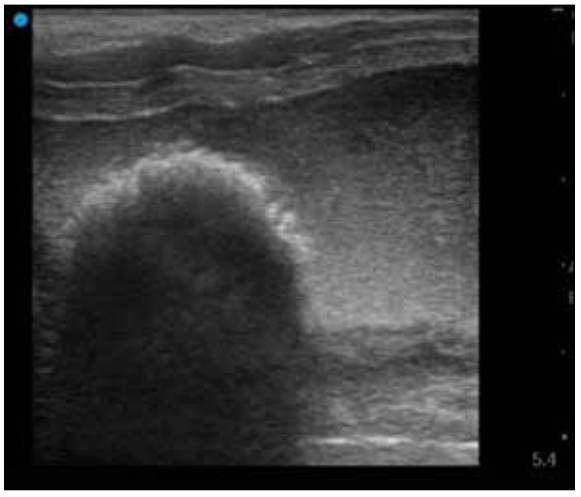

Figure 1. Transrectal ultrasound of the equine urinary bladder (image courtesy of Nora Grenager VMD, DACVIM).
Échographie transrectale de la vessie du cheval (image fournie par Nora Grenager, V.M.D., DACVIM).

2. Un hongre Quarter Horse âgé de 12 ans présente de l'hématurie après l'exercice. Son appétit, son comportement et ses performances sont normaux. L'examen physique ne révèle aucune anomalie.

Le cheval est tranquillisé à l'aide d'un agoniste des récepteurs alpha-2 (détomidine) et de butorphanol pour faciliter le nettoyage du fourreau et le passage d'un cathéter urinaire.

L'urine est macroscopiquement normale. L'examen de l'urine révèle 2+ de sang.

La palpation transrectale démontre une masse dure, de la grosseur d'une balle de golf, dans la vessie. L'échographie transrectale de la vessie décèle l'image présentée à la figure 1.

Quel est le traitement recommandé?

A. Lavage de la vessie pour enlever les débris sablonneux
B. Acidification de l'urine pour dissoudre la concrétion
C. Injection guidée par endoscopie de la masse à l'aide de cisplatine
D. L'euthanasie est recommandée étant donné le mauvais pronostic chez les chevaux
E. Ablation chirurgicale

(See p. 640 for answers./Voir les réponses à la page 640.)

The questions and answers are provided by The Zuku Review, online veterinary test prep.

Les questions et les réponses sont gracieusement fournies par le site de préparation aux examens vétérinaires Zuku Review.

2022 CVMA Convention — July 21 to 24 Connect in Halifax, Nova Scotia

Congrès de l'ACMV du 21 au 24 juillet 2022 Se retrouver à Halifax, en Nouvelle-Écosse

The 2022 Canadian Veterinary Medical Association (CVMA) Convention is approaching quickly. You can register online, until June 30, to experience the only Canadian national multi-species convention. The scientific program offers over 100 hours of Continuing Education (CE) for in-person attendees, and over 40 hours livestreamed CE for virtual attendees. All attendees will have access to the on-demand sessions for the remainder of the year.

Join your colleagues at the CVMA Annual General Meeting held on Thursday, July 21. Tickets must be purchased in advance with your registration to receive your complimentary lunch ticket. The CVMA Awards Gala is taking place on Thursday from 7 pm to 8 pm. You can observe your peers as they receive awards and are recognized for their achievements in the veterinary profession.

The CVMA Emerging Leaders Program (ELP) is kicking off with an 8-hour interactive workshop with **Rob Marr.** This workshop will focus on developing self-awareness around your personality style and preferences; building simple systems in your practice to keep you growing positively and profitably; and building strategies that keep you on track and focused. Any CVMA or Registered Veterinary Technologists and Technicians of Canada (RVTTC) member can register for a low fee of $200. This session is held on Friday July 22, from 9 am to 6 pm.

The plan for the social evening is well underway. This is an east coast party not to be missed. Join us on Saturday, July 23, for an evening of entertainment, local food and drinks, and connecting with colleagues. This is guaranteed to be a good time. Tickets are limited so grab them while they last!

We are working with Discover Halifax to create an experience like no other through a delegate landing page that will help guide

Le Congrès de 2022 de l'Association canadienne des médecins vétérinaires (ACMV) approche à grands pas! Vous pouvez vous inscrire en ligne jusqu'au 30 juin pour assister au seul congrès national multiespèces au pays. Le programme scientifique offre plus de 100 heures de formation continue en présentiel et plus de 40 heures de formation continue à distance. Tous les congressistes auront accès aux séances enregistrées pour le reste de l'année.

On vous invite à vous joindre à vos collègues lors de l'assemblée générale annuelle de l'ACMV, qui se tiendra le jeudi 21 juillet. Pour y assister, n'oubliez pas d'indiquer que vous voulez votre billet gratuit pour le dîner au moment de votre inscription, car vous devez réserver votre place à l'avance. Le gala des Prix de l'ACMV aura lieu le jeudi soir, de 19 h à 20 h. Venez soutenir vos pairs qui seront honorés et récompensés pour leurs réalisations au sein de la profession vétérinaire.

Le Programme des futurs leaders (PFL) de l'ACMV débutera par un atelier interactif de 8 heures avec **Rob Marr**. Cet atelier sera axé sur le développement de la conscience de soi selon votre style de personnalité et vos préférences, la mise en place de systèmes simples dans votre pratique pour favoriser votre croissance positive et votre épanouissement, et l'élaboration de stratégies qui vous aident à maintenir le cap. Les membres de l'ACMV et de l'association TTVAC (Technologues et techniciens vétérinaires agréés du Canada) peuvent s'inscrire au tarif réduit de 200 $. L'atelier sera offert le vendredi 22 juillet, de 9 h à 18 h.

La planification de la soirée sociale va bon train. Ce sera un « party de la côte Est » à ne pas manquer! Joignez-vous à nous le samedi 23 juillet, pour une soirée de divertissement, de cuisine et de boissons locales, et de rencontres avec des collègues. Plaisir garanti! Les places sont limitées, alors ne tardez pas à vous procurer votre billet!

DISCOVER HALIFAX

you through everything you'll need to know to make the most of your visit to the seacoast city. If you are looking for tours, inside and around the city, or restaurants, this is the site for you. A special perk for onsite attendees is the Show Your Badge program. From local food tours to souvenirs, to local experiences, you will save on all Halifax has to offer. Visit (https://businesseventshalifax.com/events/2022-cvma-convention) for more information.

Stay up-to-date with the latest event details, including the Province of Nova Scotia COVID-19 measures, and full program and registration details (https://pheedloop.com/cvma22/site/home/). We look forward to seeing you whether in-person or virtually at the 2022 CVMA Convention.

(by Sarah Cunningham, Manager, Professional Development, CVMA)

Nous travaillons avec Discover Halifax pour vous offrir une expérience unique en son genre – vous trouverez sur leur site une page d'accueil qui vous guidera pour tirer le maximum de votre séjour dans cette magnifique ville côtière. Si vous souhaitez faire une visite guidée, dans ou autour de la ville, ou obtenir des suggestions de bons restaurants, ce site est pour vous! Les participants en présentiel auront également un avantage spécial : chez divers partenaires, la présentation de leur porte-nom leur permettra de faire des économies sur ce que Halifax a de meilleur à offrir – des visites gastronomiques aux souvenirs en passant par les expériences typiquement locales! Rendez-vous sur le site de Discover Halifax (https://businesseventshalifax.com/events/2022-cvma-convention) pour en savoir plus.

Restez au courant de tous les développements concernant l'événement, y compris les mesures sanitaires en vigueur en Nouvelle-Écosse en raison de la pandémie de COVID-19, et consultez les détails du programme et les modalités d'inscription sur le site Web du Congrès (https://pheedloop.com/cvma22/site/home/). Nous avons hâte de vous voir, en personne ou virtuellement, au Congrès de l'ACMV de 2022!

(par Sarah Cunningham, gestionnaire, Perfectionnement professionnel, ACMV)

Animal Health Week 2022 — October 2 to 8
Habitat Protection = Pandemic Prevention

Semaine de la santé animale du 2 au 8 octobre 2022
Protection des habitats = Prévention des pandémies

It is time to start planning for Animal Health Week 2022! Animal Health Week is an annual national public awareness campaign organized by the Canadian Veterinary Medical Association (CVMA) and hosted by veterinarians across Canada. Each year, through Animal Health Week, the veterinary community draws attention to an important health-related message. During the first week of October, veterinary teams across Canada promote a significant animal health message and responsible animal ownership as part of Animal Health Week celebrations.

Building on the previous 2 Animal Health Week campaigns, the CVMA is further exploring the One Health theme with ***Habitat Protection = Pandemic Prevention.*** From **October 2–8, 2022,** the CVMA will raise awareness about how disruption of animal habitats in various forms, from forests to farms, can impact the health of ecosystems and affect global human health.

Canada's veterinary professionals occupy unique positions within the national One Health community and can help

Il est temps de commencer à planifier la Semaine de la santé animale de 2022! La Semaine de la santé animale est une campagne nationale annuelle de sensibilisation du public organisée par l'Association canadienne des médecins vétérinaires (ACMV) et mise en œuvre par les médecins vétérinaires du Canada. Chaque année, dans le cadre de la Semaine de la santé animale, la communauté vétérinaire attire l'attention sur un important message lié à la santé. Pendant la première semaine d'octobre, les équipes vétérinaires du pays font la promotion de ce message et de la propriété responsable des animaux dans le cadre des célébrations de la Semaine de la santé animale.

En s'appuyant sur les deux campagnes précédentes de la Semaine de la santé animale, l'ACMV pousse l'exploration de l'approche « Une seule santé » avec le thème de cette année : ***Protection des habitats = Prévention des pandémies***. Ainsi, du **2 au 8 octobre 2022**, l'ACMV cherchera à sensibiliser le public à la façon dont la perturbation des habitats des animaux, sous

educate clients about how protecting animals' health and habitats, protects everyone's health.

Promotional tools, including a robust social media campaign, resources, and articles will be available to promote Animal Health Week across the country. A free Animal Health Week poster will be included in July's issue of *The Canadian Veterinary Journal.* An additional poster will be mailed to veterinary hospitals and clinics across the country in August. As Animal Health Week nears, visit the *Animal Health Week* section of the CVMA website (www.canadianveterinarians.net) to find tips and tools to help plan your celebrations.

2022 Animal Health Week Sponsors

Generous support of the 2022 Animal Health Week campaign is provided by Program Sponsors, **iFinance Canada (Petcard)** and **Petsecure.**

toutes leurs formes allant des forêts aux fermes, peut avoir un impact sur la santé des écosystèmes et affecter la santé humaine partout dans le monde.

Les professionnels vétérinaires du Canada occupent des positions uniques au sein de la communauté nationale « Une seule santé » et peuvent aider à renseigner les clients sur la façon dont la protection de la santé et des habitats des animaux protège la santé de tous.

Des outils promotionnels, y compris une vaste campagne sur les médias sociaux, des ressources et des articles seront offerts pour promouvoir la Semaine de la santé animale d'un bout à l'autre du pays. Une affiche gratuite de la Semaine de la santé animale sera incluse dans le numéro de juillet de *La Revue vétérinaire canadienne*. Une affiche sera également envoyée par la poste aux établissements vétérinaires du pays en août. À l'approche du mois d'octobre, visitez la section sur la *Semaine de la santé animale* du site Web de l'ACMV (www.veterinairesaucanada.net) pour obtenir des conseils et des outils qui vous aideront à planifier vos célébrations.

Commanditaires de la Semaine de la santé animale de 2022

La campagne de la Semaine de la santé animale de 2022 est généreusement soutenue par **iFinance Canada (Petcard)** et **Petsecure**.

Wayne McDonell retires from Editorial Committee

After 9 years of processing, editing, and arranging for peer-review, if not peer-reviewing articles himself, **Dr. Wayne McDonell** has retired from the position of Associate Editor for *The Canadian Veterinary Journal* and as a member of the Canadian Veterinary Medical Association (CVMA) Editorial Committee.

Dr. McDonell was celebrated at his last CVMA Committee Weekend, which was held in-person in Ottawa at the end of March this year. In addition, last year Dr. McDonell received the American College of Veterinary Anesthesia and Analgesia (ACVAA) 2021 Career Achievement Award.

The ACVAA Career Achievement Award recognizes a Diplomate for accomplishments throughout a long career of outstanding performance in advancing the art and science of veterinary anesthesia and/or analgesia. The award is made based on accomplishments throughout a career distinguished by sustained, significant contributions to education, research and/or service in veterinary anesthesia and analgesia, including service to the ACVAA.

Dr. McDonell is a founding member of the ACVAA and has served the College in a variety of ways over the years (including being President of the College in 1981). He grew up on a farm in Alberta and attended the University of Guelph, Ontario Veterinary College (OVC) from 1961–65. After practicing

Wayne McDonell quitte le Comité de la rédaction

Après 9 ans à évaluer, à revoir et à organiser la révision par les pairs (quand il ne faisait pas lui-même partie des réviseurs), le **Dr Wayne McDonell** quitte son poste de rédacteur en chef adjoint de *La Revue vétérinaire canadienne* et ses fonctions en tant que membre du Comité de la rédaction de l'Association canadienne des médecins vétérinaires (ACMV).

Le Dr McDonell a été honoré lors de la dernière fin de semaine de réunions des comités de l'ACMV, qui a eu lieu en présentiel à Ottawa à la fin du mois de mars cette année. De plus, l'an dernier, le Dr McDonell a reçu le « 2021 Career Achievement Award » de l'American College of Veterinary Anesthesia and Analgesia (ACVAA).

Ce prix récompense un membre de l'ACVAA pour les réalisations accomplies au cours d'une longue carrière de performance exceptionnelle dans l'avancement de l'art et de la science de l'anesthésie et de l'analgésie vétérinaires. Le prix est décerné en fonction des accomplissements qui ont ponctué un parcours professionnel qui se distingue par des contributions soutenues et significatives à l'éducation, à la recherche et/ou aux soins en anesthésie et en analgésie vétérinaires, y compris par le service au sein de l'ACVAA.

Le Dr McDonell est un membre fondateur de l'ACVAA qu'il a servi de diverses façons au fil des ans (notamment en tant que président en 1981). Il a grandi dans une ferme en Alberta et

veterinary medicine in Alberta, he went back to Guelph in 1966, teaching anesthesia for 3 years during which time he also completed an MSc. He was employed as an Assistant Professor in 1969, and in 1971 he obtained a Medical Research Council of Canada Fellowship that funded his PhD at Cambridge University. He studied the effect of posture on respiratory function in horses, carrying out some of the earliest seminal work on respiratory function associated with anesthesia in this species. He returned to the OVC and became an Associate Professor with tenure in 1976 and continued to become a full Professor 5 years later. During his tenure at OVC, he formed the anesthesia service and was a key member and driver of this service for the rest of his career.

Dr. McDonell later became the first OVC Director of the Teaching Hospital in 1983 and he also became Assistant Dean for Research and Graduate Studies at OVC and served in that position for 7 years. During this time, he continued to support and mentor graduate students, residents and young faculty with his continuous inspiration and search for new knowledge. He was instrumental in the inception of the Doctor of Veterinary Science (DVSc) program, a clinical doctorate that replaced the residency program in 1980 and took on the first DVSc student **(Doris Dyson)** to enter this program. Many faculty and residents have subsequently benefited from this program. Dr. McDonell was also a key player in the foundation of the Pet Trust at OVC, which has raised hundreds of thousands of dollars over the years to support research efforts in companion animals by faculty and DVSc students.

Dr. McDonell has published over 120 peer reviewed papers and numerous chapters in veterinary textbooks. Although he officially retired from teaching in 2005, he helped establish Veterinarians Without Borders — Canada and has served on its Board. He has been involved with the training of many graduate students and residents in our discipline, who have themselves gone on to influence veterinary anesthesia.

a fréquenté l'Ontario Veterinary College (OVC) de l'Université de Guelph de 1961 à 1965. Après avoir pratiqué la médecine vétérinaire en Alberta, il est retourné à Guelph en 1966, où il a enseigné l'anesthésie pendant trois ans et obtenu une maîtrise. Il a été employé comme professeur adjoint en 1969, et en 1971, il a obtenu une bourse du Conseil de recherches médicales du Canada qui a financé son doctorat à l'Université de Cambridge. Il a étudié l'effet de la posture sur la fonction respiratoire chez les chevaux, en effectuant certains des premiers travaux déterminants sur la fonction respiratoire en lien avec l'anesthésie chez cette espèce. Il est retourné à l'OVC et est devenu professeur agrégé en 1976, puis professeur titulaire cinq ans plus tard. Au cours de son mandat à l'OVC, il a formé le service d'anesthésie et a été un membre clé et un ambassadeur de ce service pour le reste de sa carrière.

Le Dr McDonell est devenu le premier directeur de l'Hôpital d'enseignement de l'OVC en 1983 et, plus tard, il a occupé le poste de vice-doyen à la recherche et aux études supérieures de l'OVC durant 7 ans. Pendant ce temps, il a continué à soutenir et à encadrer les étudiants des cycles supérieurs, les résidents et les jeunes professeurs grâce à son inspiration continue et à sa recherche de nouvelles connaissances. Il a joué un rôle crucial dans la création du programme de doctorat en sciences vétérinaires (D. V. Sc.), un doctorat clinique qui a remplacé le programme de résidence en 1980, et il a recruté la première étudiante (**Doris Dyson**) à s'y inscrire. De nombreux professeurs et résidents ont par la suite bénéficié de ce programme. Le Dr McDonell a également joué un rôle clé dans la fondation du Pet Trust de l'OVC, qui a amassé des centaines de milliers de dollars au fil des ans pour soutenir les efforts de recherche sur les animaux de compagnie par les professeurs et les étudiants du programme de doctorat en sciences vétérinaires.

Le Dr McDonell a publié plus de 120 articles révisés par des pairs et rédigé de nombreux chapitres de manuels vétérinaires. Bien qu'il ait officiellement pris sa retraite de l'enseignement en 2005, il a contribué à l'établissement de Vétérinaires sans frontières – Canada et a siégé à son conseil d'administration. Il a participé à la formation de nombreux étudiants diplômés et résidents de notre discipline, qui ont par la suite eux-mêmes eu une influence sur l'anesthésie vétérinaire.

Dr./Dr Wayne McDonell

Case Report Rapport de cas

Babesia vulpes in a dog from Prince Edward Island, Canada

Anne C. Arsenault, Peter M. Foley, Noel P. Clancey

Abstract — A 12-year-old neutered male American Staffordshire terrier dog was referred to the Atlantic Veterinary College, Prince Edward Island, Canada, for suspected immune-mediated hemolytic anemia. Babesiosis *(Babesia vulpes)* was confirmed using polymerase chain reaction testing. The dog was successfully treated with a 10-day protocol of atovaquone/proguanil (TEVA Pharmaceutical Industries, Toronto, Ontario), 13.5 mg/kg BW, PO, q8h and azithromycin (Pharmascience, Montreal, Quebec), 10 mg/kg BW, PO, q24h. To the authors' knowledge, this report is the first documented case of babesiosis caused by *Babesia vulpes* in a dog from Canada.

Résumé — *Babesia vulpes* chez un chien de l'Île-du-Prince-Édouard, Canada. Un chien American Staffordshire terrier mâle castré de 12 ans a été référé au *Atlantic Veterinary College*, Île-du-Prince-Édouard, Canada, pour suspicion d'anémie hémolytique à médiation immunitaire. La babésiose (*Babesia vulpes*) a été confirmée à l'aide d'un test d'amplification en chaîne par la polymérase. Le chien a été traité avec succès avec un protocole de 10 jours d'atovaquone/proguanil (TEVA Pharmaceutical Industries, Toronto, Ontario), 13,5 mg/kg BW, PO, q8h et azithromycine (Pharmascience, Montréal, Québec), 10 mg/kg BW, PO, q24h. À la connaissance des auteurs, ce rapport est le premier cas documenté de babésiose causée par *Babesia vulpes* chez un chien du Canada.

(Traduit par Dr Serge Messier)

Can Vet J 2022;63:589–592

Babesia species are protozoal parasites that target erythrocytes in affected patients. These protozoal organisms are most often transmitted to dogs by ticks; however, they can also be spread through direct inoculation *via* dog bites and the use of blood products, or through vertical transmission (1). Canine babesiosis can range from asymptomatic to severe clinical disease, with hemolytic anemia and thrombocytopenia being the most common clinical manifestations (1). *Babesia* organisms can be visualized in erythrocytes on blood film evaluation and are classified into large and small forms based on their visual appearance (2). Molecular techniques are being used more commonly to confirm the presence of *Babesia* organisms and for species identification purposes (3). Recommendations for treatment of canine babesiosis are species-specific, with treatment guidelines generally different for large- *versus* small-form infections (2). Canine babesiosis is a well-established cause of hemolytic anemia in endemic areas in the United States (4); however, it has not been documented previously in dogs from Canada without a previous travel history. This report outlines the first documented case of *Babesia vulpes* in a dog from Canada. The aim of this report is to increase awareness and emphasize the importance of screening for canine babesiosis in patients with hemolytic anemia in regions of Canada.

Case description

A 12-year-old American Staffordshire terrier dog was referred to the Atlantic Veterinary College (AVC) for suspected immune-mediated hemolytic anemia and concurrent immune-mediated thrombocytopenia. The dog had been assessed by the referring veterinarian earlier the same day for lethargy and anorexia of several days. The dog was adopted as a stray from a local animal shelter on Prince Edward Island (PEI), Canada approximately 10 y previously and had not left PEI since adoption. The dog was healthy at the time of adoption, and the owners reported no history of health concerns. A new dog (also an American Staffordshire terrier) from a shelter in Georgia, USA had been introduced to the household 2 y previously. This more recently adopted dog had no health concerns, although it was noted that the 2 dogs engaged in fights with one another occasionally. The clinical case dog was not receiving any medications at the time of assessment and had no history of previous use of parasite preventative products. A complete

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blood (cell) count (CBC) completed by the referring veterinarian revealed a marked thrombocytopenia [platelet concentration = 15 × 10^9/L, reference interval (RI): 117 to 490 × 10^9/L] and a moderate normocytic normochromic anemia [hematocrit (HCT) = 0.21 L/L, RI: 0.33 to 0.56 L/L; red blood cell concentration (RBC) = 2.88 × 10^{12}/L, RI: 5.10 to 8.50 × 10^{12}/L; hemoglobin (HGB) = 69 g/L: RI: 110 to 190 g/L; mean corpuscular volume (MCV) = 71.2 fL, RI: 60 to 76 fL; and mean corpuscular hemoglobin concentration (MCHC) = 320 g/L, RI: 300 to 380 g/L]. No reticulocyte count(s) or information regarding polychromasia on blood smear evaluation was provided. These hematological findings prompted referral to the AVC Small Animal Internal Medicine Service for further investigation.

On general physical examination, the dog was quiet and lethargic and weighed 31.7 kg. The heart rate was 128 beats/min with no murmur or arrythmia appreciated on auscultation. The dog was panting throughout the examination, with a slightly elevated rectal temperature of 40.0°C. The mucus membranes were pale pink, with an adequate capillary refill time of < 2 s. Evaluation of the integumentary system revealed no evidence of petechiation or ecchymoses, and no ectoparasites were visualized. Slightly prominent submandibular lymph nodes were noted but otherwise peripheral lymph nodes were unremarkable on palpation. The dog's abdomen was tense on palpation, limiting a thorough evaluation, but no obvious abnormalities were appreciated. The remainder of the physical examination was unremarkable. A CBC evaluated at admission revealed a normal white blood cell concentration. An accurate platelet concentration could not be provided due to platelet clumping, but platelet numbers were deemed adequate on smear evaluation. This finding eliminated immune-mediated thrombocytopenia as a likely diagnosis. A marked normocytic hypochromic non-regenerative anemia was present (HCT = 0.11 L/L, RI: 0.40 to 0.56 L/L; RBC concentration = 1.42 × 10^{12}/L, RI: 5.7 to 8.4 × 10^{12}/L; HGB = 34 g/L, RI: 135 to 198 g/L; MCV = 73.9 fL, RI: 64 to 75 fL; MCHC = 324 g/L, RI: 334 to 357 g/L; reticulocytes = 54.81 × 10^9/L, RI: 0 to 85 × 10^9/L). Blood smear erythron findings included 2+ (out of 4+) anisocytosis, 1+ polychromasia, 2+ rouleaux, slight spherocytosis, and visual identification of small signet-ring structures consistent with small form *Babesia* organisms (Figure 1). An ethylenediaminetetraacetic acid (EDTA) anticoagulated whole blood sample was submitted to the Michigan State University Veterinary Diagnostics Laboratory (Michigan, US), for polymerase chain reaction (PCR) testing for *Babesia* species, and another was submitted to Eurofins Genomics LLC (Louisville, Kentucky, USA) for *Babesia* species identification. A serum biochemistry profile revealed a mild hyperbilirubinemia (12 μmol/L, RI: 0 to 4 μmol/L), mild hypokalemia (3.5 mmol/L, RI: 3.9 to 5.3 mmol/L), moderate hypoalbuminemia (22 g/L, RI: 30 to 36 g/L), and moderately elevated creatinine kinase (1556 U/L, RI: 44 to 249 U/L) and aspartate aminotransferase activities (117 U/L, RI: 18 to 55 U/L). A urinalysis performed on a free-catch urine sample revealed a 2+ bilirubin pad reaction, trace protein pad reaction, and 0.25 g/L protein on a sulfosalicylic acid test. A 1+ blood pad reaction was also present, but

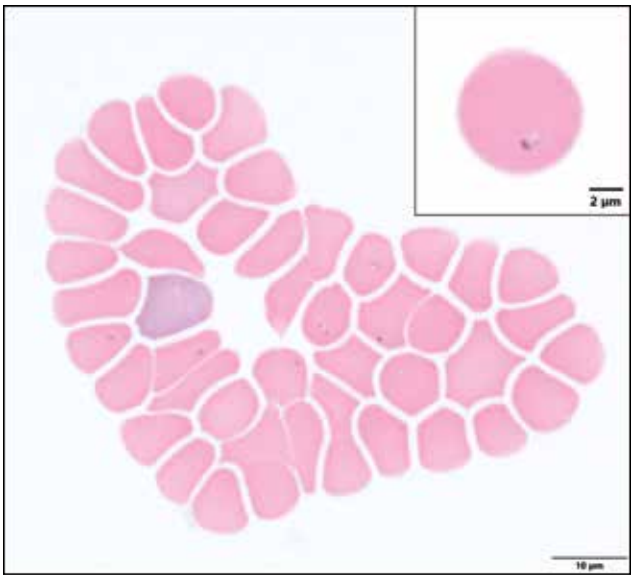

Figure 1. *Babesia vulpes* organisms visualized in several erythrocytes on blood film evaluation. Wright-Giemsa stain, 1000×. Inset: Classic signet-ring shape of small *Babesia* species. Wright-Giemsa stain, 1000×.

urine sediment examination revealed no intact erythrocytes. The dog was negative for *Dirofilaria immitis, Borrelia burgdorferi, Anaplasma* sp. and *Ehrlichia* sp. using a Snap4Dx test (IDEXX Laboratories, Portland, Maine, USA). The prothrombin time was within normal limits and activated partial thromboplastin time (aPTT) was mildly elevated at 111.0 seconds (RI: 72.0 to 102.0 seconds). The slightly prolonged aPTT was deemed clinically inconsequential. Rapid point-of-care ultrasound examination of the thorax and abdomen revealed no evidence of free fluid. Thoracic radiographs revealed a mild generalized bronchial pattern, suspected to be an age-related change. Abdominal ultrasonography revealed splenomegaly with a diffusely coarse echotexture of the splenic parenchyma. There was mild distension of the gall bladder with anechoic bile contents, but no other abnormal findings. Ultrasound-guided fine-needle aspiration cytology findings of the spleen revealed a mainly immature lymphocyte population with 56% small lymphocytes, 19% intermediate lymphocytes, 1% large lymphocytes and 24% plasma cells, and several clusters of bland spindleloid stromal cells containing low normal of enmeshed individual mast cells consistent with a reactive spleen. Extra-medullary hematopoiesis was also present. Piroplasms identical to those observed in peripheral blood were visualized within mature erythrocytes. The dog was diagnosed with hemolytic anemia secondary to suspected babesiosis.

The dog was blood typed as DEA 1.1 positive (Quick Test DEA 1; Alvedia, Lyon, France) and received a blood transfusion consisting of 1 unit of packed red blood cells (approximately 200 mL) and 1 unit of whole blood (approximately 450 mL). Packed cell volume rose to 24% following the blood transfusion, and the dog's clinical signs improved substantially. The dog was discharged 3 d later with clindamycin (TEVA Pharmaceuticals Industries, Toronto, Ontario), 25 mg/kg BW, PO, q12h, metronidazole (AA Pharma, Toronto, Ontario),

15 mg/kg BW, PO, q12h, and doxycycline (Apotex, Toronto, Ontario), 5 mg/kg BW, PO, q12h while awaiting the PCR test results. It was elected to delay targeted therapy due to owner financial constraints. Eight days later, PCR results confirmed *Babesia* organisms, with a 100% nucleotide sequence match to *Babesia vulpes.* A CBC at this time revealed a moderate macrocytic hypochromic regenerative anemia (HCT = 0.24 L/L, RI: 0.40 to 0.56 L/L; RBC concentration = 2.4 × 10^{12}/L, RI: 5.7 to 8.4 × 10^{12}/L; HGB = 71 g/L, RI: 135 to 198 g/L; MCV = 100.8 fL, RI: 64 to 75 fL; MCHC = 292 g/L, RI: 334 to 357 g/L; and reticulocytes = 500 × 10^{9}/L, RI: 0 to 85 × 10^{9}/L). A mild leukocytosis characterized by a mild neutrophilia and mild monocytosis was present (WBC concentration = 17.1 × 10^{9}/L, RI: 5.4 to 14.3 × 10^{9}/L; segmented neutrophil concentration = 10.6 × 10^{9}/L, RI: 2.9 to 10.1 × 10^{9}/L, monocyte concentration = 1.6 × 10^{9}/L, RI: 0.1 to 1.4 × 10^{9}/L). Platelet assessment was adequate. Blood smear evaluation revealed 1+ anisocytosis, 2+ macrocytosis, 3+ polychromasia, and 3+ rouleaux with continued visual evidence of *Babesia* organisms. The dog's previous medications were discontinued and a protocol of atovaquone/proguanil (TEVA Pharmaceutical Industries, Toronto, Ontario), 13.5 mg/kg BW, PO, q8h and azithromycin (Pharmascience, Montreal, Quebec), 10 mg/kg BW, PO, q24h was initiated for a 10-day course. The dog tolerated the protocol with only minor gastrointestinal upset, which responded well to maropitant citrate (Cerenia; Zoetis, Kalamazoo, Michigan, USA), 2 mg/kg BW, PO, q24h for several days.

The dog was reassessed 5 d after completing the therapeutic protocol. The owner reported that the dog was doing well at home with no reoccurrence of clinical signs. A CBC revealed a mild macrocytic hypochromic non-regenerative anemia (HCT = 0.33 L/L; RBC concentration = 3.9 × 10^{12}/L; HGB = 71 g/L; MCV = 85.6 fL; MCHC = 328 g/L; and reticulocytes = 72 × 10^{9}/L). A mild leukocytosis characterized by a mild neutrophilia (WBC concentration = 15.4 × 10^{9}/L; segmented neutrophil concentration = 12.6 × 10^{9}/L), and a mild thrombocytosis (497 × 10^{9}/L, RI: 218 to 470 × 10^{9}/L) were also present. Blood smear evaluation revealed 1+ anisocytosis, slight polychromasia, slight macrocytosis, 3+ rouleaux, and no further visual evidence of *Babesia* organisms. The owner's financial constraints precluded re-evaluation through use of a *Babesia* PCR test at this time.

Discussion

The increased use of molecular-based testing has allowed for more precise identification of *Babesia* organisms, leading to an expansion of recognized *Babesia* species responsible for canine babesiosis. The current list of recognized *Babesia* species affecting dogs includes *Babesia canis, Babesia vogeli, Babesia rossi, Babesia gibsoni, Babesia conradae,* and *Babesia vulpes* (2). *Babesia vulpes* has had several previous names, including *Babesia microti*-like and *Theileria annae* (5). *Babesia vulpes* was first reported in Spain (6), where it has a high prevalence in the red fox population, as similarly reported in Portugal, Croatia, Sweden, and France (7). *Ixodes* tick species *(*notably *Ixodes hexagonus)* are often suggested as the proposed vector between the fox population and domestic dogs, although transmission studies are lacking (3).

Despite high prevalence rates in European fox populations, foxes do not appear to experience overt clinical disease associated with *Babesia vulpes* infections (5). Similarly, *Babesia vulpes* has been documented in increasing frequency in North American red foxes, with apparently low virulence as well (8). Conversely, *Babesia vulpes* infections in dogs have been documented to result in marked clinical disease (9), similar to that observed in the dog in this report. Clinical infections with *Babesia vulpes* were previously deemed uncommon in North American dogs; however, a 2019 study evaluating 9376 dogs from North America for *Babesia* species using PCR testing, revealed *Babesia vulpes* as the second most identified species (9). Given the important clinical manifestations of *Babesia vulpes* infections in dogs, and the relatively high prevalence observed in the Barash et al (9) study, *Babesia vulpes* may be more clinically relevant in North American dogs than previously thought.

To the authors' knowledge, this is the first confirmed case of *Babesia vulpes* in a dog from Canada. *Babesia vulpes* infection in this dog was surprising as babesiosis in North American dogs is often reported in endemic areas in the United States or involves dogs with a travel history to or from endemic areas (10). Due to the absence of a deer population, PEI has previously been considered a region free of tick-borne disease. However, this perception has changed in recent years. A passive surveillance study conducted on PEI between 2016 and 2018 confirmed the presence of ticks in this region, predominantly *Ixodes scapularis* (11). There is also an established presence of *Babesia* organisms in the Prince Edward Island red fox population (7), with the first reported case of *Babesia vulpes* in a red fox from Canada documented on PEI in 2010 (12). Tick surveillance studies in several Canadian provinces have also documented the presence of other *Babesia* species (13,14). This suggests that tick-borne transmission of canine babesiosis is a valid concern and a plausible source for this dog's *Babesia vulpes* infection.

Although the dog did not have any travel history outside of PEI, the introduction of another dog from a shelter in a southern USA state with reported cases of canine babesiosis offers another possible source of transmission. Dog-to-dog transmission by direct inoculation has been demonstrated for certain *Babesia* species, specifically *Babesia gibsoni* in pitbull-type breeds (9). Given the breed of dog involved in this case, and history of occasionally fighting with the other dog in the household, direct inoculation of *Babesia vulpes* cannot be ruled out. Molecular testing for *Babesia* species in the other asymptomatic household dog was offered, but not pursued due to owner financial considerations. Regardless of disease transmission specifics, diagnosis of *Babesia vulpes* in this dog emphasizes babesiosis should remain an important differential diagnosis for dogs with hemolytic anemia.

Treatment recommendations exist in the literature for more commonly encountered *Babesia* species; however, specific treatment options for *Babesia vulpes* are limited. Treatment protocols for canine babesiosis vary depending on the species involved, although similar therapeutic recommendations are described for small-form *versus* large-form species (2). Given that *Babesia*

vulpes is a small-form species, most treatment recommendations are similar to those proposed for *Babesia gibsoni;* which are, atovaquone and azithromycin (1,3,9). The positive outcome in this case also serves as support for this recommendation. Although infection status with repeat PCR testing post-treatment was not possible in this case, the dog's improvement in clinical signs, bloodwork parameters, and absence of further visual identification of *Babesia vulpes* on blood smears were all taken as evidence of disease remission. The outcome for this dog is encouraging; however, additional studies are required to investigate therapeutic recommendations specifically for *Babesia vulpes.*

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Case Report Rapport de cas

Laparoscopic colopexy for recurrent rectal prolapse in a Maltese dog

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Abstract — A 2.5-kg castrated male Maltese dog, suspected to be older than 10 y, was presented with a prolapsed mass at the anus. This had occurred on 2 previous occasions within the last 4 mo and had been managed with manual reduction and purse-string sutures. The rectal prolapse had viable tissue and was reducible but resulted in straining and fecal accumulation. Colopexy (with intracorporeal sutures) was performed laparoscopically using 3 ports; the distal colon was retracted cranially and attached to the abdominal wall with 3 simple interrupted sutures in a single row. The dog recovered uneventfully, had good appetite and normal activity, did not strain, and defecated without issues. There were no wound-healing complications and at 12-month post-operative examination, the patient was in good condition without clinical signs. Based on this case report, laparoscopic colopexy is clinically practical for management of rectal prolapse in small-breed dogs.

Résumé — Colopexie laparoscopique pour prolapsus rectal récurrent chez un chien maltais. Un chien maltais mâle castré de 2,5 kg, suspecté d'avoir plus de 10 ans, a été présenté avec une masse faisant prolapsus à l'anus. Cela s'était produit à deux reprises au cours des quatre derniers mois et avait été géré avec une réduction manuelle et des sutures en bourse. Le prolapsus rectal avait des tissus viables et était réductible mais a entraîné des efforts et une accumulation fécale. La colopexie (avec sutures intracorporelles) a été réalisée par laparoscopie à l'aide de trois ouvertures; le côlon distal a été rétracté crânialement et attaché à la paroi abdominale avec trois sutures interrompues simples en une seule rangée. Le chien s'est rétabli sans incident, avait un bon appétit et une activité normale, ne s'est pas fatigué et a déféqué sans problème. Il n'y avait pas de complications de cicatrisation et lors de l'examen postopératoire de 12 mois, le patient était en bon état sans signes cliniques. Sur la base de ce rapport de cas, la colopexie laparoscopique est cliniquement pratique pour la gestion du prolapsus rectal chez les chiens de petite race.

(Traduit par Dr Serge Messier)

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Rectal prolapse (RP) occurs partially or completely in dogs and cats with prolonged tenesmus (1). Any urogenital or anorectal conditions causing straining can contribute to RP, including intestinal neoplasia, foreign body, urolithiasis, constipation, perineal hernia, prostatic disease, dystocia, or previous surgery in the posterior portion of the body, e.g., perineal herniorrhaphy. Rectal prolapse is common in young animals, and most frequently associated with severe internal parasitic infestation and diarrhea (1,2). There is no breed predisposition, except Manx cats with their anal laxity (1). Rectal prolapse should be differentiated from a prolapsed intussusception by insertion of a finger or probe alongside the prolapsed mass; an intussusception has a fornix that allows a probe to pass between the anus and the prolapsed tissue, whereas this is not possible in rectal prolapse (3). The prolapsed tissue may be simply red and swollen, or with excoriation, laceration, hemorrhage, desiccation, necrosis, or ulceration, depending on the duration of the RP (1,3). Self-mutilation and trauma may worsen the condition, and therefore, should be prevented (3).

The treatment of choice depends on the degree of prolapse, tissue viability, reducibility, chronicity, and previous treatment attempts. Most patients with rectal prolapse can be managed by manual reduction, transient (3 to 5 d) purse-string suture, and stool softener or low-residue diet. Importantly, the underlying causes must be addressed to prevent recurrence (1,3). Surgical treatment options include rectal amputation with resection and anastomosis for non-reducible/traumatized cases, and colopexy for multiple recurrences (1–3).

Colopexy creates a permanent adhesion between the colonal serosa and abdominal wall, preventing caudal displacement of

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Drs. Park and Moon contributed equally to the work.

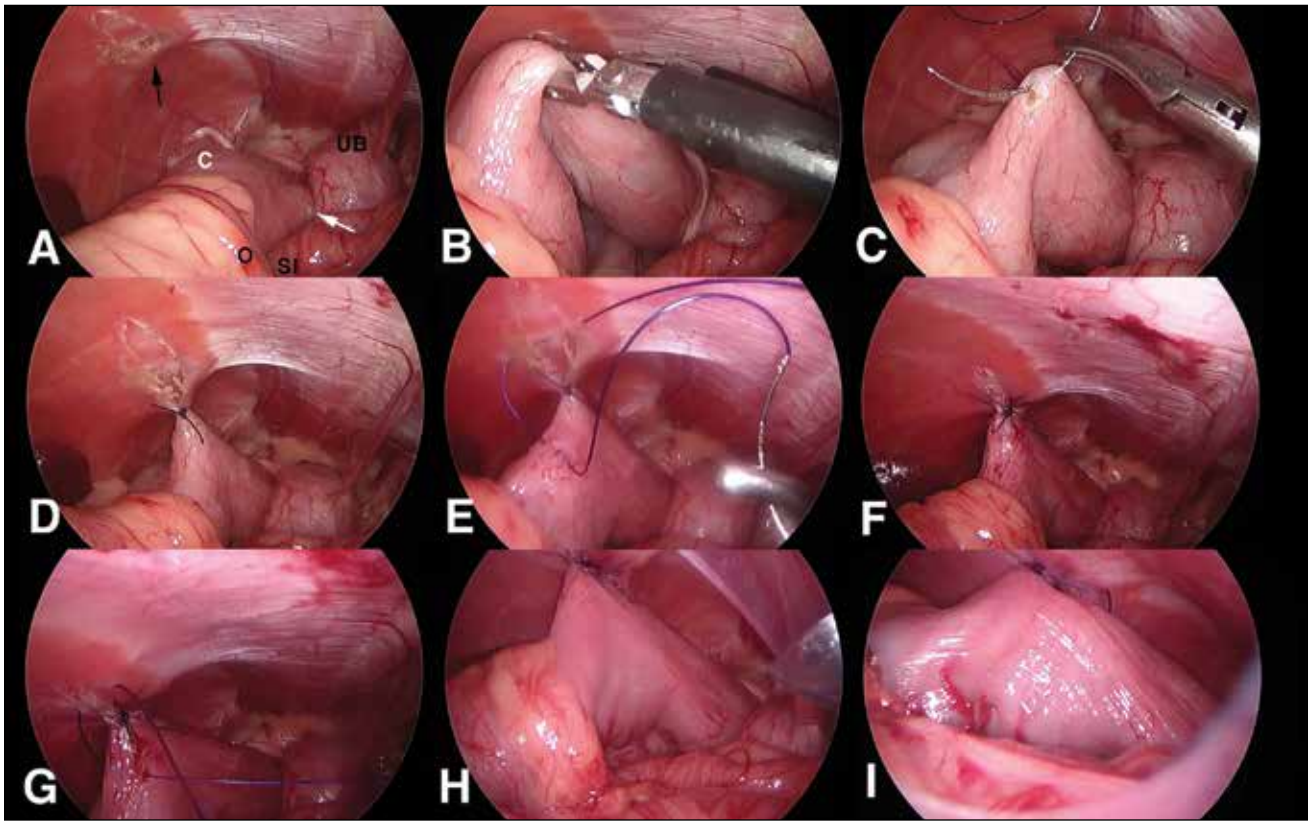

Figure 1. Laparoscopic colopexy in a dog with recurrent rectal prolapse. A – Colopexy sites on both sides indicated with cauterization; B – Final confirmation of tension before suture placement of colopexy; C – The seromuscular suture bite of the colon; D – Placement of the first caudal anchoring suture; E–G – The second and third suture bites; H – The completed colopexy; and I – The colopexy site without tension during deflation. Black arrow – Peritoneal incision of the abdominal wall with cauterization; White arrow – Pinpointed cauterization of the colon; C – Colon; O – Omentum; SI – Small intestine; UB – Urinary bladder.

the colon and rectum (1,2). It is commonly used for management of recurring RP with viable tissue, and in complicated perineal hernia, to prevent post-operative RP or recurrence of the perineal hernia (1,4). Furthermore, colopexy can be used for RP due to anal sphincter laxity (5) and a descending colonal torsion (6).

Open colopexy is most often performed; however, with increasing interest in minimally invasive surgery, a laparoscopic approach is becoming more common. During colopexy, sutures should be placed without penetrating the colon or putting excessive tension on the colon with cranial traction (1,4,7). This is important for ensuring a successful outcome, preventing local infection, or preventing failure of adhesion formation between the colon and body wall. Both incisional and non-incisional types of colopexy are effective (2).

Case description

A castrated male Maltese dog (2.5 kg), retrieved from an animal shelter, was presented with RP. The dog had a history of 2 previous surgeries (purse-string suture) since being rescued 4 mo ago. However, the RP did not resolve completely, and there was occasional bleeding. There was no internal parasitic infestation, but heartworm disease was diagnosed and treated by the referring veterinarian. The dog had dyschezia and straining on defecation, but otherwise, was bright and alert, with good appetite and normal activity. The RP had a relatively healthy mucosal eversion, ~1 cm long, that was reduced manually but relapsed soon after. Screening tests [thoracic/abdominal radiography, abdominal ultrasonography, complete blood (cell) count (CBC), serum chemistry, electrolytes, and urinalysis] revealed no specific findings except fecal accumulation. The dog was started on oral lactulose (0.5 mL/kg, q12h), and feces were manually expressed.

Figure 2. Portal sites for laparoscopic colopexy in a dog with rectal prolapse (after surgery). * Xyphoid process; Arrow – Primary port for camera.

Laparoscopic colopexy was performed 2 wk later, under general anesthesia with isoflurane inhalation (Figure 1).

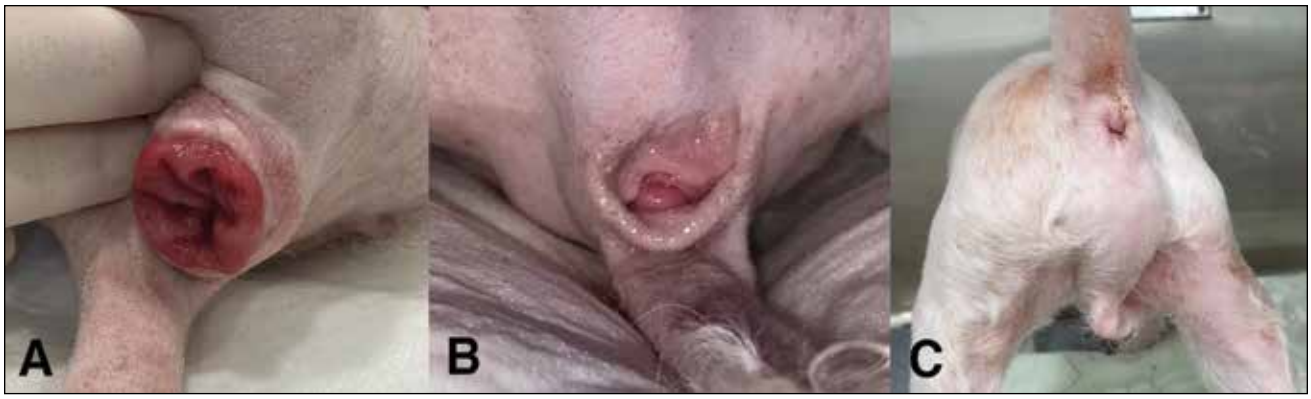

Figure 3. Gross appearance of rectal prolapse in a Maltese dog, before (A) and after (B) cranial retraction of the colon during laparoscopic colopexy, and on post-operative day 21 (C).

Midazolam (0.2 mg/kg, IV), butorphanol (0.2 mg/kg, IV), propofol (4 mg/kg, slow IV) were used for premedication and induction. Cefazolin (20 mg/kg, IV) and meloxicam (0.2 mg/kg, IV) were also given. The dog was placed in dorsal recumbency, and the surgical table was tilted as needed, to the right and laterally. The primary surgeon was on the right side of the dog, and an assistant who handled the camera stood on the left. Three 5-mm ports were placed using the Hasson technique: primary port (cranial to umbilicus) for the telescope (5 mm, 0°, 1488 HD; Stryker, Portage, Michigan, USA), and second and third instrumental ports (right paramedian around the prepuce for debakey forcep, babcock forcep, j-hook, and 2 laparoscopic needle holders with different jaw type; 1 flat and 1 curved, each) (Figure 2). Intra-abdominal pressure was maintained at $<$ 10 mmHg throughout the procedure.

Intra-abdominal exploration revealed that the omentum had adhered around the internal inguinal ring; it was cauterized with a j-hook. The distal colon was exposed and retracted cranially under external visual inspection by a nonsterile assistant to determine the degree of retraction required to resolve the RP with appropriate tension (Figure 3 A,B). Subsequently, it was lifted upward, and colopexy sites were chosen. Locations where the first anchoring suture was to be placed were indicated by pin-pointed cauterization on the colon and on the parietal peritoneum. To promote a strong adhesion, a 2-cm incision was made on the peritoneum, progressing anterior from the indicated point. Using 3-0 polydioxanone with tapered-round needle and a square knot, 3 simple interrupted sutures were placed intracorporeally, joining the abdominal wall and seromuscular layer of the colon. Intra-abdominal pressure was lowered when the first anchoring suture was tied, to allow both sides to approximate more easily, with less tension on the colon. The 2 following sutures were placed from the caudal to the cranial direction, more than 5 mm apart from each other. There was no suture failure, and bleeding was minimal. The colon was confirmed to be fixed to the body wall without a gap when the colopexy site was explored. Intra-abdominal conformation and tension on the colon were assessed during pneumoperitoneum deflation. The portal sites were closed routinely after bupivacaine infiltration.

The dog recovered uneventfully and had a good appetite and normal activity after surgery. Mild subcutaneous emphysema developed but resolved. He urinated and defecated with no indications of wound infection, peritonitis, or gastrointestinal signs. The dog had a positive perineal reflex, and the straining resolved (Figure 3 C). Compared to pre-surgery, feces were longer and of normal shape. The C-reactive protein concentration was within the normal range (10 mg/L, reference range: 0 to 20 mg/L) on post-operative day (POD) 1. Lactulose was discontinued on POD 7. There were no specific findings on abdominal radiography or ultrasonography on POD 5 and POD 37 and the colopexy maintained its intended site. A mild and transient protrusion of edematous anal mucosa was observed on POD 37. At the 12-month follow-up, he was doing well, without recurrence of RP.

Discussion

This report describes a laparoscopic colopexy in a clinical patient, a small-breed dog presenting with recurring RP despite 2 previous treatment attempts. Colopexy was achieved using a totally laparoscopic procedure with a 3-portal system, resulting in a favorable outcome. There was no need to convert, and there were no post-operative complications. This was attributed to a mild degree of prolapse of the external anal sphincter, despite the chronic pathologic course.

This is the first report of a completely laparoscopic colopexy procedure with detailed surgical information, in the English clinical literature. Previous veterinary studies on laparoscopic colopexy reported the laparoscopic-assisted technique that mostly used extracorporeal suturing and an paramedian incision of up to 5 cm (5,6,8–10). Zhang et al (6) reported less surgical trauma with a significantly lower serum C-reactive protein concentrations through this technique using a 3 to 4 cm mini-laparotomy compared to open colopexy. The C-reactive protein level in the present case was normal on POD 1, the time when these values are highest in the absence of progressive complication (6). Apart from the colopexy site, the 3 holes (each 5 mm) were the only other surgical trauma to the abdominal wall.

Laparoscopic colopexy requires skill and often considerable time to perform intracorporeal sutures, with practice needed to achieve proficiency. The author is a right-handed surgeon, and taking oblique suture bites instead of bites perpendicular to the longitudinal axis of the colon/cauterized abdominal wall, may have been more convenient for driving the needle. Furthermore, a shorter needle or ski needle with knotless barbed sutures would also have made this easier. In addition, when intracorporeal suture is not possible, a transparietal/percutaneous suture with skin only incision could be considered (11).

Regarding suture arrangement, in conventional open colopexy, the recommendation is 2 parallel rows with 5 to 8 sutures in each row, in an interrupted, continuous, or horizontal mattress pattern (1,3,5). This was also maintained in previous studies on laparoscopic-assisted colopexy (6,8,10), especially for an incisional technique. In the present case, only 3 simple interrupted sutures were placed in a single row, which induced no specific complications. This may be due to the small size and body weight of the patient; however, it is unclear how this method would work in larger patients. For example, more sutures could be placed, depending on the degree of stability. This method was supported by a study on laparoscopic-assisted colopexy that used 5 simple interrupted sutures in a single row in 7 healthy dogs (mean body weight, 13.2 kg) (11) that resulted in a favorable colopexy without complications. Necropsy and histopathology at 11 wk after surgery revealed a tight adhesion between the colon and abdominal wall, measuring 3 to 3.5 cm in length.

Five laparoscopic colopexies were included in a previous canine study (4); 3 resulted in wound complications, including local abscess formation at the colopexy site, requiring revision of laparotomy in 2 dogs for definitive treatment of infection. In another study, 1 dog had a laparoscopic-assisted colopexy but was euthanized due to bacterial peritonitis resulting from colonic leakage on POD 11 (12). Unfortunately, there was no detailed information available for surgical procedures in either report; therefore, laparoscopic colopexy may not have been attempted. In contrast, in the present case, there was no wound infection or leakage at the colopexy site, either perioperatively, or up to 12 mo after surgery. Although laparoscopy does not allow surgeons to work directly on the tissue with tactile sensation, it provides magnified visualization, which is preferable for precise suture placement in the seromuscular wall of the colon. Although the condition of the colon and its healing from surgical trauma in healthy dogs could differ from that in clinical cases with RP, previous laparoscopic colopexy in 8 healthy dogs reported no complications associated with wound infection at the colopexy site, and an appropriate permanent adhesion was achieved (7). In that study, intracorporeal sutures were performed with simple interrupted sutures in 2 rows and 3 sutures in each row.

The findings in this case supported the use of laparoscopic colopexy in small-breed dogs. It is a practical treatment option in clinical cases. However, further studies with a greater number of clinical patients and longer follow-up periods are warranted. CVJ

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Case Report Rapport de cas

Multiple session mesotherapy for management of coxofemoral osteoarthritis pain in 10 working dogs: A case series

João C. Alves, Ana Santos, Patrícia Jorge, Pilar Lafuente

Abstract — The aim of this study was to document the effects of mesotherapy in working dogs diagnosed with hip osteoarthritis (OA) and related pain. Ten police working dogs with hip OA and related pain were treated with a combination of lidocaine, piroxicam, and thiocolchicoside, injected in multiple intradermal points. Seven treatment sessions were conducted. The Canine Brief Pain Inventory (CBPI) and the Hudson Visual Analogue Scale (HVAS) were used in the assessment of response to treatment compared to evaluation before treatment (T0), after 15 d, 30 d, 60 d, 90 d, 120 d, 150 d, and 180 d after initial treatment. Results were compared using the Wilcoxon signed-rank test.

Significant differences were experienced in CBPI scores comparing moments with T0: at 15 d ($P = 0.03$ for Pain Interference Score — PIS) and $P = 0.02$ for Pain Severity Score — PSS), 30 d ($P < 0.05$ for PIS and $P < 0.05$ for PSS), 60 d ($P = 0.04$ for PIS and $P = 0.01$ for PSS) and 180 d ($P = 0.04$ for PSS). Individual treatment results were considered successful in 40% of animals at 15 d and 30 d, 66.7% at 60 d, 44% at 90 d, 37.5% at 120 d, and 25% at 150 d. The HVAS scores showed no significant differences.

Mesotherapy may be an option for the treatment of canine musculoskeletal-related pain. Further studies are required.

Résumé — Mésothérapie en plusieurs séances pour la prise en charge de la douleur arthrosique coxofémorale chez 10 chiens de travail : une série de cas. Le but de cette étude était de documenter les effets de la mésothérapie chez les chiens de travail diagnostiqués avec une arthrose de la hanche (OA) et des douleurs associées. Dix chiens de travail policiers souffrant d'OA et de douleurs associées ont été traités avec une combinaison de lidocaïne, de piroxicam et de thiocolchicoside, injectée en plusieurs points intradermiques. Sept séances de traitement ont été réalisées. Le *Canine Brief Pain Inventory* (CBPI) et l'échelle visuelle analogique de Hudson (HVAS) ont été utilisés dans l'évaluation de la réponse au traitement par rapport à l'évaluation avant traitement (T0), après 15 j, 30 j, 60 j, 90 j, 120 j, 150 j et 180 j après le traitement initial. Les résultats ont été comparés à l'aide du test des rangs signés de Wilcoxon.

Des différences significatives ont été observées dans les scores CBPI comparant les moments avec T0 : à 15 jours ($P = 0{,}03$ pour *Pain Interference Score* – PIS) et $P = 0{,}02$ pour *Pain Severity Score* – PSS), 30 jours ($P < 0{,}05$ pour PIS et $P < 0{,}05$ pour PSS), 60 jours ($P = 0{,}04$ pour PIS et $P = 0{,}01$ pour PSS) et 180 jours ($P = 0{,}04$ pour PSS). Les résultats du traitement individuel ont été considérés comme réussis chez 40 % des animaux à 15 jours et 30 jours, 66,7 % à 60 jours, 44 % à 90 jours, 37,5 % à 120 jours et 25 % à 150 jours. Les scores HVAS n'ont montré aucune différence significative.

La mésothérapie peut être une option pour le traitement des douleurs musculosquelettiques canines. Des études complémentaires sont nécessaires.

(Traduit par Dr Serge Messier)

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Introduction

Osteoarthritis (OA) affects all animals (1,2). It has an estimated prevalence of 20% in dogs, particularly working dogs with high physical demands. The most common and relevant clinical sign, and a hallmark of the disease, is chronic pain (3–5). Prevalence of this condition is expected to increase due to a simultaneous increase in life expectancy and obesity. In one study, OA was identified in 98% of dogs followed until their end of life (6). Osteoarthritis is incurable and challenging to treat despite being a common condition (7,8). The condition has an effect on gait, posture, activity, and overall performance in working dogs.

Mesotherapy is an administration technique in which drugs or other substances are deposited in small quantities in the dermis. From these microdeposits created in the skin over the area of the condition being treated, the drugs are slowly released to the surrounding tissues, muscles, tendons, and ligaments, which are also a source of pain in OA (9,10). Mesotherapy has a rapid onset of action, a prolonged local action, and a drug-sparing effect, having been described as superior to systemic therapy for musculoskeletal pain relief in humans (11,12). Mesotherapy has been described in the treatment of various musculoskeletal conditions, such as back pain and osteoarthritis, in humans, horses, and dogs (13–16).

Evaluation of chronic pain in animals is challenging, and can be performed by subjective and objective methods. The Canine Brief Pain Inventory (CBPI) is a questionnaire designed to assess owners' perception of the impact of chronic pain on their dog. It has been used to detect improvements in the treatment of OA in dogs receiving NSAIDs (17). The CBPI is divided into 2 components: a pain severity score (PSS) that assesses the magnitude of pain experienced by a dog, and a pain interference score (PIS) that evaluates the degree to which pain affects daily activities (18). The Hudson Visual Analogue Scale (HVAS) is a validated tool for assessing lameness in dogs (19).

This report aims to describe the use and effectiveness of mesotherapy in working dogs with hip OA-related pain.

Materials and methods

This study is a part of a project approved by the Ethical Review Group of the Association of Veterinary Anaesthetists (No. 2020-010). Written, informed consent was obtained from the Institution responsible for all the animals (Guarda Nacional Republicana, Portuguese Gendarmerie). Animals were included from the population of working dogs of the Grupo de Intervenção Cinotécnico (Portuguese Gendarmerie Canine Unit). Dogs were selected based on history, trainer complaints (difficulty rising, jumping, and maintaining obedience positions, stiffness, and decreased overall performance), physical (pain during joint mobilization, stiffness, and reduced range of motion), and radiographic findings consistent with bilateral hip OA. Dogs with other illnesses were excluded based on physical, orthopedic, and neurological examination, complete blood (cell) count, and serum chemistry profile. Animals included in the study could not be under any other treatment.

In this single-blinded study (trainers were unaware of the type of treatment their animals received), dogs were treated with a solution of 40 mg of lidocaine (Anestesin; Laboratório Sorológico, Amadora, Portugal), 20 mg of piroxicam (Feldene; Pfizer, Porto Salvo, Portugal), and 4 mg of tiocolchicoseide (Relmus; Sanofi, Porto Salvo, Portugal), based on an identical protocol used for the treatment of OA in humans (20). A total solution volume of 4 mL was prepared, regardless of the animal's weight. In each injection point, 0.1 mL was injected intradermally, using 27-G needles, 4-mm in length (Mesoram; Miami, Florida, USA). Injection sites were spaced approximately 2 cm apart (10,21), along the skin area corresponding to the location of the coxofemoral joint: laterally on a 4×4 cm area with the greater trochanter at its center, and medially on a similar-sized area, having the coxofemoral joint at the center. Thirty-five to 40 injections were done on each animal, depending on the dog's size. Injections were conducted with the needle at an average inclination of 30° at a depth of up to 4 mm (21,22). Only mild restraint and no sedation were required to conduct treatment sessions. Animals were rested for 3 d after the initial treatment session and then resumed normal activity over 5 d (16).

The assisting veterinarian examined all animals 1 and 4 d after initial treatment for any abnormal findings induced by the treatment. If none were detected, the animal was permitted to return to normal work. A total of 7 injection sessions were conducted for each animal; 4 weekly sessions followed by 3 sessions 15 d apart (21). With mesotherapy, adverse effects are extremely rare and mild, and if they occur, include nausea, vomiting, diarrhea, mild pain, edema, pruritus, and erythema (23). Signs of any possible adverse effects were recorded during the follow-up examination.

Response to treatment as measured with the CBPI and HVAS, was evaluated before treatment (T0), after 15 d (after 2 treatment sessions), 30 d (after 4 treatment sessions), 60 d (after 6 treatment sessions), 90 d (after all 7 treatment sessions), 120 d, 150 d, and 180 d after initial treatment. The trainers completed these without seeing their previous evaluation. The CBPI includes a question to classify the animals' overall quality of life, comprising 5 levels: bad, reasonable, good, very good, and excellent.

Normality was assessed with a Shapiro-Wilk test. Results of each evaluation moment were compared with those before treatment with the Wilcoxon signed ranks test. IBM SPSS Statistics version 20 was used for the statistical analysis, $P < 0.05$.

Results

Ten animals comprised the sample, representing 5 breeds, German shepherd (n = 5), Labrador retriever (n = 2), Belgian Malinois shepherd (n = 1), Dutch shepherd (n = 1), and catch dog of São Miguel Island (n = 1). Eight males and 2 females were included, with a mean weight of 32.3 kg ($\pm$ 4.9 kg) and a mean age of 6.7 y ($\pm$ 1.05 y). Of the animals enrolled, 2 had to be excluded. One was excluded due to the impossibility of medical follow-up after 30 d. Another dog was eliminated after 90 d, as he suffered a third phalanx avulsion of the second digit of the right thoracic limb. Data obtained from these animals up to the moment of exclusion was included in the analysis. The CBPI and HVAS answers were collected in all evaluation moments, up to the study's end or when an animal was excluded. The number

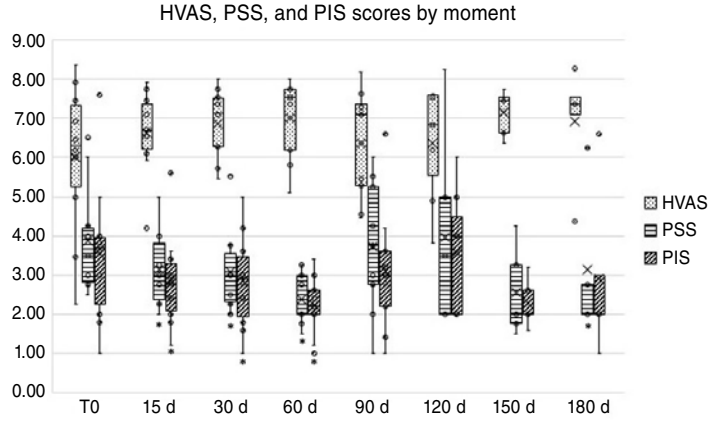

Figure 1. Overall Hudson Visual Analogue Scale (HVAS), Pain Severity Score (PSS), and Pain Interference Score (PIS) registered, by moment.
* Indicates significant variation.

of injections performed in each animal varied with its size to cover the area being injected. No adverse effects were detected.

When comparing results for each moment with T0, differences were observed at 15 d ($P = 0.03$ for PIS and $P = 0.02$ for PSS), 30 d ($P < 0.05$ for PIS and $P < 0.05$ for PSS), 60 d ($P = 0.04$ for PIS and $P = 0.01$ for PSS) and 180 d ($P = 0.04$ for PSS) (Figure 1). Individual treatment success, as measured by the CBPI, has been defined as a reduction of ≥ 1 in PSS and ≥ 2 in PIS (24). Treatment was successful in reducing PSS in 4 out of 10 animals at 15 d and 30 d (40%), 6/9 at 60 d (67%), 4/9 at 90 d (44%), 3/8 at 120 d (37.5%), 2/8 at 150 d (25%) and none at 180 d. In addition, PSS results improved for 8/10 animals at 15 d (80%), 8/9 at 60 d (88.9%), 6/9 at 90 d (67%), 4/8 at 120 d (50%) and 3/8 at 150 and 180 d (37.5%). Considering PIS, treatment was a success in 1 out of 10 animals at 15 d and 30 d (10%), 3/9 at 60 d (33.3%), 1/9 at 90 d (11.1%,), 2/8 at 120 d (25%), and 1/8 at 150 d and 180 d (12.5%). Treatment also improved PIS scores for 6/10 animals at 15 and 60 d (60%), 6/9 at 90 d (67%), 2/8 at 120 and 150 d (25%), and 1/8 at 180 d (12.5%).

No significant differences were registered in the results of the HVAS in each moment with T0 (Figure 1). When considering individual results, an improvement in results was observed in 5/10 animals at 15 d (50%), 8/10 at 30 d (80%), 7/9 at 60 d (77.7%), 5/9 at 90 d (55.6%), 3/8 at 120 d and 150 d (37.5%), and 2/8 at 180 d (25%). Mean scores for PSS, PIS, and HVAS at the various times, are presented in Table 1. Individual scores for PSS, PIS, and HVAs are presented in Tables 2, 3, and 4, respectively.

Considering trainers' classification of the quality of life at T0, 4/10 of animals were considered to have a very good quality of life, another 4/10 as good, 1/10 as reasonable, and 1/10 as bad. This distribution of classifications changed at 15 d, with 6/10 of animals classified as having a very good quality of life and 3/10 as good and 1/10 as reasonable. At 30 d and 60 d, animals were classified as having very good (5/10 and 2/9, respectively) or good (5/10 and 7/9, respectively) quality of life. At 90 d, 3/9 animals were classified as having a very good quality of life,

Table 1. Significant improvements in Pain Severity Score (PSS) and Pain Interference Score (PIS) of the Canine Brief Pain Inventory (CBPI), and improvements in HVAS scores, by moment.

	T0		T1		T2		T3		T4		T5		T6		T7	
Survey	Score	*P*-value	Score	*P*-value	Score	*P*-value	Score	*P*-value	Score	*P*-value	Score	*P*-value	Score	*P*-value	Score	*P*-value
PSS	3.9 ± 1.36	—	3.1 ± 0.93	0.02	2.9 ± 1.03	0.04	2.4 ± 0.68	0.01	3.7 ± 1.69	0.68	3.9 ± 2.33	0.49	3.1 ± 1.18	0.14	2.58 ± 1.79	0.04
PIS	3.6 ± 1.85	—	2.9 ± 1.21	0.03	2.8 ± 1.21	0.04	2.2 ± 0.77	0.04	3.1 ± 1.65	0.17	3.6 ± 1.61	0.92	2.3 ± 0.63	0.46	2.9 ± 2.17	0.28
HVAS	6.0 ± 1.93	—	6.6 ± 1.07	0.11	6.9 ± 0.86	0.07	7 ± 1.03	0.17	6.4 ± 1.42	0.59	6.3 ± 1.48	0.92	7.1 ± 0.59	0.07	6.6 ± 6.56	1

Table 2. Evolution of individual of Pain Severity Scores (PSS) and percentual variation compared with T0, by moment.

	PSS													
	T0	15		30		60		90		120		150		180	
Patient	Score	Score	%	Score	%	Score	%	Score	%	Score	%	Score	%	Score	%
1	3.5	2.0*	42.9	5.5	−57.1	2.0**	42.9	2.0**	42.9	2.0**	42.9	1.5**	57.1	2.8	20.0
2	4.3	4.0*	7.0	3.8*	11.6	3.3**	23.3	5.5	−27.9	5.0	−16.3	4.3	0.0	4.3	0.0
3	2.8	3.3	−17.9	2.3*	17.9	2.0*	28.6	1.0**	64.3	2.0**	28.6	1.8**	35.7	2.0*	28.6
4	2.8	2.0*	28.6	2.0*	28.6	2.8	0.0	4.3	−53.6	2.0*	28.6	2.0*	28.6	2.0*	28.6
5	2.5	2.8	−12.0	2.5	0.0	1.5**	40.0	2.0*	20.0	2.5	0.0	2.5	0.0	2.5	0.0
6	3.0	2.3*	23.3	2.0**	33.3	2.0**	33.3	2.8*	6.7	3.5	−16.7	3.3	−10.0	2.8*	6.7
7	4.0	3.0**	25.0	3.0**	25.0	—	—	—	—	—	—	—	—	—	—
8	6.5	5.0**	23.1	2.8**	56.9	3.0**	53.8	5.3**	18.5	5.0**	23.1	6.3	3.1	6.3	3.1
9	6.0	4.0**	33.3	3.0**	50.0	1.8**	70.0	3.8**	36.7	8.3	−38.3	7.0	−16.7	7.5	−25.0
10	3.5	2.3**	34.3	3.0*	14.3	3.3*	5.7	3.5	0.0	—	—	—	—	—	—

* Indicates score improvement.
** Indicates significant score improvement.

Table 3. Evolution of individual of Pain Interference Scores (PIS) and percentual variation compared with T0, by moment.

	PIS													
	T0	15		30		60		90		120		150		180	
Patient	Score	Score	%	Score	%	Score	%	Score	%	Score	%	Score	%	Score	%
1	5.0	3.4*	32.0	5.0	0.0	2.2**	56.0	2.2**	56.0	2.0**	60.0	1.6**	68.0	1.0**	80.0
2	3.6	3.6	0.0	3.6	0.0	2.6*	27.8	3.2*	11.1	4.0	−11.1	2.6*	27.8	3.6	0.0
3	1.8	1.8	0.0	2.8	−55.6	2.0	−11.1	1.0*	44.4	2.0	−11.1	2.0	−11.1	2.0	−11.1
4	2.0	2.0	0.0	1.6*	20.0	2.2	−10.0	4.2	−110.0	2.0	0.0	2.0	0.0	2.0	0.0
5	1.0	1.2	−20.0	1.0	0.0	1.0	0.0	1.4	−40.0	1.0	0.0	1.0	0.0	1.2	−20.0
6	3.0	2.4*	20.0	1.8*	40.0	2.4*	20.0	2.8*	6.7	4.0	−33.3	3.2	−6.7	3.0	0.0
7	3.8	3.0*	21.1	3.0*	21.1	—	—	—	0.0	—	—	—	—	—	—
8	7.6	5.6**	26.3	4.2**	44.7	3.4**	55.3	6.6	13.2	5.0**	34.2	6.6	13.2	6.6	13.2
9	4.0	2.8*	30.0	2.4*	40.0	1.2**	70.0	3.6*	10.0	6.0	−50.0	5.0	−25.0	5.0	−25.0
10	3.8	2.8*	26.3	3.0*	21.1	3.0*	21.1	3.8	0.0	—	—	—	—	—	—

* Indicates score improvement.
** Indicates significant score improvement.

Table 4. Evolution of individual of Hudson Visual Analogue Scale (HVAS) scores and percentual variation compared with T0, by moment.

	HVAS													
	T0	15		30		60		90		120		150		180	
Animal	Score	Score	%	Score	%	Score	%	Score	%	Score	%	Score	%	Score	%
1	8.4	7.7	−8.3	7.5	−10.7	7.4	−11.9	7.6	−9.5	7.6	−9.5	7.5	−10.7	7.4	−11.9
2	6.5	6.5	0.0	7.2	10.8	5.1	−21.5	4.5	−30.8	6.5	0.0	6.4	−1.5	6.4	−1.5
3	7.5	7.5	0.0	7.1	−5.3	7.6	1.3	7.4	−1.3	7.5	0.0	7.5	0.0	7.5	0.0
4	7.9	7.9	0.0	8.0	1.3	8.0	1.3	8.2	3.8	8.0	1.3	8.2	3.8	8.3	5.1
5	6.2	6.1	−1.6	7.4	19.4	7.5	21.0	7.3	17.7	6.2	0.0	6.2	0.0	6.0	−3.2
6	6.9	7.1	2.9	7.7	11.6	7.7	11.6	7.1	2.9	6.2	−10.1	6.6	−4.3	3.0	−56.5
7	6.0	6.7	11.7	6.3	5.0	6.0	0.0	5.5	−8.3	5.8	−3.3	6.0	0.0	5.8	−3.3
8	2.3	4.2	82.6	5.7	147.8	5.8	152.2	4.5	95.7	4.9	113.0	5.5	139.1	6.6	187.0
9	3.5	6.6	88.6	6.3	80.0	7.7	120.0	5.3	51.4	3.8	8.6	4.0	14.3	3.5	0.0
10	5.0	5.9	18.0	5.5	10.0	6.2	24.0	5.0	0.0	5.0	0.0	4.8	−4.0	4.8	−4.0

* Indicates score improvement.

4/9 as having a good quality of life, and 2/9 had a reasonable classification. From 120 d on, 4/8 had a very good quality of life, 2/8 had a good quality of life, and 2/8 had a reasonable classification.

Discussion

Osteoarthritis management focuses mainly on controlling symptoms, predominantly pain (25,26). Our results show that mesotherapy can provide significant short-term pain relief in working dogs with OA, making it an interesting tool in managing the disease. Joint pain and function are influenced by sensory innervation of all composing and surrounding tissues, such as muscle, tendons, ligaments, and remaining joint tissues (1,9). Mesotherapy targets all of these tissues. It is postulated that the applied drugs diffuse from the microdeposit to all underlying tissues, even those with poor vascularization,

reaching high concentration levels superior to those obtained with other administration routes (10).

The CBPI survey is frequently used in veterinary medicine to assess chronic pain in dogs (17,24,27,28). It has the advantage of quantifying the owner's assessment of the dog in their environment and over time. In dogs with OA, successful treatment has been set as a decrease in PSS $\geq$ 1 and PIS $\geq$ 2 (24,28). Mesotherapy significantly reduced scores of working dogs with hip OA, particularly PSS. The entirety of individual treatment sessions distributed over 10 wk, and the beneficial effects of the treatment were observed throughout this period and, for some animals, well beyond this time. Even though a significant reduction was not observed for all animals, 80% of animals showed a PSS reduction between 15 and 60 d, 55% at 90 d, 50% at 120 d, and 37.5% at 150 and 180 d (37.5%), with peak improvements being registered after the first 4 sessions, conducted once a week. This prolonged effect has been previously described (10), and it is probably due to a combination of local drug action and improved joint function resulting from the use of a less painful joint.

Results for PIS registered less significant improvements, but at 30 d, 60% of animals showed a score reduction; a value that declined up to 180 d, in which 12.5% of animals still registered better results than initial scores. Some factors may account for this fact. Since most of the treated animals showed only mild clinical signs, PIS scores were low initially, making it difficult to reduce this score significantly. In addition, as these dogs have high work motivation, they may still exhibit good performance in daily activities, leading to a low perception of pain interference. When trainers were asked to classify the animal's quality of life, all but one was seen to have very good or at least good quality of life on the first evaluation points after beginning treatment (15 d), and all up to 2 mo (60 d), this corresponding to the evaluation point in which better results were registered with the CBPI. From this point on, most animals were still considered to have a good quality of life. The fact that the animals enrolled in this study are working dogs means that their musculoskeletal structures are in greater demand compared with a companion animal. With that in mind, it is possible that results may remain evident for a longer period of time in companion animals due to the lower physical demand. On the other hand, most of the animals included in this study had only mild symptoms since signs of the disease are usually detected early, which may not be true for a companion animal. Difficulty jumping is a common complaint in working dogs; even in dogs without apparent musculoskeletal disease (29). Visual analog scales are commonly used to evaluate the severity of pain, allowing comparisons between or among analgesic regimens. The Hudson Visual Analogue Scale (HVAS) has been validated against force plate analysis (19). We did not observe significant variations in HVAS scores, even though individual results seemed to improve in almost all animals. Since visual analog scales are more sensitive in detecting and recording changes in more overt cases of lameness, and most of the animals included in the study showed only mild signs, a significant change may be harder to detect with the HVAS.

We chose a specific drug combination based on a protocol described for management of human OA (20). In addition to being described in humans, this particular drug combination seemed to make sense to address all the tissues involved in OA-related pain (1). However, other drug combinations are described (20), and their evaluation may be a topic for future research. Also, it would be interesting to evaluate the effect of a single drug compared to that of combined drugs. The effect of a single drug is hard to determine, as most described mesotherapy protocols present the combined use of different drugs (20,21), and recommendations for the use of a single drug are based on a reduced risk of drug-drug interactions and local side effects, not on the effect of the drug itself (10).

We also chose these specific evaluation moments based on previous reports on the evaluation of OA treatment in dogs (30–33). However, additional or different evaluation moments can be selected, for example, to correspond with treatments times. The selection of treatment moments can also be adjusted. We chose this protocol based on the treatment frequency suggested for human musculoskeletal pain management (21). The authors also indicate the possibility of monthly or every 15-day sessions, as needed. As this was the first description of the use of mesotherapy in the management of hip OA in working dogs, we considered it interesting to evaluate the longevity of the results. The treatment has been described as having a long-lasting effect, amounting to months in some cases (16,34). It is possible that additional sessions, 3 or 4 mo following initial treatment, would produce different outcomes. These variables and their effects, from drug selection to treatment algorithm and the effect of mesodermal modulation, must be evaluated in future studies (22). No adverse effects were observed in the animals treated. Mesotherapy can be combined with other systemic therapies and may also be an option if other therapies are not a choice due to existing comorbidities. Further studies addressing this possibility are required.

This study had some limitations, namely its sample size, the lack of a control group, and the fact that it was only single-blinded. For this study, we selected the CBPI and HVAS as outcome measures, as they have been validated for the evaluation of pain and lameness in dogs, and focus on 2 major clinical signs of OA: pain and mobility (35). Further studies should include other evaluation methods, such as other available clinical metrology instruments (the Liverpool Osteoarthritis in Dogs or the Canine Orthopedic Index). Although these scales are useful in clinical settings, they are susceptible to bias, as in the case of the caregiver placebo effect (36,37), particularly in the absence of a control group. Also, for these reasons, future studies should include objective measures, such as Force Plate Gait Analysis. Since study herein presented positive hip OA-related pain management results, future studies should enroll larger numbers of animals and a control group.

In conclusion, mesotherapy may be a treatment option in dogs with OA. In this study, it resulted in lower pain severity scores in some police working dogs with hip OA-related pain, with improvements lessening after the last treatment session. Further studies are required, with more animals, with different hip OA grades, and evaluating other medications or combinations. The present treatment algorithm is safe and adequate to treat this clinical problem. CVJ

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Article

Description and validation of a new descriptive and multiparametric numeric rating scale to assess sedation in cats

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Abstract — The objective of this study was to design and assess the validity and reliability of a new feline multiparametric sedation scale (FMSS). A total of 89 household cats were recruited, enabling a total of 534 sedation assessments. Every assessment was performed by 3 blinded observers with varying expertise levels (Level 1: Student; Level 2: RVT; Level 3: ACVAA diplomate or senior resident). For comparison purposes, a visual analogue scale (VAS) and a Simple Qualitative Scale (SQS) were also used concurrently, with the VAS considered the gold standard. The new scale had excellent inter-observer agreement among experience groups with weighted *Kappa* scores of 0.84 (Levels 1 *versus* 2), 0.82 (Levels 2 *versus* 3), and 0.84 (Levels 1 *versus* 3), with $P < 0.0001$ for all comparisons. There was a high degree of association between FMSS and VAS ($r = 0.90$, $P < 0.0001$) and between FMSS and SQS ($r = 0.89$, $P < 0.0001$). Final FMSS numerical values were paired with levels of sedation with None = 0 (0 to 5), Mild = 4 (1 to 7), Moderate = 6 (2 to 10), and Profound = 12 (7 to 12); furthermore, differences were detected between pre- and post-sedation evaluations ($P = 0.001$). This scale demonstrated internal consistency and sensitivity even when evaluating drugs or doses with minimal sedative effects and there was very strong interrater reliability, independent of experience level. Based on this clinical study, we concluded that the use of this sedation scale is appropriate when objective numerical sedation quantification is required, in either a clinical or research setting.

Résumé — Description et validation d'une nouvelle échelle d'évaluation numérique descriptive et multiparamétrique pour évaluer la sédation chez le chat. L'objectif de cette étude était de concevoir et d'évaluer la validité et la fiabilité d'une nouvelle échelle de sédation multiparamétrique féline (FMSS). Un total de 89 chats domestiques a été recruté, permettant un total de 534 évaluations de sédation. Chaque évaluation a été effectuée par trois observateurs en aveugle avec différents niveaux d'expertise (Niveau 1 : étudiant; Niveau 2 : RVT; Niveau 3 : diplomate de l'ACVAA ou résident senior). À des fins de comparaison, une échelle visuelle analogique (VAS) et une échelle qualitative simple (SQS) ont également été utilisées simultanément, VAS étant considérée comme l'étalon. La nouvelle échelle présentait un excellent accord inter-observateurs parmi les groupes d'expérience avec des scores *Kappa* pondérés de 0,84 (niveaux 1 *versus* 2), 0,82 (niveaux 2 *versus* 3) et 0,84 (niveaux 1 *versus* 3), avec $P < 0{,}0001$ pour toutes les comparaisons. Il y avait un degré élevé d'association entre FMSS et VAS ($r = 0{,}90$, $P < 0{,}0001$) et entre FMSS et SQS ($r = 0{,}89$, $P < 0{,}0001$). Les valeurs numériques FMSS finales ont été appariées avec les niveaux de sédation avec Aucun = 0 (0 à 5), Léger = 4 (1 à 7), Modéré = 6 (2 à 10) et Profond = 12 (7 à 12); en outre, des différences ont été détectées entre les évaluations pré- et post-sédation ($P = 0{,}001$). Cette échelle a démontré une cohérence interne et une sensibilité même lors de l'évaluation de médicaments ou de doses avec des effets sédatifs minimes et il y avait une très forte fiabilité inter-évaluateur, indépendamment du niveau d'expérience. Sur la base de cette étude clinique, nous avons conclu que l'utilisation de cette échelle de sédation est appropriée lorsqu'une quantification numérique objective de la sédation est requise, dans un cadre clinique ou de recherche.

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Introduction

Based on recent census data from the Canadian Animal Health Institute (CAHI), cat and dog populations in Canada have risen since 2014 (1). Approximately 38% of households in Canada have a cat, and cats outnumber dogs with 8.8 million cats considered household pets in 2016. The Canadian Veterinary Medical Association, however, estimates that cat owners (46%) are far less likely than dog owners (77%) to have taken their pet to the veterinarian within the last year (2). Resistance to and stress caused by transportation and examination appear to be some of the main factors contributing to cat owners not pursuing regular wellness examinations (3). After the combined stressors of confinement and transportation, cats can be in a state of high arousal or anxiety, increasing the possibility of resistance and aggression. Handling difficult or fractious patients may preclude a thorough examination or lead to increased risk of injury to veterinary staff (4).

Administration of oral or parenteral sedatives is a useful strategy to attempt sedation/anxiolysis prior to hospital visits, facilitate diagnostic or minor procedures such as catheterization before general anesthesia, decrease induction doses, or to facilitate cage rest or exercise restriction post-operatively. Administration of sedatives also aids in reducing stress levels on pets, owners, and staff members. Many studies have described the sedation properties of various drugs in cats (5–9). However, sedation scales for quantifying degree of sedation in domestic cats have not been formally assessed for validity and reliability (9,10). Many of the existing scales vary substantially in their content, with researchers often modifying existing scales used in other species, increasing variability among published results, and hindering comparisons of sedation data (11,12). For example, the scale described by Slingsby et al (13) is a simple descriptive scale that only includes posture and lack of response to sound. This scale has been used and modified by other authors to include a more detailed description of the posture and response to touch and sound (14,15). More descriptive scales have been designed that include various categories to capture more specific signs of sedation in cats. Categories included in these scales vary widely among studies, with some including or excluding variables such as muscle relaxation, response to noise, or restraint, whereas others include more specific signs tailored to the study (16,17).

Determining validation and reliability offers information on whether a sedation scale correctly measures what it is supposed to, and the degree of measurement errors coinciding with the scale of choice. When measuring sedation, verifying evidence for the validity and reliability of the scale is essential to ensuring appropriate scale sensitivity, when assessing various levels of sedation, as well as appropriate inter-rater agreement (12). Moreover, having a reliable scale capable of detecting even mild levels of sedation and one that is easy to use, irrespective of observer experience, should improve reproducibility of future studies and comparisons of results.

The primary objective was to design and assess the validity and reliability of a newly developed sedation scale and determine concordance between raters with varying levels of expertise. We hypothesized that this scale detects differences among various levels of sedation and has acceptable inter-rater reliability when used by multiple raters with varying experience.

Materials and methods

Animals

The study was performed in accordance with an approved Animal Utilization Protocol from the University of Guelph. All feline assessments were completed on client-owned animals at the Ontario Veterinary College Small Animal clinic (OVC-HSC) Canada. Owner consent was obtained for administration of sedatives, either as part of the anesthetic protocol or to facilitate diagnostic procedures. All animals included in the study were cats that required intravenous (IV), or intramuscular (IM) sedation prior to physical examination, general anesthesia, or to perform diagnostic procedures, e.g., radiographs or blood collection. An assessment was completed before and 30 min after drug administration to assess scale performance under pre- and post-sedation for a population of cats with non-homogeneous sedation protocols.

Sedation scale

The feline multiparametric sedation scale (FMSS) is a descriptive multiparametric numeric rating scale designed for the purpose of this study (Appendix 1). Some of the components of this scale were modified from other composite multiparametric scales used for cat sedation studies (14–18). We only included categories considered relevant to all degrees of sedation, excluding end points such as muscle relaxation that are most prominent when using some sedation protocols (18). Before study initiation, this scale was widely trialed and refined by several anesthesia technicians and residents, to ensure clarity and ease of use. For comparison purposes, a visual analogue scale (VAS) and a Simple Qualitative scale (SQS) were also used at the same time points (Appendix 1). Therefore, the sedation assessment sheet had 3 sections.

The first section of the sedation sheet was the FMSS, which allowed observers to rank an animal's posture, behavior, response to sound, and response to restraint, on a scale of 0 to 3. Each numerical choice was accompanied by a descriptor. Posture was assessed by observing the cat in their cage from the other side of the room (distance of approximately 2 m). Behavior was assessed through interacting with the animal by petting its head or body. Response to sound was determined by an animal's reaction to a loud single clap inside the cage while they were not looking at the operator. Lastly, response to restraint was assessed by the animal's reaction to being held for an intramuscular injection or placement of an intravenous catheter. The final resulting scale was a number out of 0 to 12, with 0 and 12 representing no and maximum sedation, respectively. Cats were never scruffed, and all interactions with them were standardized. Restraint for IM injections was always performed by covering the cat with a towel and applying moderate pressure to ensure contact of the cat with the cage floor. For IV catheterization, cats were gently wrapped in a towel, positioned in sternal recumbency, and the restrainer positioning 1 hand under the jaw to control the head while using the other hand to extend the leg to facilitate catheter placement.

Table 1. Drug protocols for sedating cats with FMSS final scores expressed as median (range) and SQS for all 3 observers.

Drug protocol	*n*	FMSS final score[a]	SQS[b]
Pre-sedation			
None	85	1 (0 to 5)	None
Gabapentin (PO)	4	3 (0 to 7)	Mild
Post-sedation			
Opioid (IM or IV)	7	4 (3 to 12)	Moderate
Dexmedetomidine + opioid (IM)	36	11 (2 to 12)	Profound
Dexmedetomidine + opioid + ketamine (IM)	1	10 (10)	Profound
Dexmedetomidine + opioid + alfaxalone (IM)	2	12 (12)	Profound
Gabapentin (PO) + dexmedetomidine + opioid (IM)	1	12 (12)	Profound
Acepromazine + opioid (IM)	25	5 (2 to 12)	Moderate
Acepromazine + opioid + ketamine (IM)	10	11 (5 to 12)	Profound
Gabapentin (PO) + acepromazine + opioid (IM)	3	10 (8 to 11)	Profound
Alfaxalone + opioid	1	4 (4)	Mild

[a] FMSS final score — Range of 0 to 12 with 0 being no sedation and 12 being maximal sedation.
[b] SQS word choice: None, Mild, Moderate, or Profound.

Table 2. Lins concordance correlation analysis testing for agreement between all raters for visual analogue scoring (VAS) and various Spearman's correlations for Level 3 raters for sedating cats.

VAS concordance	Level[a] 2 *versus* Level 3	Level 2 *versus* Level 1	Level 1 *versus* Level 3
Lin's *r*-value	0.94	0.95	0.96
Lower limit	0.92	0.93	0.95
Upper limit	0.96	0.96	0.97
Spearman's correlation	Final score[b] *versus* VAS[c] (Res)	Word choice[d] *versus* VAS (Res)	Final score *versus* Word choice (Res)
r-score[e]	0.90	0.96	0.89
R^2	0.81	0.91	0.80
P-value	< 0.0001*	< 0.0001*	< 0.0001*

* Indicates significant correlation.
[a] Level 1 — Student; Level 2 — RVT; Level 3 — ACVAA resident/boarded.
[b] FMSS final score: Range of 0 to 12 with 0 being no sedation and 12 being maximal sedation.
[c] VAS score: Range of 0 to 100 with 0 being no sedation and 100 being maximal sedation.
[d] Word choices: None, Mild, Moderate, or Profound.
[e] *R* score indicates the correlation. R^2 is the square of the correlation.

The second portion of the assessment was a Simple Qualitative scale (SQS) consisting of a simple word choice. The observer was asked to circle the option that better described the level of sedation: none, mild, moderate, or profound. This assessment is commonly used in multiple practices, including our institution, as part of the pre-medication sedation assessment on the anesthetic record (19). It was included to determine if there was a correlation between final FMSS values and various levels of sedation.

Lastly, the third section was a Visual Analogue Scale (VAS). This scale has been extensively used to assess sedation in multiple species, including cats (20), and it is commonly used in humans as clinimetric measure of wakefulness or sedation (21,22). The VAS used in this study consisted of a straight line measuring from 0 to 100 mm, with observers drawing a point on that line to indicate the level of sedation. The final score, therefore, was a number ranging from 0 to 100 (none and maximal sedation, respectively).

Observers

To assess inter-observer variability, 3 observers independently assessed the animals at each time point. One of the 3 observers was trained and familiar with the scale; they oversaw interactions of cats to ensure standardization. The other 2 observers were not trained and only watched the interactions. To evaluate if clinical experience level affected the use of this new scale, observers were classified into 3 expertise groups, based on their knowledge and experience in the use of sedatives on cats.

- Level 1: Undergraduate DVM students with minimal experience;
- Level 2: Registered veterinary technicians with years of experience in anesthesia; and
- Level 3: Board-certified ACVAA faculty members or ACVAA senior residents considered experts in the field.

Individual observers varied from case to case, but assessments were always performed by 1 member of each group and all observers were blinded to sedation protocol and route of administration.

Statistical methods

To determine if there was a significant difference in VAS score between the 4-word choice categories, a VAS value out of 100 was treated as a visual analog scale variable. A Kruskal-Wallis 1-way analysis of variance (ANOVA) was used to compare the median VAS among the 4-word choice categories.

Pairwise comparisons were based on the Dwass, Steel, Critchlow-Fligner Method (DSCF). The FMSS final score was compared among word choice groups with a Kruskal-Wallis test with pairwise comparisons using DSCF. Lins concordance correlation analysis, including Bland-Altman plots, was used to test for agreements between raters for VAS scoring. A weighted *Kappa* was used to test for agreement between raters for FMSS final scores and SQS. Spearman's correlation was used to test degrees of association between final score, SQS, and VAS scores. To determine if sedation score was sensitive enough to identify differences of sedation between pre- and post-scores for FMSS and VAS among all observer classifications, a Wilcoxon sign-ranked test was used. Significance was set to $\alpha = 0.05$ for all statistical testing.

Results

A total of 89 cats was recruited, enabling 178 individual pre- and post-sedation assessments to be included in the statistical analyses. As each case was assessed by 3 observers, a total of 534 sedation assessments was recorded. The cats were of the following breeds: domestic short hair ($n = 65$), domestic medium

Table 3. Weighted *Kappa* scores for agreement between all levels of raters[a] for FMSS final scores[b] and word choices[c] for sedating cats.

	Levels 1 *versus* 2	Levels 2 *versus* 3	Levels 1 *versus* 3
Final score comparison			
Weighted *Kappa*	0.84	0.82	0.84
Probability (2-sided)	< 0.0001	< 0.0001	< 0.0001
Word choice comparison			
Weighted *Kappa*	0.85	0.84	0.87
Two-sided *P*-value	< 0.0001	< 0.0001	< 0.0001

[a] Level 1 — Student; Level 2 — RVT; Level 3 — ACVAA resident/boarded.
[b] FMSS final score: Range of 0 to 12 with 0 being no sedation and 12 being maximal sedation.
[c] Word choices: None, Mild, Moderate, or Profound.

Table 4. Relationship between word choice and FMSS final score expressed as median (range) for sedating cats.

Word choice[a]	Final score[b]	Hypothesized range
None	0 (0 to 3)	0 to 2
Mild	4 (1 to 5)	3 to 6
Moderate	6 (2 to 10)	7 to 9
Profound	12 (7 to 12)	10 to 12

[a] Word choices: None, Mild, Moderate, or Profound.
[b] FMSS final score: Range of 0 to 12 with 0 being no sedation and 12 being maximal sedation.

hair (n = 7), domestic long hair (n = 6), Bengal (n = 3), Siamese (n = 3), Maine coon (n = 1), ragdoll (n = 2), Scottish fold (n = 1), and Russian blue (n = 1). Mean age was 5.1 ± 3.8 y (range: 7 mo to 16 y). Mean body weight was 5.4 ± 1.1 kg (range: 3.2 to 9.1 kg). Reasons for sedation included premedication for surgery (n = 26), blood donation (n = 27), diagnostic imaging (n = 7), and minor procedures such as nasogastric tube or jugular catheter placement (n = 28).

Nine drug combinations were used (Table 1). Opioids included butorphanol, buprenorphine, hydromorphone, and fentanyl. All drug regimens were approved by a Board-certified ACVAA anesthesiologist. No major complications or side effects were observed in any cats undergoing sedation. Four animals received oral gabapentin at home before the initial assessment.

For all categories of observers and pre-/post-assessments, VAS values had moderate to substantial concordance, with no difference ($P > 0.05$) in VAS scores amongst the 3 experience groups (Table 2). For both FMSS and SQS, weighted *Kappa* scores had good agreement and significant *P*-values, indicating a high level of comparison between all observer groups (Table 3). Based on the high level of concordance and agreement amongst observers, the remaining statistics were completed only on the Level 3 group of experience. A comparison of FMSS and VAS revealed a high *r*-score and significant *P*-value Spearman's correlation, indicating a high degree of association between both scales. Similar values were obtained between SQS and VAS and between SQS and final FMSS (Table 2). The relationship between word choice and FMSS final score expressed as median (range) is reported in Table 4. Multiple comparisons analysis of the differences between the median values of the FMSS scores in the 4 groups of word choice showed all pairwise comparisons where significant at $P < 0.016$ (Table 5). The VAS and FMSS evaluations

Table 5. Pairwise comparisons of final FMSS scores[a] for all sedation levels[b].

Sedation levels	*P*-value
None *versus* Mild	< 0.0001
None *versus* Moderate	< 0.0001
None *versus* Profound	< 0.0001
Mild *versus* Moderate	0.0161
Mild *versus* Profound	< 0.0001
Moderate *versus* Profound	< 0.0001

[a] FMSS final score: Range of 0 to 12 with 0 being no sedation and 12 being maximal sedation.
[b] Word choices: None, Mild, Moderate, or Profound.

for each experience level examiner differed ($P < 0.0001$) for the median difference in pre- *versus* post-sedation scores (Table 6).

Discussion

The main objective was to design and assess the validity and reliability of a newly developed sedation scale and determine concordance between raters with varying levels of expertise. The final goal of this project was to validate a sedation scale specific for cats that could be easily used for research and clinical cases. This numerical descriptive scale, designed using influences from published scales and clinical experience, was described by all observers as being easy or very easy to use.

Since there is no true gold standard in veterinary literature for sedation scores, we selected VAS and SQS for comparison. The former was selected because it has been used in human and animal studies and is considered by some as the gold standard, whereas the latter is commonly used in clinical settings and many veterinarians are familiar with it. Based on the excellent correlations between FMSS and both VAS and SQS, we concluded that there was a strong relationship between levels of sedation and overall score. It is noteworthy that VAS is considered the goal standard in human medicine (23). To the authors' knowledge, no sedation scales have been validated against VAS, but it has proven to be repeatable and valid for use in assessing the degree of pain and lameness in dogs (24) and has been used as comparison for newly developed pain or lameness scales (25,26). Although VAS is an effective scale for measuring sedation and pain in humans, scales that include multiple descriptive parameters perform better and may be easier to use (26,27). Despite the 3 scales performing well in our population, the major advantages of FMSS are a more descriptive nature that facilitates accounting for specific feline behaviors, while also providing a final numerical value for statistical comparisons.

An ideal sedation scale should not only be reliable but also easy to use and require minimal training. Most observers in this study did not receive any training on how to use the scale prior to the study. Our results indicated not only good interindividual agreement, but also near perfect agreement amongst all experience groups tested, eliminating this as source of variability for future studies.

It may be difficult to detect small changes in sedation levels and some scale systems may fail to detect differences, especially between none *versus* mild sedation. This behavioral scale was designed to consider cats with a wide range of personalities,

Table 6. Pre- *versus* Post-FMSS and VAS scores compared with Wilcoxon sign-ranked test.

Score	Experience[a] level	Median pre (range)	Median post (range)	Median difference	Wilcoxon signed-rank *P*-value
FMSS[b]	1	0 (0 to 7)	9 (2 to 12)	7	< 0.0001
FMSS	2	1 (0 to 7)	9 (1 to 12)	7	< 0.0001
FMSS	3	1 (0 to 9)	9 (0 to 12)	7	< 0.0001
VAS[c]	1	0 (0 to 35)	80 (10 to 100)	75	< 0.0001
VAS	2	0 (0 to 65)	80 (15 to 100)	75	< 0.0001
VAS	3	0 (0 to 50)	80 (0 to 00)	75	< 0.0001

[a] Level 1 — Student; Level 2 — RVT; Level 3 — ACVAA resident/boarded.
[b] FMSS final score: Range of 0 to 12 with 0 being no sedation and 12 being maximal sedation.
[c] VAS score: Range of 0 to 100 with 0 being no sedation and 100 being maximal sedation.

and based on our results, it was sensitive enough to detect small changes in awareness. Consequently, FMSS can potentially be used to assess drugs that only cause mild sedation or anxiolysis such as gabapentin or trazodone. This is particularly true if a baseline is obtained on the same animal before drug administration to compute individual personality quirks in the comparison.

As an additional objective, a numerical range was associated with each sedation level and expressed in word format. Based on statistical results, it appears word choice appropriately captured final sedation values. For example, for word choice "none," final scores amounted to zero, whereas for word choice "profound," final scores ranged from 9 to 12. This was demonstrated throughout all word choice selections, and accurately related to final sedation score ranges. The main reason for doing so was to enable the user to easily equate a familiar descriptive word to a specific quantity of sedation, making this sedation score user-friendly. This practice is commonly used in human medicine settings and is known as Simple Descriptive Scoring. Many studies have been compiled that validate the use of words paired with numerical ranges, to quantify pain levels appropriately and accurately in adults and children (27–29). To put our sedation scale into a more clinical context, final sedation scores of 1 to 5 were common in cats with signs of mild sedation that was sufficient to perform non-invasive diagnostic procedures such as radiographs or abdominal ultrasound. Furthermore, final scores of 6 to 9 indicated a degree of sedation that allowed small procedures such as blood collection, catheterization, or fine-needle aspiration with minimal restraint. Scores higher than 9 were often recorded with sedation protocols that included dexmedetomidine or ketamine; this degree of sedation facilitated manipulation of highly aggressive patients or to perform more invasive procedures such as wound debridement or biopsies.

In conclusion, the scale used in this study had excellent internal consistency and very good reliability between multiple untrained raters with varying expertise levels. Therefore, we inferred that we developed a reliable, sensitive, and validated feline sedation scale which is easy to use and universal in terms of application (both observer and drug selection). To our knowledge, there is no validated sedation scale in drug-related veterinary research specifically designed for cats. Therefore, this scale may be a useful tool when testing new drug protocols in cats or when sedation levels need to be quantified. CVJ

Appendix 1 Feline Multiparametric Sedation Score (FMSS).

Posture (observe from far away first)
- 0 Sitting up and/or walking around, no ataxia
- 1 Sternal recumbency head up and/or able to stand with mild ataxia if walking
- 2 Sternal or lateral recumbency with head down, severe ataxia if walking
- 3 Recumbent even when stimulated

Behavior
- 0 Alert, normal interaction with assessor*
- 1 Alert, but slower response than normal to interaction with assessor
- 2 Minimal response to interaction with assessor
- 3 No response to interaction

Response to sound
- 0 Reacts quickly to clapping# or too distracted to react
- 1 Slower or milder response than normal to clapping
- 2 Very mild response to clapping
- 3 No response to clapping

Response to restrain and/or IM injection/IV catheter (if responses to restrain and needle correlate with different numbers, always circle the lowest value)
- 0 Readily resist restrain or very interactive with handler, strong response to needle insertion
- 1 Initial resistance to restrain but gives up, moderate response to needle
- 2 Minimal resistance, easy to restrain, mild response to needle
- 3 No resistance to restrain, no response to needle

Final Score (0–12):

Select one:

None **Mild** **Moderate** **Profound**

* Contact with the assessor includes opening cage door and attempt to pet, record what normal interaction is (friendly vs aggressive behavior). If the cat is showing strong aggressive behaviors (growling, hissing, trying to bite/scratch), assign a 0.
# If cat does not respond to clapping because is actively focusing on something else such as getting out of the cage, assign a 0.

Please include below any other specific behaviors observed such as purring, kneading, rolling exposing abdomen…

Behaviors observed (Notes):

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Article

Is training necessary for efficacious use of the Glasgow Feline Composite Measure Pain Scale?

Carly M. Moody, Lee Niel, Daniel J. Pang

Abstract

Objective

The Glasgow Feline Composite Measure Pain Scale (CMPS-F) is a validated cat pain assessment tool for clinical use. No research has examined how training impacts use of this tool. Thus, we examined whether seminar-style training improves the identification of cat pain when using the CMPS-F. Veterinarians (n = 17) and non-veterinarian staff (n = 33; N = 50) were recruited to participate.

Procedure

Seminars included: i) pre-training use of the CMPS-F to score cat videos with varying degrees of pain; ii) cat pain assessment training; and iii) post-training use of the CMPS-F. Participant CMPS-F ratings were compared to experts' ratings of the same videos. Average CMPS-F scores and analgesic decision ratings were compared pre- and post-training.

Results

Most participants were female non-veterinarian staff who had not heard of the CMPS-F. Participant and expert analgesic decision-making did not differ pre- (P = 1.0) and post-training (P = 0.1). In addition, analgesic decision-making was similar between participants and experts for all but 3/20 videos.

Conclusion and clinical relevance

Seminar training may not be necessary for efficacious use of the CMPS-F. Further research is needed to explore strategies for improving awareness of cat pain assessment tools and increasing in-clinic use.

Résumé

Une formation est-elle nécessaire pour une utilisation efficace de l'échelle de mesure de la douleur féline composite de Glasgow?

Objectif

L'échelle de mesure de la douleur féline composite de Glasgow (CMPS-F) est un outil validé d'évaluation de la douleur chez le chat à usage clinique. Aucune recherche n'a examiné l'impact de la formation sur l'utilisation de cet outil. Ainsi, nous avons examiné si la formation de type séminaire améliore l'identification de la douleur du chat lors de l'utilisation du CMPS-F. Des vétérinaires (n = 17) et du personnel non vétérinaire (n = 33; N = 50) ont été recrutés pour participer.

Procédure

Les séminaires comprenaient : i) l'utilisation du CMPS-F avant la formation pour noter des vidéos de chats avec différents degrés de douleur; ii) formation à l'évaluation de la douleur chez le chat; et iii) l'utilisation du CMPS-F après la formation. Les notes CMPS-F des participants ont été comparées aux notes des experts des mêmes vidéos. Les scores CMPS-F moyens et les cotes de décision analgésique ont été comparés avant et après la formation.

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Résultats

La plupart des participants étaient du personnel féminin non vétérinaire qui n'avait jamais entendu parler du CMPS-F. La prise de décision des participants et des experts en matière d'analgésie ne différait pas avant (P = 1,0) et après la formation (P = 0,1). De plus, la prise de décision analgésique était similaire entre les participants et les experts pour toutes les vidéos sauf 3/20.

Conclusion et pertinence clinique

La formation en séminaire peut ne pas être nécessaire pour une utilisation efficace du CMPS-F. Des recherches supplémentaires sont nécessaires pour explorer des stratégies visant à améliorer la sensibilisation aux outils d'évaluation de la douleur chez les chats et à accroître leur utilisation en clinique.

(Traduit par Dr Serge Messier)

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Introduction

Adequate and consistent pain assessment is imperative for recognizing and treating pain in cats. However, pain assessment in companion cats is particularly challenging due to several factors including, amongst others, the inability to recognize low and moderate levels of pain, limited use of pain assessment tools in veterinary clinics, and lack of training for those assessing cat pain (1–3). Observer pain assessment techniques are commonly used for cat pain assessment, but these methods are subjective, involving an inherent risk of bias influencing evaluations and subsequent decisions on pain management. For example, a veterinarian's attitudes towards companion animal pain, gender, and graduation year impacts analgesic use in veterinary clinics (1,4–7). This is a welfare concern given that unrecognized or underestimated pain cannot be properly managed and may lead to suffering. It is crucial, therefore, that clinical pain assessment in cats be improved. One solution is to increase the acceptance and use of validated pain assessment tools. Limited research has examined current use of cat pain assessment tools in a clinical setting; however, a study conducted in 2013 surveying UK veterinary surgeons suggested it was likely quite low, as 17% (122/720) of questionnaire respondents used a feline assessment tool (2).

For cats, there are 3 validated acute pain scales: the Glasgow Feline Composite Measure Pain Scale (CMPS-F) (8); the UNESP-Botucatu multidimensional composite pain scale for evaluating post-operative pain in cats (UNESP-Botucatu MCPS) (9); and a feline grimace scale (10,11). The CMPS-F and UNESP-Botucatu MCPS were published at the time of data collection for this study. The UNESP-Botucatu MCPS has been validated for assessing ovariohysterectomy pain in cats (9), whereas the CMPS-F has been validated for various acute pain states such as post-operative pain, trauma, and medical conditions (8). In addition, the CMPS-F is a shorter pain scale, making it potentially quicker and easier to apply in a clinical setting.

The CMPS-F examines both spontaneous and evoked behaviors, which is beneficial for providing information on the degree of pain experienced (8). The tool consists of 3 parts and 7 questions, a scale range of 0 to 20, and a derived analgesic intervention level of $\geq$ 5. A major advantage of the CMPS-F is that it can also be used to guide clinicians with analgesic decision-making. The tool uses a numerical measurement scale to generate a score, to which an analgesic intervention level of 5 is then applied. Cats receiving scores above this level have a greater probability of being in pain (and *vice versa*). This scale provides a good level of sensitivity such that painful cats have a high probability of being correctly classified as requiring an analgesic (8). This is practical and important from a clinical perspective, providing more value as a clinical tool than pain assessment alone.

It remains to be explored if user training has an impact on pain scores when using the CMPS-F tool. Research examining training for pain assessment scoring in laboratory rodents suggests behavior-based pain assessment can be quickly taught (12), and that combining interactive participant discussions about pain assessment techniques with scoring practice may be more effective than practicing scoring alone (13). The objective of the current study, therefore, was to examine whether seminar-style training improved veterinarian and non-veterinarian staff identification of cat pain when using the CMPS-F. We predicted that before training there would be a larger difference between participant and expert scores pre-training compared to post-training.

Materials and methods

The study protocol was reviewed and approved by the University of Guelph's Research Ethics Board (# 18-03-016) and Animal Care Committee (# 3902).

Cat videos and expert CMPS-F scores

Videos of female domestic shelter cats pre- and post-ovariohysterectomy were used in the cat pain assessment training seminars. Ovariohysterectomy surgery was chosen given that it is performed routinely and has the potential to result in pain due to its invasive nature. The cats belonged to 1 of 3 city shelter facilities in the greater Toronto area, Ontario, Canada, and all surgeries and video recordings took place in veterinary hospitals in the same region. All cats were scheduled for surgery, regardless of the current study. The researchers had no influence or involvement with the surgeries, including the anesthesia and pain management provided to the cats. Drugs used were typical for these procedures, and included dexmedetomidine, butorphanol, acepromazine, propofol, ketamine, meloxicam, and buprenorphine. In addition, the clinic veterinarians and veterinary staff carrying out the surgical and post-operative care procedures were unaware of the study goals. A convenience

sample of 20 shelter cats elected to be spayed at 1 of 3 veterinary clinics (Clinic 1 = 9 cats, Clinic 2 = 6 cats, and Clinic 3 = 5 cats) with a median age of 1.0 y (range: 0.58 to 3 y) were selected. All cats were housed individually in standard stainless-steel kennels with a towel and/or brown paper covering the kennel floor, litter box, and a purple or green translucent plastic shelter (33 cm long × 40 cm wide × 21.5 cm high; Igloo Hideout; Kaytee Products, Chilton, Wisconsin, USA).

The following CMPS-F protocol was video-recorded by a research assistant and conducted by 1 researcher for consistency (CM; hands-on training received from a veterinary anaesthesiologist, DP):

i) assess undisturbed cat behavior in the kennel;
ii) slowly open kennel door;
iii) remove litter box;
iv) stroke cat from head to tail 3 consecutive times;
v) pick up cat and move to a standing position (if not already standing); and
vi) palpate caudal abdominal midline area (site of surgical incision) (8).

Cat demeanor assessment (score based on visual and hands-on assessment) (14); was scored based on the cat's responses during the pre-surgical videos. Pre-surgical videos were taken at least 1 h after arrival at the clinic. Post-operative video recording commenced 2 h after surgery and every 30 min for 2 (n = 6 cats; 1 clinic) or 3 (n = 26; 2 clinics) 30-minute time points. At the first post-surgical time point, the cat was propped up into a standing position and a sedation scale used no sedation: 0 = stand normally, sedation: 1 = stand but wobbly, 2 = cannot stand on own; revised from Slingsby et al (15). If the cat was still sedated (score = 1 or 2), no video was recorded, and sedation assessment occurred at the next time point for up to 1 to 2 more time points. If the cat was not sedated (score = 0), a post-surgical video was recorded, and sedation was not assessed for the remaining time points. Of the post-operative videos, 2 cats were not video-recorded for 1 post-operative time point due to sedation. The resulting 72 videos were reviewed (CM and DP) and those that were dark and/or of poor quality were removed from the study.

One caveat when using the CMPS-F for clinical cat pain assessment was the potential confounding impact of cat demeanor on pain scores (16,17). For example, when using the CMPS-F, non-painful cats that were shy or aggressive were at risk of being misclassified as painful simply due to being in a clinical setting which may be perceived negatively by some cats (17). Therefore, cat videos with high demeanor scores ($\geq$ 6; shy and aggressive cats) were excluded and those with lower scores ($<$ 6; friendly cats) were included to reduce confounding with pain assessment (17). The 45 remaining videos were edited (increased brightness, clarity, and sharpness) to optimize image quality (Adobe Photoshop v.19; Adobe, San Jose, California, USA), and sound removed to reduce potential bias from background noise. Cat vocalizations were indicated with text appearing at the relevant time in the videos.

The videos were initially scored by a Board-certified veterinary anesthesiologist (DP), an expert in cat pain assessment with experience conducting and publishing studies using a range of pain assessment scales including the CMPS-F (10,17–19). Based on these scores, 20 videos (10 pre-training, 10 post-training) consisting of a broad range of CMPS-F scores and cat demeanor scores were chosen for the seminars. The pre- and post-training periods each included 5 videos with demeanor scores in the lower end of the friendly category (scores 0–3) and 5 videos in the higher end of the friendly category (scores 4–5). The 20 videos were then scored by a second Board-certified veterinary anesthesiologist who was involved in the original development of the CMPS-F but was not involved in the current study. Both experts (DP, AB) scoring the videos were blind to the pre- and post-operative context of the videos. "Expert scores" were created by calculating a mean score from the 2 anesthesiologists. Since the videos in the pre- and post-training phases were different, average expert pain scores were used for comparison with participant scores.

Cat pain assessment training seminars

The target population were veterinarians and non-veterinarian staff members that currently perform pain assessment on companion cats in Ontario, Canada. Ontario veterinary and animal shelter organizations (Ontario Veterinary Medical Association, Ontario Association of Veterinary Technicians, College of Veterinarians of Ontario, the Ontario Shelter Medicine Association, and the Ontario Veterinary College Alumni Association) were asked to share a study advertisement to their member listserv, website, and social media accounts. In addition, advertisements to participate were distributed using Ontario Veterinary College social media accounts. Incentive to participate included 2.5 continuing education credits for registered Ontario veterinarians and Ontario veterinary technicians, as approved by the Ontario Veterinary Medical Association and Ontario Association of Veterinary Technicians, upon completion of the seminar. The advertisement link led to an online consent form; upon consent, respondents could sign up for 1 of 4 seminars.

Four 2.5-hour seminars took place between May 25 and May 27, 2018, each in a different location across the greater Toronto and southwestern Ontario areas. The seminars consisted of 4 parts in the following order: i) introduction and participant questionnaire; ii) pre-training cat pain video assessment; ii) cat pain assessment training; and iv) post-training cat pain video assessment. The seminars used a revised CMPS-F score sheet which included check boxes instead of the numerical scoring system and did not identify the analgesic intervention level. This was intended to encourage participants to focus on the behaviors displayed rather that the numerical score or potential for intervention.

All seminars were conducted by the same researcher (CM) who has extensive knowledge about cat behavior and received hands-on cat pain-assessment training by 2 cat pain experts. First, participants were provided background information about cat pain management (definition of pain, multi-dimensionality of pain, importance of pain assessment, and challenges in cats), then orientated to the revised CMPS-F score sheet. Participants completed a short questionnaire collecting demographic information, frequency of cat pain assessment, and previous use

of the CMPS-F. For all cat videos played during the seminar, participants were blind to the procedures that the cats had undergone. The 10 pre-training cat videos were then played consecutively; new videos were not played until all participants had finished their assessments. Participants received a 20-minute break, then cat pain assessment training commenced.

Training involved reviewing all aspects of the revised CMPS-F score sheet, including each scale item and associated behavior. Behaviors included in the score sheet were: vocalizations, lip licking, posture, attention to the painful area/wound, ear position, muzzle shape, tail position, response to stroking, response to palpation around the potentially painful area, and demeanor of the cat. Each of the behaviors described in the score sheet was reviewed in detail using operational definitions, pictures, videos, and sound clips. After going through the cat behaviors listed in the scale, we practiced scoring CMPS-F behaviors as a group using pictures and videos, and 1 full cat video using the revised CMPS-F. Participants were free to ask questions and comment throughout the training phase. After the training phase, participants scored 10 new videos of cats in varying degrees of pain using the revised CMPS-F score sheets. During the post-training phase, participants followed the same protocol as the pre-training phase.

Data analyses

Since different cat videos were used before and after training, we could not directly compare participant scores before and after training. Instead, we used mixed linear regression modeling to examine the expert by time-point interaction effect, with the hypothesis that expert scores would remain consistent for both sets of videos, and that participant scores would be more similar to expert scores following training. In these models we also assessed whether participant demographic data explained differences in CMPS-F scores among participants. In addition, we created a binary variable using CMPS-F scores (≥ 5 analgesic is needed, yes; scores < 5 no analgesic is needed, no) to compare participant and expert analgesic decision-making before and after training.

Analyses were conducted using SAS Studio v3.71 (SAS Institute, Cary, North Carolina, USA) with $P < 0.05$ considered statistically significant. Responses from the 4 seminars (Seminar 1, n = 12; Seminar 2, n = 7; Seminar 3, n = 20; and Seminar 4, n = 11; total participants: N = 50) were combined and descriptive statistics (frequencies, percentages; Tables 1, 2) were generated using participant questionnaire responses.

Mixed linear regression models were used to examine associations between participant cat pain scores, average expert score, participant demographics, and time point (pre-training phase, and post-training phase). Since all veterinarian participants had attended post-secondary education but not all non-veterinarian participants had, non-veterinarian and veterinarian responses were initially analyzed separately for the purposes of the participant cat pain score analyses. However, to allow assessment of differences between veterinarians and non-veterinarians, a secondary analysis combined all participant data, excluding information about post-secondary education. All regression models included the outcome variable participant pain score, with participant ID and time point (pre-training phase, post-training phase) as random effects. Explanatory variables were average expert score, timepoint, gender (female, male), previous experience handling painful cats (yes, no), position (veterinarian, non-veterinarian), and year of graduation (2017 to 2007, 2006 to 1996, ≤ 1995, did not graduate). The non-veterinarian model had the additional explanatory variable post-secondary education (yes, no), and a different position variable (veterinary technician/technologist, veterinary assistant, other).

Table 1. Categorical demographic information for veterinarians ($n = 17$) and non-veterinarian staff ($n = 33$; N = 50) participating in 1 of 4 cat pain assessment seminars in the greater Toronto area.

Variable	Veterinarian *n* (%)	Non-veterinarian *n* (%)	N
Attended veterinary-related program for position			
Yes	17 (100)	18 (62.0)	35
No	0 (0)	11 (37.9)	11
Total	17	29	46
Year of graduation			
2007–2017	1 (5.9)	6 (27.3)	7
1996–2006	5 (29.4)	5 (22.7)	10
1985–1995	6 (35.3)	1 (4.5)	7
< 1984	1 (5.9)	1 (4.5)	2
Have not graduated	0 (0)	9 (40.9)	9
Prefer not to answer	4 (23.5)	0 (0)	4
Total	17	22	39
Gender			
Female	7 (41.2)	30 (90.9)	37
Male	10 (58.8)	3 (9.1)	13
Total	17	33	50

Models used a stepwise elimination process and included fitting of interaction terms into the model. We also tested for quadratic effects, which have a U-shaped curve, such as expert by expert interactions. Model fit was assessed using residual plots, normality test ($P < 0.05$), and AIC (with a lower value preferred). For all final models, only participant ID was significant as a random effect and thus left in the models. The errors were normally distributed and homoscedastic, and there were no violations of model assumptions. For all pair-wise comparisons, the Tukey-Kramer adjustment was used.

To assess analgesic decision-making, participant and average expert scores were consolidated into a binary outcome with scores ≥ 5 indicating an analgesic is needed (yes), and scores < 5 indicating no analgesic is needed (no). McNemar's test was used to compare the binary expert and participant CMPS-F scores for indicating analgesic decision-making (yes/no), before and after training. The Mantel-Haenszel odds ratio for $2 \times 2 \times k$ tables was computed to provide a summary effect size.

Results

Participants

Overall, data provided by 50 seminar participants were analyzed. Participants were practicing veterinarians (n = 17), veterinary technicians/technologists (registered and non-registered; n = 10), veterinary assistants (n = 6), veterinary students (n = 6), and other (e.g., clinic manager; n = 11; N = 50). Demographic responses received by participants are outlined

in Table 1. Most participants were non-veterinarians (33/50, 66%), female (37/50, 74%), perform cat pain assessment in a small animal clinic (31/45, 69%), handle potentially painful cats (42/50, 84%), and had not heard of the CMPS-F (44/50, 88%). Participant responses indicated that their places of work provided standard analgesia protocols for various procedures (38/40, 95%) and generally did not use a scoring tool for pain assessment (29/40, 72.5%; Table 2).

Table 2. Summary statistics for pre-training questions describing cat pain assessment information for veterinarians ($n = 17$) and non-veterinarian staff members ($n = 33$; N = 50) participating in 1 of 4 cat pain assessment seminars in the greater Toronto area.

Variable	*n*	Frequency (%)
Location of pain assessment		
Small animal clinic	31	68.9
Animal shelter	6	13.3
Laboratory/Research facility	3	6.7
Other	5	11.1
Total	45	100
Handle potentially painful cats		
Yes	42	84.0
No	8	16.0
Total	50	100
Frequency of pain management in cats		
Daily	26	54.1
Weekly	6	12.5
Monthly	3	6.3
Annually	2	4.2
Never	11	22.9
Total	48	100
Uses standard analgesia protocols for various procedures		
Yes	38	95.0
No	2	5.0
Total	40	100
Uses a standard protocol for pain assessment in cats		
Yes	16	40.0
No	24	60.0
Total	40	100
Uses a scoring tool for pain assessment in cats		
Yes	11	27.5
No	29	72.5
Total	40	100
Participant has heard of the Glasgow Feline Composite Measure Pain Scale		
Yes	26	52.0
No	24	48.0
Total	50	100
Participant has used the Glasgow Feline Composite Measure Pain Scale		
Yes	6	12.0
No	44	88.0
Total	50	100
How confident are you assessing pain in cats? (1 = no confidence, 5 = high confidence)		
1	2	4.1
2	10	20.4
3	20	40.8
4	16	32.7
5	1	2.0
Total	49	100

Cat pain assessment scores

All participants model. A significant quadratic effect was detected between expert and participant CMPS-F scores. The relationship was positive up to a maximum expert score of 9.77, then expert scores declined with increasing participant scores ($F_{1596} = 5.8$; $P = 0.016$). Those graduating between 1996 and 2006 gave higher average pain scores by 1.42 (95% CI: 0.78, 2.06; $F_{3596} = 7.03$; $P < 0.0001$) and by 1.08 (95% CI: 0.45, 1.71; $P = 0.004$) points than those graduating before 1996 and those that had not graduated, respectively. Male seminar participants gave average CMPS-F pain scores that were 1.4 points (95% CI: 0.14, 1.27; $F_{1596} = 6.04$; $P = 0.014$) higher than female participants. We examined the interaction between expert score and time point to test the effect of training, but we did not detect a significant effect ($P > 0.05$).

Veterinarian-only model. Veterinarian CMPS-F scores were different ($F_{1214} = 185.6$; $P < 0.001$) from expert scores; for every 1-point change in expert score, the average change in the mean participant score was 1.14 points (95% CI: 0.98, 1.31). Veterinarians graduating between 1996 and 2006 reported higher pain scores by an average 2.40 points (95% CI: 0.77, 4.03; $F_{2214} = 12.58$; $P < 0.041$) and 2.01 points (95% CI: 1.18, 2.83; $P < 0.0001$), compared to those graduating between 2007 and 2017 and before 1996, respectively. We did not detect a significant interaction between expert score and time point.

Non-veterinarian staff model. There was a significant quadratic effect detected between expert and participant CMPS-F scores. The relationship was positive up to a maximum expert score of 10.0, then expert scores declined with increasing participant scores ($F_{1377} = 7.79$; $P = 0.006$). Non-veterinarian staff that had not attended post-secondary education for their position reported pain scores that were on average 1.9 points higher (95% CI: 0.31, 3.42; $F_{1377} = 5.59$; $P = 0.0186$) than those that had attended post-secondary education. Recent graduates (2007 to 2017) reported higher pain scores on average by 1.0 points (95% CI: 0.23, 1.78; $F_{2377} = 3.27$; $P = 0.012$). On average, veterinary students reported higher pain scores by 0.9 points (95% CI: 0.09, 1.76; $F_{2377} = 6.87$; $P = 0.03$) and by 1.8 points (95% CI: 0.83, 2.77; $P = 0.0003$) compared to veterinary technicians and staff that were not technicians or assistants, respectively. Male non-veterinarian staff reported higher pain scores by 1.5 points (95% CI: 0.35, 2.70; $F_{1377} = 6.55$; $P = 0.01$) compared to female non-veterinarian staff. We did not detect a significant interaction between expert score and time point.

Analgesic intervention level

Participant and expert scores did not differ in analgesic intervention decision-making when using the CMPS-F tool before ($P = 1.0$) and after ($P = 0.10$) training. Regardless of training, the odds of agreement between participants and experts for having similar analgesic decision-making was 2.0 (95% CI: 0.52, 7.71). Overall, experts and participants had similar analgesic decision-making for 17 of the 20 cat videos; however, there were differences for video numbers 1 and 4 before training, and number 19 after training (Figure 1).

Discussion

Overall, participants and experts showed similar analgesic decision-making for all but 3 of the 20 cat videos when using

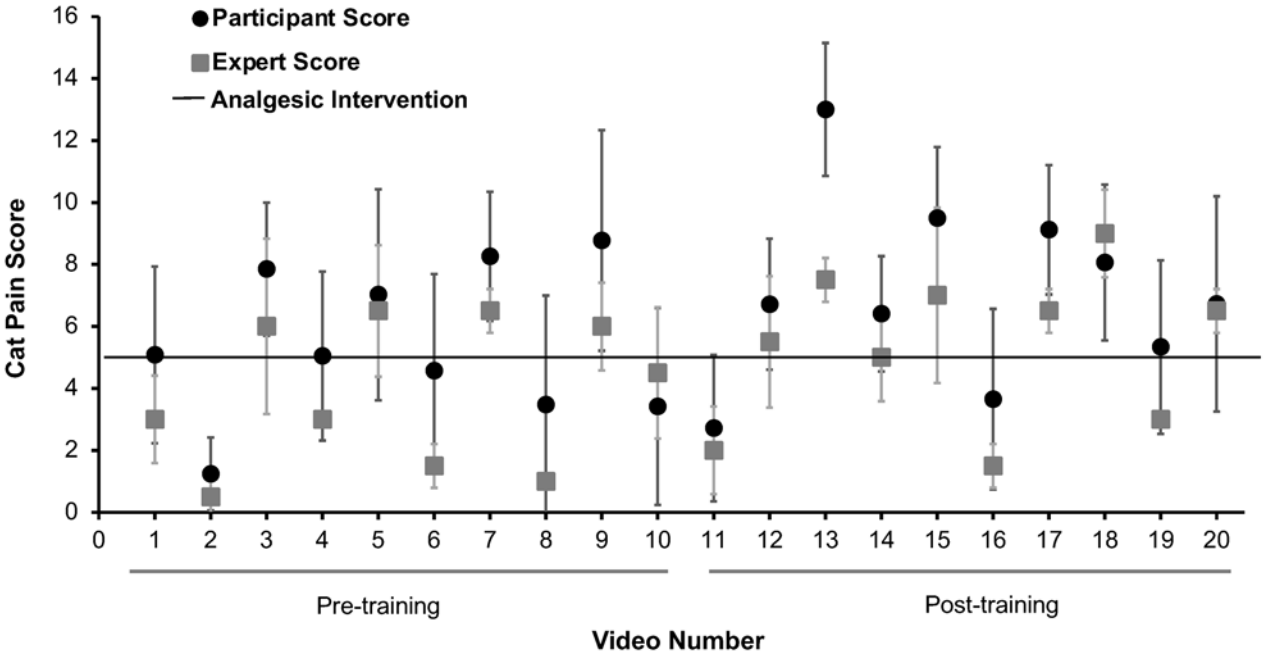

Figure 1. Average (± SD) expert ($n = 2$) and participant ($n = 50$) scores for each video watched during the training ($n = 10$) and post-training ($n = 10$; N = 20) phases during the 4 cat pain assessment seminars in the greater Toronto area.

the CMPS-F tool. The magnitude of the difference between average expert and participant scores for these 3 videos was between 2 to 3 points, with a moderate odds ratio (OR) = 2 (20) of agreement. Although a significant difference was detected between the participant and expert average pain scores, this difference was 1 point (scale range: 0 to 20). We do not consider this clinically relevant given the composite nature of the scale, and that the derived analgesic intervention threshold is intended to serve as a guide for analgesic management. The similarities between average participant and expert scores were likely due to the composite nature of the pain scale, which uses multiple measures of acute pain assessment for overall analgesic decision-making. This type of scale allows for a holistic approach and does not rely on only 1 or 2 items. However, since a deviation of a few points led to differences in analgesic decision-making for 3 videos, these results supported the use of the analgesic intervention threshold for guiding analgesic decisions rather than for definitive judgments (8).

We failed to detect an interaction effect between expert score and timepoint, suggesting that seminar training did not substantially alter the relationship between participant and expert scores. This was a compelling result, as most of our study participants had not previously used or were even aware of the CMPS-F. It is possible that training is not necessary for efficacious use, as the authors of the CMPS-F tool do not report training as a requirement to use this tool (8). In addition, the training seminar may not have been effective for improving participant cat pain assessment when using the CMPS-F to score cat videos. However, it is difficult to assess efficacy of the seminar-style training, given the similarities between the participant and expert scores both before and after training. Although the study results suggested expert and participant scores diverged when average CMPS-F scores were > 10, only 1 video had an average participant score exceeding 10 (Figure 1). Thus, the study results may only be relevant for lower levels of cat pain (scores < 10). A larger sample size incorporating a broader range of CMPS-F scores would provide a more comprehensive assessment of the seminar-style training. In addition, it remains unexplored as to whether scoring videos using the CMPS-F yields the same result as scoring cats in a real-time clinical setting.

The study results indicated that average expert CMPS-F scores tended to be lower than average participant scores in all but 2 videos (pre-training video Number 18; post-training video Number 10). There was a larger difference detected between expert and participant CMPS-F scores when participants rated pain higher. This indicates that when participants scored cat pain higher, experts tended to be more conservative in their ratings. It is possible that the experts may have been less sensitive when examining cats showing higher levels of pain than were non-experts. Underestimation of human pain by professionals in a clinical setting has been identified (21). Alternatively, given that participants were aware they were attending a pain assessment seminar, this may have inflated scores if participants were overly focused on identifying indicators of pain in the videos. It is also important to recognize that the experts have received formal training in pain assessment and have used the CMPS-F tools extensively in clinical practice. Comparatively, the majority of participants had not used the CMPS-F in clinical practice and this was their first time seeing and using the tool.

We inferred that previous education impacted participant cat pain scores. Non-veterinarian staff that had not attended

post-secondary education tended to report higher pain scores than those that had attended post-secondary education. In addition, those graduating between 1996 and 2006 tended to score pain higher in the videos, than those graduating before 1996, and those that had not graduated. No other graduate year effects were detected, but sample sizes for some groups were relatively small. It was reported that differences in education and experience levels may influence cat pain assessment (22). In recent years there has been an increase in availability of validated scoring tools for cats (8–11,17). It would be beneficial, therefore, to assess how various types of student training impacts later clinical pain assessment methods used post-graduation. This could provide information on educational strategies for improving cat pain assessment in clinical practice.

Interestingly, male study participants reported higher cat pain scores than did female participants. This was unexpected given that companion animal literature reports that female veterinarians are more likely to provide an analgesic in a clinical setting (1,4,6), suggesting a higher identification of pain by female veterinarians or a greater motivation to provide pain control. However, our sample had gender differences in terms of position, with most of our female participants identifying as non-veterinarians, and most male participants as veterinarians. More research is needed to examine differences in cat pain assessment and analgesic decisions between veterinarians and non-veterinarian staff, as well as the influence of gender on these respective groups.

A potential study limitation was the use of subtitles to indicate when cats were vocalizing. This was done as there was often background noise present in the video clips and we did not want to introduce potential sources of bias or distraction to the scoring procedure. In addition, the study sample included a relatively small number of veterinarians and non-veterinarian staff from 1 region in Ontario, Canada, which is a limitation in terms of generalizability. Future research should examine the use of the CMPS-F in a larger population to better assess the influence of various parameters that may impact the use of the CMPS-F and analgesic decision-making in a clinical setting. Finally, research is needed to explore strategies for improving awareness of cat pain assessment tools and increasing in-clinic use.

Supplementary material

Demographic questionnaire completed by the seminar participants (N = 50) at the beginning of the cat pain assessment training seminars.

Questions and answers

Are you a:
- a) Practicing Veterinarian
- b) Veterinary Technician/Technologist (registered/non-registered)
- c) Veterinary Assistant
- d) Veterinary Student
- e) Other

If you are a non-veterinarian, did you attend a veterinary-related program for your position:
- a) Yes
- b) No

If you attended a veterinary-related program for your position, what year did you graduate?
- a) 2017–2007
- b) 2006–1996
- c) 1995–1985
- d) < 1985
- e) Have not graduated yet
- f) Prefer not to answer
- g) Not applicable

Are you:
- a) Female
- b) Male
- c) Other
- d) Prefer not to answer

Do you handle potentially painful cats?
- a) Yes
- b) No

How often do you assess cats for pain management
- a) Daily
- b) Weekly
- c) Monthly
- d) Annually
- e) Never

Which location(s) do you assess pain in cats? (Choose all that apply)
- a) Small Animal Clinic
- b) Mixed Animal Practice
- c) Animal Shelter
- d) Laboratory/Research Facility
- e) Other

Do any of these locations provide standard analgesia (pain relief) protocols for different procedures? Ex. Spay (ovariohysterectomy/ovariectomy)?
- a) Yes
- b) No
- c) Not applicable

Do any of these locations have a standard protocol (assessment tool) for pain assessment in cats?
- a) Yes
- b) No
- c) Not applicable

In general, on a scale from 1–5, how confident are you assessing pain in cats? (1= no confidence, 5 = high confidence)
- a) 1
- b) 2
- c) 3
- d) 4
- e) 5

Have you heard of the Glasgow Feline Composite Measure Pain Scale?
- a) Yes
- b) No

Have you used the Glasgow Feline Composite Measure Pain Scale before?
- a) Yes
- b) No

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Article

Diagnostic evaluation of insulin and glucose dynamics in light-breed horses receiving dexamethasone

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Abstract

Objective

Insulin dysregulation is a hallmark of equine metabolic syndrome (EMS) and increases the risk for development of laminitis. Accurate diagnosis of insulin dysregulation is crucial for implementation of preventative strategies in this population. The objective was to assess the effects of dexamethasone administration on insulin and glucose dynamics in light-breed horses and assess the agreement of various diagnostic tests for insulin dysregulation [basal [insulin] (BI), oral sugar test (OST), and combined glucose-insulin test (CGIT)].

Animal

Fourteen adult light-breed horses.

Procedure

Prospective, experimental study to assess insulin and glucose dynamics by performing basal insulin, OST, and CGIT before (baseline) and post-dexamethasone administration (0.08 mg/kg, PO, q24h) for 7 d. Insulin and glucose dynamics were assessed by the BI, OST, CGIT, and insulin sensitivity proxy measurements (RISQI, QUICKI, FGIR, HOMA-IR, IG) at the baseline and post-dexamethasone time points.

Results

The OST area under the insulin and glucose curves were increased following dexamethasone treatment ($P < 0.001$ and $P < 0.01$, respectively). Basal insulin, OST [insulin] at 60 min and CGIT [insulin] at 45 min were increased at the post-dexamethasone time point ($P < 0.001$, < 0.001, and < 0.01). Similarly, time spent in the positive glucose phase during the CGIT was longer at the post-dexamethasone time point ($P < 0.001$). The proxy measurements for insulin sensitivity (RISQI, QUICKI, FGIR) were decreased ($P < 0.01$) and the proxy measurements for insulin resistance (HOMA-IR) and β-cell function (IG) were increased after dexamethasone administration ($P < 0.01$). More horses were classified with following dexamethasone administration, based on the diagnostic criteria for basal insulin ($P = 0.03$), OST ($P = 0.01$), and CGIT ($P < 0.01$). *Kappa* coefficients, measuring agreement between basal insulin, OST, and CGIT, showed none to moderate agreement at the baseline time point.

Conclusion

Dexamethasone administration at 0.08 mg/kg, PO, q24h for 7 d worsened insulin dysregulation in adult light-breed horses based on findings of a basal insulin, OST, CGIT, and insulin sensitivity proxy measurements. There was none to moderate agreement between the basal insulin, OST, CGIT for the diagnosis of insulin dysregulation.

Clinical relevance

Horses administered dexamethasone at a dose of 0.08 mg/kg, PO, q24h for 7 d should be considered insulin dysregulation and appropriate preventative strategies should be implemented. The variability of diagnostic performance of common tests for insulin dysregulation (basal insulin, OST, CGIT) may affect clinical decisions; therefore, performing multiple tests, including proxy measurements, may improve diagnostic accuracy of insulin dysregulation.

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Résumé

Évaluation diagnostique de la dynamique de l'insuline et du glucose chez les chevaux de race légère recevant de la dexaméthasone

Objectif

La dysrégulation de l'insuline est une caractéristique du syndrome métabolique équin (EMS) et augmente le risque de développement de la fourbure. Un diagnostic précis de la dysrégulation de l'insuline est crucial pour la mise en œuvre de stratégies préventives dans cette population. L'objectif était d'évaluer les effets de l'administration de dexaméthasone sur la dynamique de l'insuline et du glucose chez les chevaux de race légère et d'évaluer la concordance de divers tests de diagnostic pour le dérèglement de l'insuline [insuline basale] (BI), test de sucre oral (OST) et un test glucose-insuline combiné (CGIT).

Animal

Quatorze chevaux adultes de race légère.

Procédure

Étude prospective et expérimentale pour évaluer la dynamique de l'insuline et du glucose en effectuant l'insuline basale, l'OST et le CGIT avant (valeur de base) et après l'administration de dexaméthasone (0,08 mg/kg, PO, q24h) pendant 7 jours. La dynamique de l'insuline et du glucose a été évaluée par les mesures indirectes de BI, de l'OST, du CGIT et de la sensibilité à l'insuline (RISQI, QUICKI, FGIR, HOMA-IR, IG) aux points temporels de base et post-dexaméthasone.

Résultats

La zone OST sous les courbes d'insuline et de glucose a augmenté après le traitement à la dexaméthasone ($P < 0,001$ et $P < 0,01$, respectivement). L'insuline basale, l'OST [insuline] à 60 minutes et le CGIT [insuline] à 45 minutes ont augmenté au point temporel post-dexaméthasone ($P < 0,001$, $< 0,001$ et $< 0,01$). De même, le temps passé dans la phase de glucose positif pendant le CGIT était plus long au moment post-dexaméthasone ($P < 0,001$). Les mesures indirectes de la sensibilité à l'insuline (RISQI, QUICKI, FGIR) ont diminué ($P < 0,01$) et les mesures indirectes de la résistance à l'insuline (HOMA-IR) et de la fonction des cellules β (IG) ont augmenté après l'administration de dexaméthasone ($P < 0,01$). Plus de chevaux ont été classés avec l'administration suivante de dexaméthasone, sur la base des critères de diagnostic de l'insuline basale ($P = 0,03$), OST ($P = 0,01$) et CGIT ($P < 0,01$). Les coefficients *Kappa*, mesurant la concordance entre l'insuline basale, l'OST et le CGIT, ont montré une concordance nulle à modérée au point de référence.

Conclusion

L'administration de dexaméthasone à 0,08 mg/kg, PO, toutes les 24 h pendant 7 jours a aggravé la dysrégulation de l'insuline chez les chevaux adultes de race légère d'après les résultats d'une insuline basale, d'OST, de CGIT et de mesures indirectes de la sensibilité à l'insuline. Il n'y avait aucun accord à modéré entre l'insuline basale, l'OST, le CGIT pour le diagnostic de dysrégulation de l'insuline.

Pertinence clinique

Les chevaux ayant reçu de la dexaméthasone à une dose de 0,08 mg/kg, PO, q24h pendant 7 jours doivent être considérés comme ayant un dérèglement de l'insuline et des stratégies préventives appropriées doivent être mises en œuvre. La variabilité des performances diagnostiques des tests courants de dysrégulation de l'insuline (insuline basale, OST, CGIT) peut affecter les décisions cliniques; par conséquent, la réalisation de plusieurs tests, y compris des mesures indirectes, peut améliorer la précision du diagnostic du dérèglement de l'insuline.

(Traduit par Dr Serge Messier)

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Introduction

Insulin dysregulation, a hallmark feature of equine metabolic syndrome (EMS), is associated with an increased risk for development of laminitis (1). The underlying pathophysiology is not completely understood, but induction of prolonged hyperinsulinemia using the euglycemic-hyperinsulinemic clamp (EHC) has induced laminitis in previously healthy equids (2,3). Glucocorticoids are commonly used in equine practice for treatment of inflammatory and immune-mediated disorders; however, corticosteroids can influence insulin and glucose dynamics, leading to development of insulin dysregulation in otherwise healthy horses (4,5). The administration of glucocorticoids has also been associated with development of laminitis (6), and may be more likely to occur in horses that are systemically ill while concurrently receiving glucocorticoid therapy (7–9). Laminitis induced through the EHC and glucocorticoid-induced laminitis results in similar histopathologic findings, characterized by separation of the dermo-epidermal junction as well as lengthening and attenuation of the primary and secondary lamellae (3,6), thus supporting a possible shared mechanism of laminitis induction.

The diagnostic accuracy of insulin dysregulation, regardless of the cause, is crucial in identifying horses at-risk for development

of laminitis and other metabolic derangements associated with insulin dysregulation, to implement preventative treatment strategies in at-risk equids. There are several diagnostic tests used to diagnose insulin dysregulation in horses, but the sensitivity, repeatability, and the agreement among these tests is highly variable (10–12). Gold standard tests for the diagnosis of insulin dysregulation, such as the EHC and frequently sampled insulin-modified intravenous glucose tolerance test (FSIGTT), are technical and cumbersome to perform in traditional field settings. However, fasting basal insulin and glucose concentrations are easy to perform and enable calculation of insulin sensitivity proxy measurements to further evaluate insulin and glucose dynamics. Proxy measurements are commonly used in human medicine to assess insulin sensitivity, insulin resistance, and pancreatic β-cell function and have been well-validated when compared to gold standard testing in humans (13); however, specific diagnostic cut-off values have not been validated in horses. Furthermore, values obtained from a single baseline blood glucose and insulin concentration measurement may not consistently identify horses with insulin dysregulation, as external factors such as length of fasting (14), sampling time (15), stress-induced cortisol release (16), and concurrent medications (17) can affect insulin and glucose concentrations. The oral sugar test (OST) was designed to evaluate a horse's glucose-induced insulin response following oral administration of non-structural carbohydrates, thereby also assessing the enteroinsular axis or incretin response (18,19). The combined glucose and insulin test (CGIT), another dynamic test, was designed to assess peripheral insulin sensitivity through intravenous administration of glucose and insulin (12). Performance of these dynamic tests is extremely variable among cohorts (10,20,21), making continued evaluation of these testing strategies warranted.

The objective of this study was to evaluate insulin and glucose responses in adult light-breed horses before and after dexamethasone administration (0.08 mg/kg, PO, q24h for 7 d) through assessment of baseline blood [insulin] and [glucose], calculation of insulin sensitivity proxy measurements, and evaluation of the OST and CGIT at 2 time points, baseline and post-dexamethasone. A second objective was to compare the degree of agreement between the basal insulin and dynamic tests (OST, CGIT) in the same cohort of horses prior to administration of dexamethasone. We hypothesized that administration of dexamethasone for 1 wk would induce or exacerbate insulin dysregulation as assessed by baseline blood [insulin] and [glucose], insulin sensitivity proxy measurements, and results of dynamic testing for insulin dysregulation (OST, CGIT). In addition, we hypothesized that for the diagnosis of insulin dysregulation, there would be low agreement between the basal insulin and dynamic testing (OST, CGIT) based on commonly used diagnostic criteria.

Materials and methods

Experimental design

The experimental procedures in this study were approved by the OSU Institutional Animal Care and Use Committee (Protocol 2014A00000029) in accordance with the NIH Guide for the Care and Use of Laboratory Animals. Fourteen adult light-breed horses owned by the Ohio State University College of Veterinary Medicine and housed at the OSU Veterinary Medical Center (VMC) were included in this prospective experimental study. Inclusion criteria for the study included age > 4 and ≤ 15 y and an endogenous [adrenocorticotrophic hormone (ACTH)] (Animal Health Diagnostic Center, Cornell University, Ithaca, New York, USA) < 35 pg/mL tested in May. The horses were housed in individual stalls at the OSU VMC and fed grass hay and given *ad libitum* access to water for a 5-day acclimation period prior to the start of the experimental protocols. The grass hay fed was submitted for nutritional analysis (Equi Analytical, Ithaca, New York, USA) (Table 1).

Insulin and glucose dynamics were assessed at 2 time points, baseline and post-dexamethasone, and testing occurred over 2 d. Baseline sampling was performed following the acclimation period; a basal insulin and OST were performed on Day 5, and a CGIT was performed on Day 6 of the study. Then, all horses were treated with dexamethasone (0.08 mg/kg, PO, q24h), beginning on Day 7, for 7 d. Testing for the post-dexamethasone timepoint occurred on Days 14 (basal insulin, OST) and 15 (CGIT). All testing took place in July to August 2019.

Oral sugar test (OST)

The OST was performed as described (22). The horses were fasted for approximately 12 h before the start of the test. Briefly, approximately 1 h prior to the start of the study, an IV catheter (Abbocath-T Catheter 14 G × 5.5″; Abbott Animal Health, Chicago, Illinois, USA) was placed in a jugular vein for blood collection. Catheter patency was maintained with heparinized saline irrigation after blood collection and every 6 h thereafter for 36 h. Prior to sample collection, a minimum of 10 mL of blood was collected from the IV catheter and discarded. A baseline blood sample (T0) was collected for blood [glucose] and [insulin] measurements. Then, light corn syrup (Karo Light Corn Syrup; ACH Food Companies, Inc., Oakbrook, Illinois, USA), 0.15 mL/kg, PO to deliver about 150 mg/kg of digestible carbohydrates. Subsequent blood samples were collected at 30, 60, 90, 120, 150, 180, and 240 min post-corn syrup administration to determine blood [glucose], with samples at 60, 120, and 150 min also used to determine plasma [insulin].

Combined glucose and insulin test (CGIT)

The horses were fasted as for the OST. The CGIT was performed as described (12). Briefly, the IV catheter placed the previous day for the OST was used for blood sample collection, and patency was maintained with heparinized saline irrigation. Prior to sample collection, a minimum of 10 mL of blood was collected from the IV catheter and discarded before each sample collection. Baseline (T0) blood samples were collected to determine blood [glucose] and [insulin]. Then, a 50% dextrose solution (VetOne, MWI Animal Health, Boise, Idaho, USA), 150 mg/kg, IV immediately followed by regular insulin (Humulin R; Eli Lilly and Company, Indianapolis, Indiana, USA), 0.1 U/kg in the opposite jugular vein *via* a 19-gauge winged infusion (SURFLO Winged infusion set; Terumo Medical, Somerset, New Jersey, USA) set, over 1 to 2 min. The infusion set was flushed with 10 mL of heparinized saline and removed. Additional blood samples were collected at

1, 5, 15, 25, 35, 45, 60, 75, 90, 105, 120, 135, and 150 min after dextrose and insulin administration to determine blood [glucose], with samples at 45, 90, and 120 min also used to determine plasma [insulin].

Sample analyses

Blood samples taken during the OST and CGIT were collected in ethylenediaminetetraacetic acid (EDTA) (K_2 EDTA Vacutainer tubes; Becton Dickinson, Franklin Lakes, New Jersey, USA) and silicone-coated tubes (Silicone-coated Vacutainer tubes; Becton Dickinson) and immediately placed on ice. A hand-held glucometer (AlphaTRAK blood glucose monitoring system meter; Zoetis, Kalamazoo, Michigan, USA), previously validated for equine whole blood (23), was used to measure blood [glucose] at the time of collection. All blood samples were centrifuged within 6 h after collection; serum and plasma were aliquoted and stored at −80°C until analysis. Plasma [insulin] was measured using a commercial enzyme-linked immunosorbent assay (ELISA) (Insulin ELISA 07M-60102; MP Biomedicals, Solon, Ohio, USA) validated for use in horses (24).

Data analysis

A power calculation was performed using statistical software (G*Power 3.1; Heinrich Heine Universitat, Düsseldorf, Germany). To determine differences between insulin and glucose parameters and proxy measurements using a paired Student's *t*-test or Wilcoxon signed-rank test, a minimum sample size of 6 horses was required based on a power calculation of 0.95 and $\alpha = 0.05$. To assess changes in categorical classification of insulin dysregulation using a Fisher's Exact test, a minimum sample size of 14 horses, with 7 horses in each group, was required based on a power calculation of 0.8 and a pre-test probability of 0.15 and post-test probability of 0.85.

The basal [insulin] and [glucose] measurements were obtained from samples collected at Time 0 of the OST at both time points: baseline and post-dexamethasone. The area under the curve for glucose ($AUC_{gluc0\text{-}240}$), area under the curve for insulin ($AUC_{insulin0\text{-}150}$), and the insulin concentration at 60 min ($[Insulin]_{60}$) were calculated for the OST at both time points. The CGIT parameters calculated included insulin concentration at 45 min ($[Insulin]_{45}$), glucose concentration at 45 min ($[Glucose]_{45}$), and the positive phase duration of the glucose curve ($PP\text{-}D_{glu}$) at both time points. Outliers were identified using the ROUT method with a Q of 1% and removed prior to statistical analysis (25). Quantitative variables were assessed for normality using the D'Agostino & Pearson omnibus normality test. The basal insulin, OST($AUC_{gluc0\text{-}240}$), OST($AUC_{insulin0\text{-}150}$), OST$[Insulin]_{60}$, and CGIT$[Insulin]_{45}$ were normally distributed and are displayed as mean ± standard deviation (SD) (Table 2). The basal [glucose] and the ($PP\text{-}D_{gluc}$) were not normally distributed and are displayed as median [interquartile range (IQR)]. A paired Student's *t*-test was used to compare time points of normally distributed data (BI, OST($AUC_{gluc0\text{-}240}$), OST($AUC_{insulin0\text{-}150}$), OST$[Insulin]_{60}$, and CGIT$[Insulin]_{45}$) and a Wilcoxon matched-pairs signed rank test was used to compare time points of non-normally distributed data (basal [glucose], $PP\text{-}D_{gluc}$). Statistical significance was set at $P < 0.05$.

Table 1. Proximate analysis of forage consumed by study subjects.

	As sampled	Dry matter
Digestible energy (Mcal/kg)	1.92	2.05
Crude protein (%)	8.7	9.3
Water-soluble carbohydrate (%)	8.5	9.1
Non-fiber carbohydrate (%)	16.9	18.1

Equi-Analytical Laboratory Services, Ithaca, New York, USA.

To further assess the effects of dexamethasone on insulin and glucose dynamics, proxy measurements of insulin sensitivity were calculated for all horses at the baseline ($n = 14$) and post-dexamethasone ($n = 14$) time points, using the following formulae:

RISQI = $\text{Insulin}^{-0.5}$ (= $1/\sqrt{\text{Insulin}}$)
QUICKI = $[\log(\text{fasting glucose} \times \text{fasting insulin})]^{-1}$
HOMA-IR = [Fasting insulin × fasting glucose]/405
MIRG = $(800\text{-}0.3 \times [\text{Insulin-}50]^2)/(\text{Glucose-}30)$
I:G = Fasting Insulin/Fasting Glucose
FGIR = Fasting Glucose/Fasting Insulin

The [glucose] and [insulin] measurements obtained from the Time 0 sample of the OST testing days were used for proxy calculations. Outliers were identified using the ROUT method with a Q of 1% and removed prior to statistical analysis (25). As a result, 1 horse was removed from statistical analysis of basal blood [glucose], plasma [insulin], MIRG, and IG. Assessment of normality was performed using the D'Agostino and Pearson omnibus test. The proxy measurement data and basal plasma [insulin] were normally distributed. A Student's paired *t*-test was performed to evaluate differences in proxy measurements between the baseline and post-dexamethasone time points. Commercial statistical software (GraphPad Prism 8; GraphPad Software, La Jolla, California, USA) was used for all data analyses.

A positive diagnosis of insulin dysregulation was determined based on a basal insulin > 20 μIU/mL, OST$[Insulin]_{60}$ > 60 μIU/mL, OST$[Insulin]_{60}$ > 45 μIU/mL, CGIT$[Gluc]_{45}$ > baseline [glucose], and CGIT$[Insulin]_{45}$ > 100 μIU/mL at each time point. A Fisher's Exact test was used to assess the categorical classification of insulin dysregulation between baseline and post-dexamethasone time points according to the previously mentioned diagnostic criteria for basal insulin, OST, and CGIT. In addition, agreement of categorical classification of insulin dysregulation at the baseline time point between BI > 20 μIU/mL and OST$[Ins]_{60}$ > 60 μIU/mL, OST$[Ins]_{60}$ > 45 μIU/mL, CGIT$[Gluc]_{45}$ > baseline[glucose], and CGIT$[Ins]_{45}$ > 100 μIU/mL, and BI > 20 μIU/mL performed 24 h apart were assessed using Cohen's *Kappa* (0.8 to 1.0 indicates almost perfect agreement, 0.6 to 0.8 substantial agreement, 0.2 to 0.4 fair agreement, 0.0 to 0.2 slight agreement, and < 0.0 poor agreement).

Results

Fourteen adult, light-breed horses were used in the study. The study population consisted of 9 mares and 5 geldings of

Table 2. Effects of dexamethasone administration on fasting basal insulin and glucose concentrations, parameters of the CGIT, OST, and insulin sensitivity proxy measurements.

Effect measured	Measurement	Baseline	Post-dexamethasone
Basal insulin	Insulin (μIU/mL)	13.10 ± 6.90[a]	50.9 ± 27.2***
Basal glucose	Glucose (mg/dL)	94 (85 to 123)[b]	128 (109 to 184)***
OST($AUC_{Insulin0-150}$)	Insulin (μIU/mL × min)	3770 ± 3119[a]	14 666 ± 6510***
OST($AUC_{gluc0-240}$)	Glucose (mg/dL × min)	4037 ± 3321[a]	8851 ± 5326**
OST$[Insulin]_{60}$	Insulin (μIU/mL)	44.87 ± 25.68[a]	151.20 ± 73.34***
CGIT$[Insulin]_{45}$	Insulin (μIU/mL)	28.23 ± 11.46[a]	101.3 ± 72.80**
CGIT($PP\text{-}D_{gluc}$)	Time (min)	46 (15 to 150)[b]	160 (75 to 180)***
Insulin sensitivity	QUICKI	0.32 ± 0.03[a]	0.26 ± 0.03***
	RISQI	0.29 ± 0.08[a]	0.15 ± 0.06***
	FGIR	8.90 ± 4.38[a]	3.26 ± 2.13***
Insulin resistance	HOMA-IR	3.24 ± 1.81[a]	17.31 ± 10.93***
β-cell function	MIRG	2.86 ± 2.32[a]	6.09 ± 1.92
	IG	0.13 ± 0.07[a]	0.38 ± 0.18***

[a] Indicates mean ± SD.
[b] Indicates median and range.
Different from baseline time point; $^{**}P < 0.01$; $^{***}P < 0.001$.
SD — Standard deviation; $AUC_{Insulin0-150}$ — Area under the curve insulin 0 to 150 min; $AUC_{gluc0-240}$ — Area under the curve glucose 0 to 240 min; $[Insulin]_{60}$ — Insulin concentration at 60 min; $[Insulin]_{45}$ — Insulin concentration at 45 min; $PP\text{-}D_{gluc}$ — Positive phase duration glucose; QUICKI — Quantitative insulin sensitivity check index; RISQI — Reciprocal of the square root of insulin; FGIR — Fasting glucose-to-insulin ratio; HOMA-IR — Homeostasis model of assessment for insulin resistance; MIRG — Modified insulin-to-glucose ratio; IG — Insulin-to-glucose ratio.

various breeds (3 Warmbloods, 3 American Quarter Horses, 3 Thoroughbreds, 2 Trakehners, 1 American Paint Horse, 1 Standardbred, and 1 grade horse). The endogenous [ACTH] was within a normal seasonally adjusted reference range for all horses, with a mean of 19.0 ± 5.4 pg/mL. The mean age and weight of the horses were 12 ± 3 y and 527 ± 67.8 kg.

The baseline plasma [insulin] and the blood [glucose] concentrations were significantly increased at the post-dexamethasone time point compared to baseline ($P < 0.00$ and < 0.001, respectively). The OST parameters measured of $AUC_{insulin0-150}$, $AUC_{gluc0-240}$, and $[insulin]_{60}$ were increased at the post-dexamethasone time point compared to baseline ($P < 0.001$, < 0.01, and < 0.001, respectively; Table 2). Similarly, the CGIT parameters measured of $[insulin]_{45}$ and $PP\text{-}D_{gluc}$ were increased at the post-dexamethasone time point compared to baseline ($P < 0.01$ and < 0.001, respectively; Table 2). In addition, the proxy measurements of insulin sensitivity (QUICKI, RISQI, FGIR) were all decreased at the post-dexamethasone time point compared to the baseline timepoint ($P < 0.01$, < 0.01, and < 0.01, respectively; Table 2). The proxy measurement for insulin resistance (HOMA-IR) was increased at the post-dexamethasone time point compared to the baseline time point ($P < 0.01$). The IG, a proxy measurement for β-cell function, was elevated at the post-dexamethasone time point compared to the baseline time point ($P < 0.1$). However, the MIRG, another proxy measurement for β-cell function, was not different between time points ($P = 0.30$).

The diagnosis of insulin dysregulation was made at each time point according to the diagnostic criteria for basal insulin, OST, and CGIT. At the baseline time point, a basal insulin > 20 μIU/mL diagnosed 4 horses as insulin dysregulation, but at the post-dexamethasone time point, 13 horses were classified as insulin dysregulation using this test and cutoff. Similarly, at the baseline time point, an $OST[Ins]_{60}$ > 60 μIU/mL diagnosed 6 horses as insulin dysregulation, whereas at the post-dexamethasone time point, 13 horses met the criteria for insulin dysregulation diagnosis. At the baseline time point, an $OST[Ins]_{60}$ > 45 μIU/mL identified 8 horses as insulin dysregulation, which increased to 14 horses at the post-dexamethasone basal insulin time point. According to a $CGIT[Gluc]_{45}$ return to baseline [glucose], 5 horses were diagnosed with insulin dysregulation at the baseline time point, and all 14 horses were classified as insulin dysregulation at the post-dexamethasone time point. However, based on $CGIT[Ins]_{45}$ > 100 μIU/mL, only 2 horses were classified with insulin dysregulation at the baseline time point, which only increased to 5 horses classified with insulin dysregulation at the post-dexamethasone time point. When comparing changes in the categorical classifications of insulin dysregulation, dexamethasone administration for 7 d at 0.08 mg/kg, PO, q24h resulted in significantly more horses being classified as insulin dysregulation based on basal insulin > 20 μIU/mL ($P = 0.03$), $OST[Ins]_{60}$ > 60 μIU/mL ($P = 0.01$), $OST[Ins]_{60}$ > 45 μIU/mL ($P = 0.01$), and $CGIT[Gluc]_{45}$ return to baseline [glucose] ($P < 0.01$), but not for $CGIT[Ins]_{45}$ > 100 μIU/mL ($P = 0.38$) (Figure 1).

Cohen's *Kappa* coefficients were calculated to compare the degree of agreement between > 20 μIU/mL and the standard diagnostic criteria for the OST and CGIT (Table 3). The agreement between 2 basal insulin assessments performed 24 h apart was moderate (0.444). Similarly, the agreement between basal insulin and the OST analysis ($OST[Ins]_{60}$ > 60 μIU/mL,

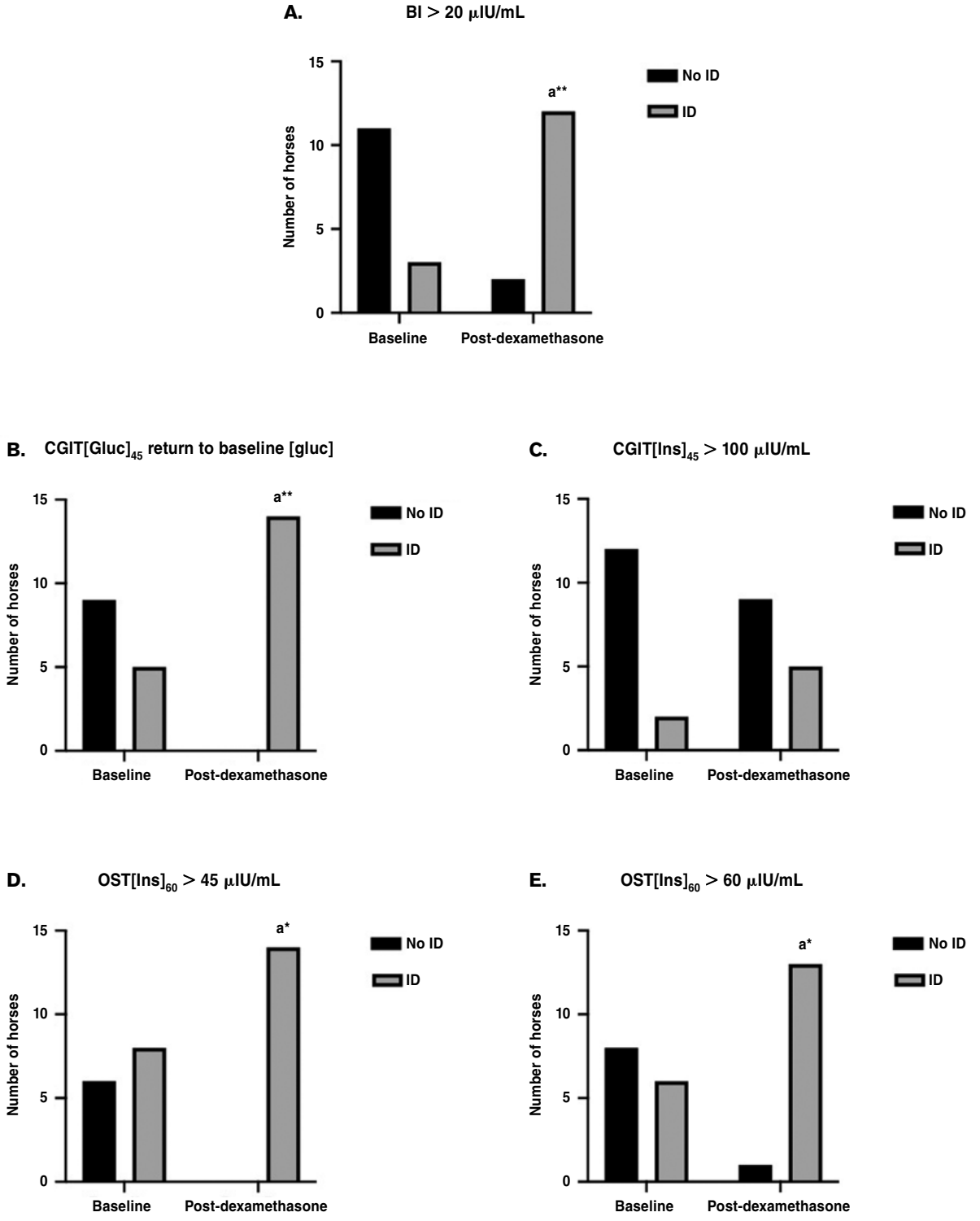

Figure 1. Changes in categorical classification of insulin dysregulation following treatment with dexamethasone. Graph A demonstrates that significantly more horses were classified as insulin dysregulation using the basal insulin following dexamethasone treatment. Graph B demonstrates that significantly more horses were classified as insulin dysregulation using the criteria of $CGIT[Gluc]_{45}$ returning to baseline blood [glucose]. Graph C demonstrates no statistical difference in the number of horses classified as insulin dysregulation based on the $CGIT[Ins]_{45} > 100$ μIU/mL. Graph D demonstrates that significantly more horses were diagnosed with insulin dysregulation based on the $OST[Ins]_{60} > 45$ μIU/mL. Graph E demonstrates that significantly more horses were diagnosed with insulin dysregulation based on $OST[Ins]_{60} > 60$ μIU/mL.

[a] Indicates significance from baseline time point; $^*P < 0.05$.
$AUC_{gluc0\text{-}240}$ – Area under the glucose curve from 0 to 240 min; $AUC_{ins0\text{-}150}$ – Area under the insulin curve from 0 to 150 min; $[Ins]_{60}$ – Insulin concentration at 60 min; $AUC_{gluc0\text{-}150}$ – Area under the glucose curve from 0 to 150 min; $PP\text{-}D_{gluc}$ – Positive phase duration of the glucose curve; $[Ins]_{45}$ – Insulin concentration at 45 min.

Table 3. Cohen's *Kappa* degree of agreement between indices used to diagnose insulin dysregulation based on basal insulin, OST, and CGIT.

Agreement with basal insulin > 20 μIU/mL	Cohen's *Kappa*	Level of agreement
$OST[Ins]_{60}$ > 60 μIU/mL	0.512	Moderate
$OST[Ins]_{60}$ > 45 μIU/mL	0.444	Moderate
$CGIT[Gluc]_{45}$ > baseline [glucose]	−0.026	Poor
$CGIT[Ins]_{45}$ > 100 μIU/mL	0.122	Slight
Basal insulin > 20 μIU/mL performed 24 h apart	0.444	Moderate

OST — Oral sugar test; CGIT — Combined glucose and insulin test.

$OST[Ins]_{60}$ > 45 μIU/mL) was also moderate (0.512, 0.444, respectively). However, the agreement between basal insulin and the CGIT analysis was poor ($CGIT[Gluc]_{45}$ return to baseline [glucose]; −0.026) and slight ($CGIT[Ins]_{45}$ > 100 μIU/mL; 0.122), depending on the diagnostic criteria.

Discussion

The current study demonstrated that dexamethasone administered at 0.08 mg/kg, PO, q24h for 7 d induced worsening insulin dysregulation as assessed by the basal insulin, OST, CGIT, and insulin sensitivity proxy measurements. We also performed an evaluation of level of agreement between frequently used tests for insulin dysregulation (basal insulin, OST, CGIT) and detected variable agreement between tests for the diagnosis of insulin dysregulation at the baseline time point.

Treatment with dexamethasone for 7 d increased basal blood [glucose] ($P < 0.01$) and basal plasma [insulin] ($P < 0.01$), demonstrating an alteration in insulin and glucose dynamics. This finding differed from a previous study, which reported dexamethasone administration (0.08 mg/kg, IV, q48h) to significantly increase [insulin], but not [glucose] after 7 d of treatment (5). The $AUC_{glucose}$ and $AUC_{insulin}$ calculated from the OST positively correlate to those achieved by the FSIGTT and therefore can be used as an indirect measurement of insulin sensitivity (22). The $OST(AUC_{Insulin0\text{-}150})$ and $OST(AUC_{glucose0\text{-}240})$ were increased following treatment with dexamethasone ($P < 0.001$ and < 0.01, respectively), thus indicating a progressive decrease in insulin sensitivity following dexamethasone administration. Similarly, the $OST[insulin]_{60}$ was increased at the post-dexamethasone time point ($P < 0.001$), further demonstrating an exacerbation of insulin dysregulation following dexamethasone administration. Furthermore, the $CGIT[insulin]_{45}$ was increased subsequent to dexamethasone administration ($P < 0.01$), indicating a decrease in tissue insulin sensitivity. Moreover, the $CGIT(PP\text{-}D_{gluc})$ remained longer in the positive phase of the glucose curve ($P < 0.001$), thus corroborating the findings that dexamethasone worsens insulin dysregulation by decreasing peripheral tissue insulin sensitivity. Therefore, administration of dexamethasone at 0.08 mg/kg, PO, q24h for 7 d can worsen insulin dysregulation in adult light-breed horses, based on insulin and glucose dynamics assessed by the basal insulin, OST, and CGIT.

Proxy measurements for insulin sensitivity have been widely used in human clinical practice and epidemiologic studies for assessment of insulin dysregulation (13). Proxy measurements were assessed in this study to evaluate effects of dexamethasone administration on various aspects of insulin dysregulation (insulin sensitivity, insulin resistance, and pancreatic β-cell response). The proxy measurements for insulin sensitivity (QUICKI, RISQI, FGIR) were all decreased following dexamethasone treatment ($P < 0.001$). Similarly, in a previous study, there was a significantly reduced RISQI in horses treated with dexamethasone for 7, 14, and 21 d compared to control horses (5). The proxy measurement for insulin resistance (HOMA-IR) was increased following dexamethasone administration for 7 d ($P < 0.001$), indicating an exacerbation of insulin resistance with treatment. The IG, a proxy measurement assessing β-cell responsiveness, was increased following dexamethasone treatment ($P < 0.001$). However, the MIRG, which is also a proxy measurement assessing β-cell responsiveness, increased following dexamethasone treatment; however, this difference was not significant ($P = 0.59$). Again, these findings supported a previous report of a significantly increased MIRG value following dexamethasone treatment for 21 d (5). Therefore, we inferred that dexamethasone induced a state of compensated insulin resistance, as markers of insulin sensitivity decreased, whereas β-cell responsiveness increased.

More horses were classified as having insulin dysregulation following dexamethasone treatment based on a BI cut-off value of > 20 μIU/mL ($P = 0.03$) (1). Similarly, 2 diagnostic criteria were used to make the diagnosis of insulin dysregulation based on the OST: an $[Ins]_{60}$ > 60 μIU/mL and an $[Ins]_{60}$ > 45 μIU/mL. Using both the original cut-off value of [insulin] being > 60 μIU/mL (26) and a newly recommended, more sensitive cut-off value of [insulin] > 45 μIU/mL (27) at 60 min, more horses were classified with insulin dysregulation following 7 d of dexamethasone treatment ($P = 0.01$). These findings were further supported by more horses being classified as insulin dysregulation based on the CGIT criteria of the blood [glucose] returning to baseline by 45 min ($P < 0.01$) (28). In contrast, when assessing for insulin dysregulation based on the CGIT criteria of an $[Ins]_{45}$ > 100, there was no significant difference in the number of horses diagnosed with insulin dysregulation following dexamethasone treatment. The discrepancy in the CGIT-based diagnoses could be due to development of uncompensated insulin resistance, in which blood [glucose] remains elevated, accompanied by a lower peak [insulin] (1). We inferred that the degree of exacerbation of insulin dysregulation caused by the administration of dexamethasone for 1 wk can lead to a significant proportion of horses becoming diagnostically insulin dysregulation. Consequently, horses administered dexamethasone should be considered at-risk for development of insulin dysregulation.

Our findings demonstrated that dexamethasone (0.08 mg/kg, PO, q24h) administered for 7 d exacerbated insulin dysregulation, consistent with other studies with similar findings following glucocorticoid administration (various dosages and routes) (4,5). The exact mechanism by which glucocorticoids induce insulin dysregulation is not yet completely understood;

however, it is likely multifactorial. Humans treated with long-term glucocorticoids often develop Cushingoid features, such as abdominal obesity, dyslipidemia, cervical fat deposits, insulin resistance, and hyperglycemia (29). Glucocorticoids increase hepatic gluconeogenesis by activating genes regulating carbohydrate metabolism, such as phosphoenolpyruvate carboxykinase (PEPCK), which enhances gluconeogenesis within the liver (30). In addition, glucocorticoids negatively impact secretion, proliferation, and survival of pancreatic β-cells (29). Glucocorticoids induce insulin resistance in adipose tissue through decreased phosphorylation of insulin receptor substrate-1 (IRS-1), which directly impacts insulin signaling following initial activation of the insulin receptor (31). In addition, glucocorticoids decrease insulin-induced glucose uptake within adipocytes due to decreased expression of the GLUT4 transporter and decreased translocation of GLUT4 to the plasma membrane (29). These mechanisms likely contributed to the observed insulin dysregulation that developed in our study following dexamethasone treatment.

Glucocorticoids are often used in equine medicine for treatment of inflammatory and immune-mediated disorders (32). Importantly, treatment with glucocorticoids in horses has been associated with development of laminitis (6). Glucocorticoid-induced laminitis produces similar histological changes in the digital lamellae compared to laminitis induced by hyperinsulinemia induced with the euglycemic-hyperinsulinemic clamp (6). Therefore, insulin dysregulation induced by glucocorticoids likely has a major role in the induction of laminitis that can be observed following this treatment. In our study, treatment with dexamethasone at a common dose worsened insulin dysregulation within 7 d. Therefore, previously healthy horses treated with glucocorticoids should be considered at-risk for development of insulin dysregulation and the subsequent deleterious health side effects; this may be a particularly important consideration for those horses with other risk factors for endocrinopathic laminitis, such as obesity, breed predisposition, high-carbohydrate diet, and pituitary *pars intermedia* dysfunction (PPID).

An accurate diagnosis of insulin dysregulation is critical to identify horses at-risk for laminitis and other metabolic derangements associated with insulin dysregulation (hypertriglyceridemia, hyperleptinemia, and hypoadiponectinemia) to initiate appropriate treatment, such as dietary modifications and exercise (27,33). This study investigated the agreement between commonly used tests to diagnose insulin dysregulation, with moderate agreement between a basal insulin $>$ 20 μIU/mL and the diagnostic criteria used to assess the OST (OST[Ins]$_{60}$ $>$ 60 μIU/mL, OST[Ins]$_{60}$ $>$ 45 μIU/mL). The agreement between the basal insulin $>$ 20 μIU/mL and the diagnostic criteria used to assess the CGIT (CGIT[Gluc]$_{45}$ return to baseline [glucose] CGIT[Ins]$_{45}$ $>$100 μIU/mL) was poor, with only slight to no agreement, respectively. Furthermore, there was only moderate agreement between the results of the same test (basal insulin) repeated in the same horses 24 h later. These findings were consistent with a previous study that reported similar variability and poor agreement among the FSIGTT, basal insulin, OST, and CGIT (10).

Only moderate agreement was identified between 2 basal insulin tests performed 24 h apart. Insulin and glucose dynamics are affected by many factors, including meal feeding and fasting (14), sampling time (15), stress level (16), and medications (17). Therefore, it was not unexpected to have only moderate agreement for the diagnosis of insulin dysregulation between 2 sampling days using basal insulin. However, this test should be used as a screening test for insulin dysregulation in clinical practice, and a follow-up dynamic test should be performed if the basal insulin is $<$ 20 μIU/mL but clinical suspicion for insulin dysregulation remains high. Similarly, diagnosis of insulin dysregulation based on the OST also resulted in moderate agreement with the basal insulin, indicating that the OST performed differently than basal insulin in the diagnosis of insulin dysregulation. The repeatability of the OST was good for the binary classification of insulin dysregulation; however, the absolute [insulin] varied greatly with repeated testing in the same horse (20). Furthermore, the OST has had poor repeatability and performed significantly different in fasted *versus* unfasted states (11). Alternatively, the basal insulin and the CGIT had only poor to no agreement in the diagnosis of insulin dysregulation at the baseline time point. The number of horses identified as insulin dysregulation based on the CGIT[Gluc]$_{45}$ return to baseline blood [glucose] was greater than the number of horses identified as insulin dysregulation based on the basal insulin. Conversely, the number of horses identified as insulin dysregulation based on the CGIT [Ins]$_{45}$ $>$ 100 μIU/mL was less than those identified as insulin dysregulation from the basal insulin. As a result, the CGIT was both more and less sensitive compared to the basal insulin, depending on the diagnostic criteria utilized for the diagnosis of insulin dysregulation. Parameters calculated from the glucose curve following a CGIT had low repeatability compared to a moderate-to-high repeatability obtained from calculated insulin parameters (21). Therefore, when diagnosing insulin dysregulation based on the CGIT, using the glucose parameters alone should be done with caution.

The results of this study demonstrated a wide and variable level of agreement between commonly used tests for the diagnosis of insulin dysregulation. Based on these findings, performing multiple tests, in addition to insulin sensitivity proxy measurements, may be useful for a more consistent and accurate diagnosis of insulin dysregulation, particularly for monitoring response to treatment over time. The basal insulin is easy to perform and can be paired with calculation of insulin sensitivity proxy measurements and the OST or the CGIT on the same testing day. Use of the OST allows for evaluation of the enteroinsular axis following administration of an enteral carbohydrate load, which may better represent a horse's natural response to a diet high in non-structural carbohydrates (18,19). Alternatively, the CGIT provides a better assessment of peripheral tissue insulin sensitivity (19). The insulin tolerance test (ITT) could also be performed as an alternative to the CGIT for the assessment of tissue insulin sensitivity, which would preclude the need for an insulin measurement (1). Therefore, it may be beneficial to perform both the OST and CGIT (or ITT) in a horse with suspected insulin dysregulation that was not diagnosed based on the basal insulin, as these tests evaluate different components to the pathogenesis

of insulin dysregulation, resulting in a higher likelihood of an accurate diagnosis and insight as to the underlying cause.

A limitation of this study was a relatively small sample size. Furthermore, 1 horse was identified as an outlier and removed from statistical analysis of the basal insulin and glucose concentrations, MIRG, and IG, further decreasing sample size. Dexamethasone was administered orally, which may have resulted in inconsistent drug administration over time. In addition, the ELISA used to measure the insulin concentrations did not have specific cut-off values determined. However, the insulin concentration cut-off values used in this study were determined from the previously used, albeit no longer available, radioimmunoassay (RIA) (12,27,34). At insulin concentrations measured < 175 μIU/mL the RIA and ELISA had good agreement (35). We did not perform a gold-standard test for the diagnosis of insulin dysregulation, such as the FSIGTT or the EHC technique. As a result, we were unable to assess the sensitivity or specificity of the performance of the basal insulin, OST, or CGIT in the diagnosis of insulin dysregulation. However, we assessed more commonly used diagnostic tests in clinical practice and demonstrated a high degree of variability in their results, which emphasized the possibility of making an inconsistent, and potentially inaccurate, diagnosis regarding the presence or absence of insulin dysregulation if only performing 1 test.

In conclusion, dexamethasone administered at 0.08 mg/kg, PO, q24h for 7 d can induce insulin dysregulation based on insulin sensitivity proxy measurements and basal insulin, OST, and CGIT. Therefore, horses treated with glucocorticoids should be considered at risk for development of insulin dysregulation, and appropriate precautions should be implemented during the treatment period. In addition, these results demonstrated that common diagnostic tests used to diagnose insulin dysregulation have variable agreement, ranging from none to moderate; performing multiple tests may support a more accurate diagnosis of insulin dysregulation. Furthermore, if the clinician suspects insulin dysregulation based on the patient's clinical signs and/or risk factors, then treatment strategies should be instituted, regardless of test results, as there could be a high likelihood of misdiagnosis depending on the diagnostic test(s) performed. Additional studies are required to determine more appropriate testing strategies for the diagnosis of insulin dysregulation, including which test or combination of tests should be performed and to determine more appropriate cut-off values for the diagnosis of insulin dysregulation.

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Erratum

Prevalence of and risk factors for equine glandular and squamous gastric disease in polo horses
Can Vet J 2018;59:880–884

In Table 2, under Exercise duration, $>$ 270 min/wk should be the referent value and $\leq$ 270 min/wk should be the increased risk. Also, in Table 2 Hay frequency should be categorized as $\geq$ 3 (38%; 14/37) and $<$ 3 (77%; 20/26); in addition, this should be corrected in the Materials and methods.

The authors apologize for any inconvenience.

Erratum

Ultrasonic characteristics of the portal venous system of 37 healthy, unsedated, student-owned cats: A prospective study
Can Vet J 2022;63:373–378

In the Abstract and Résumé, change 14.6 cm · s ($\pm$ 4.3 cm · s) to 14.6 cm/s ($\pm$ 4.3 cm/s).

Article

Vertebral heart size is associated with cardiac enlargement in Chihuahuas with myxomatous mitral valve disease

Daisuke Ito

Abstract — Although breed-specific vertebral heart size (VHS) reference ranges have been reported, the relationship between VHS and severity of cardiac enlargement has not been clarified. The objective was to assess the influence of cardiac enlargement on VHS in Chihuahuas with myxomatous mitral valve disease (MMVD). Ten clinically normal Chihuahuas (Normal) and 97 Chihuahuas with MMVD were recruited. Chihuahuas with MMVD were classified according to the values of left atrium to aorta ratio (LA/AO) and left ventricular internal dimension in diastole normalized (LVIDDN). These dogs were allocated into 3 groups: LA1 (LA/AO $<$ 1.6), LA2 (1.6 $\leq$ LA/AO $<$ 2.0), LA3 (LA/AO $\geq$ 2.0), and into 2 groups: LV1 (LVIDDN $<$ 1.7), LV2 (LVIDDN $\geq$ 1.7). Vertebral heart sizes, measured as mean $\pm$ SD, were compared among groups. Optimal cutoff values of VHS were determined for mild (LA/AO $\geq$ 1.6, LVIDDN $\geq$ 1.7) and severe (LA/AO $\geq$ 2.0, LVIDDN $\geq$ 1.7) cardiac enlargement. Vertebral heart sizes (mean $\pm$ SD) were Normal: 9.66 $\pm$ 0.36, LA1: 10.13 $\pm$ 0.64, LA2: 10.87 $\pm$ 0.71, LA3: 11.71 $\pm$ 0.78, LV1: 10.04 $\pm$ 0.71, LV2: 11.21 $\pm$ 0.78. LA2–3 had significantly greater VHS than Normal and LA1, whereas LA3 had the greatest VHS. LV2 had significantly greater VHS than Normal and LV1 and a VHS of 10.5 and 11.1 had optimal diagnostic accuracy for identifying mild and severe cardiac enlargement, respectively. In conclusion, VHS increased according to cardiac enlargement in Chihuahuas with MMVD; a VHS of 10.5 and 11.1 might be useful in evaluating the extent of cardiac enlargement.

Résumé — La taille du cœur vertébral est associée à une hypertrophie cardiaque chez les Chihuahuas atteints d'une maladie valvulaire mitrale myxomateuse. Bien que des plages de référence de taille du cœur vertébral (VHS) spécifiques à la race aient été rapportées, la relation entre le VHS et la gravité de l'hypertrophie cardiaque n'a pas été clarifiée. L'objectif était d'évaluer l'influence de l'hypertrophie cardiaque sur le VHS chez des Chihuahuas atteints de maladie myxomateuse de la valve mitrale (MMVD). Dix Chihuahuas cliniquement normaux (Normal) et 97 Chihuahuas avec MMVD ont été recrutés. Les Chihuahuas avec MMVD ont été classés selon les valeurs du rapport oreillette gauche sur aorte (LA/AO) et de la dimension interne ventriculaire gauche en diastole normalisée (LVIDDN). Ces chiens ont été répartis en trois groupes : LA1 (LA/AO $<$ 1,6), LA2 (1,6 $\leq$ LA/AO $<$ 2,0), LA3 (LA/AO $\geq$ 2,0), et en deux groupes : LV1 (LVIDDN $<$ 1,7), LV2 (LVIDDN $\geq$ 1,7). Les tailles du cœur vertébral, mesurées comme la moyenne $\pm$ SD, ont été comparées entre les groupes. Les valeurs seuil optimales de VHS ont été déterminées pour l'hypertrophie cardiaque légère (LA/AO $\geq$ 1,6, LVIDDN $\geq$ 1,7) et sévère (LA/AO $\geq$ 2,0, LVIDDN $\geq$ 1,7). Les tailles du cœur vertébral (moyenne $\pm$ SD) étaient normales : 9,66 $\pm$ 0,36, LA1 : 10,13 $\pm$ 0,64, LA2 : 10,87 $\pm$ 0,71, LA3 : 11,71 $\pm$ 0,78, LV1 : 10,04 $\pm$ 0,71, LV2 : 11,21 $\pm$ 0,78. LA2-3 avait un VHS significativement plus élevé que Normal et LA1, tandis que LA3 avait le plus grand VHS. LV2 avait un VHS significativement plus élevé que Normal et LV1 et un VHS de 10,5 et 11,1 avait une précision diagnostique optimale pour identifier l'hypertrophie cardiaque légère et sévère, respectivement. En conclusion, le VHS a augmenté en fonction de l'hypertrophie cardiaque chez les Chihuahuas avec MMVD; un VHS de 10,5 et 11,1 pourrait être utile pour évaluer l'étendue de l'hypertrophie cardiaque.

(Traduit par Dr Serge Messier)

Can Vet J 2022;63:627–632

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Introduction

Assessment of heart size is important in evaluation of myxomatous mitral valve disease (MMVD). Furthermore, the American College of Veterinary Internal Medicine guideline recommends thoracic radiography and echocardiography for assessments of heart size (1).

Vertebral heart size (VHS) is an objective measurement of heart size, as proposed by Buchanan and Bücheler (2). They reported that the VHS reference range of normal dogs was 9.7 ± 0.5 vertebral bodies, whereas VHS > 10.5 indicated cardiomegaly, although there were some exceptions, e.g., miniature Schnauzer and Dachshund. Since that report, several studies have described breed-specific differences of VHS reference ranges for various breeds (3–14). Small breeds, e.g., Chihuahua or toy poodle, are popular in Japan (15) and have a high prevalence of MMVD. Therefore, breed- and disease-specific VHS reference ranges are required.

A standard VHS reference range is helpful for distinguishing normal *versus* enlarged hearts; however, it is difficult to identify the degree of cardiomegaly. Although the normal reference range of the VHS was reported recently (14), VHS related to cardiac enlargement was not investigated in Chihuahuas. Furthermore, when echocardiography is not available, the VHS would invaluable as an indicator of cardiac enlargement since heart size must be assessed by radiography alone. The objective of this study, therefore, was to investigate the relationship between VHS and echocardiographic values for heart size in Chihuahuas with MMVD.

Materials and methods

Animals

The medical records of Chihuahuas examined at 6 veterinary facilities between September 2009 and April 2017 were evaluated retrospectively. All dogs had undergone a physical examination, echocardiography, and thoracic radiography, and some had also undergone an electrocardiogram, blood pressure measurement, complete blood (cell) count, blood chemistry examination, and abdominal ultrasound.

Chihuahuas without MMVD were classified as a normal group (Normal), whereas those with MMVD were classified according to echocardiographic indices using left atrial to aorta ratio (LA/AO) (16) and left ventricular internal dimension in diastole normalized (LVIDDN) (17). According to previous reports, they were classified into 3 groups: LA1 group as normal LA (LA/AO < 1.6); LA2 group as mild LA enlargement (1.6 ≤ LA/AO < 2.0); and LA3 group as severe LA enlargement (LA/AO ≥ 2.0) (1,18). Similarly, the Chihuahuas were classified into 2 groups: LV1 group as normal LV (LVIDDN < 1.7) and LV2 group as LV enlargement (LVIDDN ≥ 1.7) (17).

Dogs with factors that can affect VHS (e.g., heart diseases except for valvular disease, hydration disorder, abnormal vertebra, and Addison's disease) were excluded. In addition, cases that had valvular disease with right-sided enlargement were also excluded.

Examination

All data included were from Chihuahuas that had radiographic and echocardiographic examinations performed on the same day.

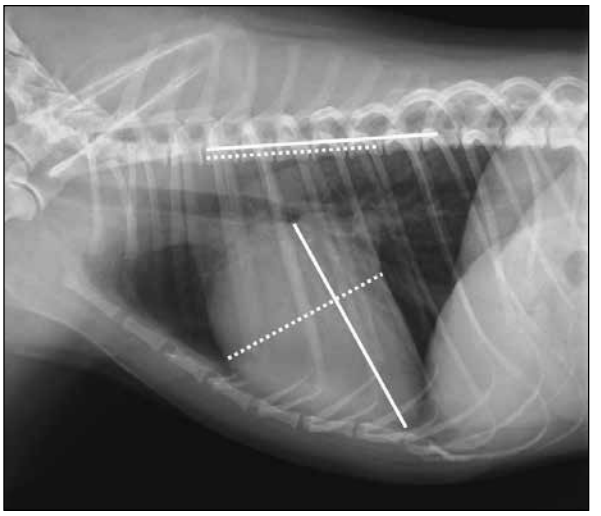

Figure 1. Measurements of vertebral heart size in a left to right lateral (RL) image in a Chihuahua. The long- and short-axis diameters of the heart are represented by solid and dashed lines, respectively.

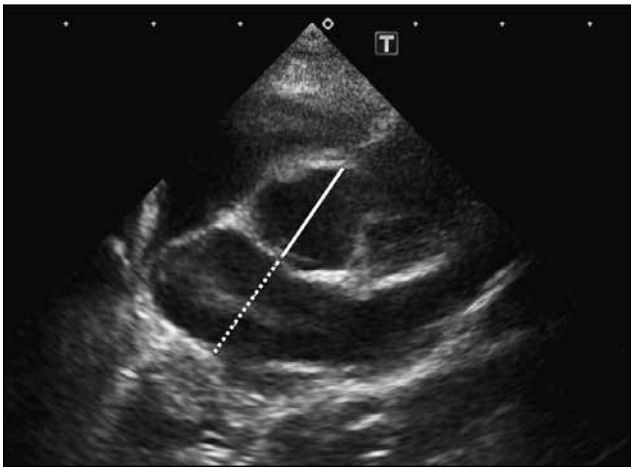

Figure 2. Measurements of the left atrium to aorta ratio (LA/AO) in the right parasternal short-axis view in a Chihuahua. Diameters of the aorta and left atrium are represented by solid and dashed lines, respectively.

Chihuahuas in the Normal group were examined once during the study period. Of the 97 Chihuahuas with MMVD, 50 had a single examination and 47 had multiple examinations in the same period (median: 1, average: 2.5, range: 1 to 32).

All thoracic radiographic and echocardiographic studies were performed by the same observer (DI). In all cases, radiographs were performed before echocardiography, so the observer was unaware of the echocardiographic results when the VHS was measured.

All VHS measurements were performed as described (2), with left to right lateral (RL) images. The long axis of the heart was measured from the ventral border of the carina to the most distant ventral contour of the cardiac apex. The short axis of the heart was measured perpendicular to the long axis at the widest point of the central third region. The long- and short-axis dimensions were expressed as vertebral body length, beginning with the cranial edge of the fourth thoracic vertebral

Table 1. Signalment and medications of Chihuahuas in the Normal, LA, and LV groups.

	Normal	LA1	LA2	LA3	LV1	LV2
N	10	50	24	23	44	53
Age (y) (mean ± SD)	6.1 ± 2.9	10.4 ± 2.49	10.1 ± 2.39	10.1 ± 1.86	10.7 ± 2.57	9.86 ± 2.02
Sex (M, F, MC, FS)	0/5/2/3	8/16/2/24	7/4/3/10	9/7/3/4	9/11/2/22	15/17/6/15
Weight (kg) (mean ± SD)	3.3 ± 1.4	2.7 ± 0.9	3.1 ± 0.8	2.9 ± 0.7	2.8 ± 0.9	3.0 ± 0.7
Loop diuretic [number (%)]	0 (0)	6 (12.0)	6 (25.0)	11 (47.8)	4 (9.1)	20 (37.7)
Pimobendan [number (%)]	0 (0)	9 (18.0)	13 (54.2)	15 (65.2)	6 (13.6)	31 (58.5)

M — Male intact; F — Female intact; MC — Male castrated; FS — Female spayed.

body (Figure 1). Both lengths were rounded to the nearest 0.1 vertebra. Then, long- and short-axis dimensions were summed to obtain a VHS value.

In echocardiography, LA/AO measurement as an index of LA size with Sweden method (16) and LVIDDN measurement as an index of LV size were conducted (17). All echocardiographic measurements were obtained from 2-dimensional images. LA/AO was obtained from the right parasternal short-axis view at the level of the aortic valve in early diastole. Dimensions of AO and LA were measured by the inner edge-to-inner edge technique. Dimensions of AO were measured from the midpoint of the convex curvature of the wall of the right aortic sinus to the point of the aortic wall and the noncoronary and left coronary aortic cusps merged. Dimensions of the LA were measured on the extended line that was used for AO measurement (Figure 2). Then, the ratios of LA to AO were calculated to the nearest 0.01. LVIDDN was calculated from the following formula:

$$\text{LVIDDN} = \text{left ventricular internal diameter in diastole (cm)}/[\text{BW (kg)}]^{0.294}$$

Left ventricular internal diameter in end diastole was measured in a right parasternal short-axis view.

Equipment for digital radiography systems and echocardiographs were as follows. Digital radiography systems: REGIUS110 (KONICA MINOLTA, Tokyo, Japan); FCR CAPSULA-2V (FUJIFILM, Tokyo, Japan); FCR XG-1 (FUJIFILM); NAOMI (RF, Nagano, Japan) and echocardiographs: Aplio300 (TOSHIBA Medical Systems, Tokyo, Japan); LOGIQ P5 (GE Healthcare Japan, Tokyo, Japan).

Statistical analyses

Multiple measurement case data were converted into representative values by using averages to avoid excessive influences on analyses. Data for each group are reported as mean ± standard deviation (SD) and 95% confidence interval (CI). Statistical analyses were performed by analysis of variance, followed by *post-hoc* Tukey. Statistical analysis of sex (male, female, spayed, and neutered) was performed using the Chi-square test. Echocardiographic data in Chihuahuas with MMVD were plotted against VHS values. Scatter plots of 2 echocardiographic measurements (ordinates) were made against VHS (abscissa) in Chihuahuas with MMVD. Regression equations were obtained by least-squares method on scatter plots, whereas the coefficients of determination (R^2) between VHS and LA/AO and VHS and LVIDDN were calculated by Spearman's correlation analysis. Receiver operating characteristic (ROC) analyses were done to define optimal cut-off values for VHS in detecting mild and severe cardiac enlargement. Definitions of mild and severe left-sided cardiac enlargement were LA/AO ≥ 1.6 and LVIDDN ≥ 1.7, LA/AO ≥ 2.0 and LVIDDN ≥ 1.7, respectively. The ROC curves were created based on the sensitivity and the specificity of the VHS. The area under the curve (AUC) was calculated. For all analyses, $P < 0.05$ was considered significant. Statistical analyses were conducted with software packages Stat View Ver.5.0 (SAS Institute, Cary, North Carolina, USA) and EZR Ver.1.40 (Saitama Medical Center, Jichi Medical University, Shimotsuke, Japan).

Results

In this study, 107 Chihuahuas (57 males and 50 females) were included. The mean age was 10.4 ± 2.8 y, and the mean body weight was 2.9 ± 0.9 kg. Ten Chihuahuas were included in the Normal group. Furthermore, 97 Chihuahuas with MMVD were classified, with 50 in the LA1 group, 24 in the LA2 group, and 23 in the LA3 group. Likewise, the Chihuahuas were classified, with 44 in the LV1 group and 53 in the LV2 group. Characteristics of these 6 groups are shown (Table 1). Only age was different between the Normal group and the other groups ($P < 0.01$ *versus* Normal), but sex and body weight were not different in all groups ($P = 0.10$ for sex and $P = 0.16$ for body weight).

Vertebral heart size (mean ± SD; 95% CI) of the Normal group were 9.66 ± 0.36; 95% CI: 9.40 to 9.92. Vertebral heart size of the LA groups were LA1: 10.13 ± 0.64; 95% CI: 9.95 to 10.31, LA2: 10.87 ± 0.71; 95% CI: 10.56 to 11.17, and LA3: 11.71 ± 0.78; 95% CI: 11.37 to 12.05, respectively. Comparisons between the VHS values of the Normal group and all LA groups were as follows: no significant differences between Normal and LA1 (Figure 3 A); LA2 greater VHS than Normal and LA1 ($P < 0.01$, Figure 3 A); and LA3 greater VHS than Normal, LA1, and LA2 ($P < 0.01$, Figure 3 A). There were significant positive relationships of VHS to LA/AO, and the regression equation was:

$$y = 0.3969x - 2.5483 \ (R^2 = 0.56)$$ (Figure 3 B).

Vertebral heart size of LV groups were LV1: 10.04 ± 0.71; 95% CI: 9.83 to 0.26 and LV2: 11.21 ± 0.78; 95% CI: 10.99 to 11.42, respectively. The results of comparisons with the VHS values in the Normal group and all LV groups are as follows: there were no significant differences between Normal and LV1 (Figure 3 C) and LV2 had significantly greater VHS than Normal and LV1 ($P < 0.01$, Figure 3 C). There were significant

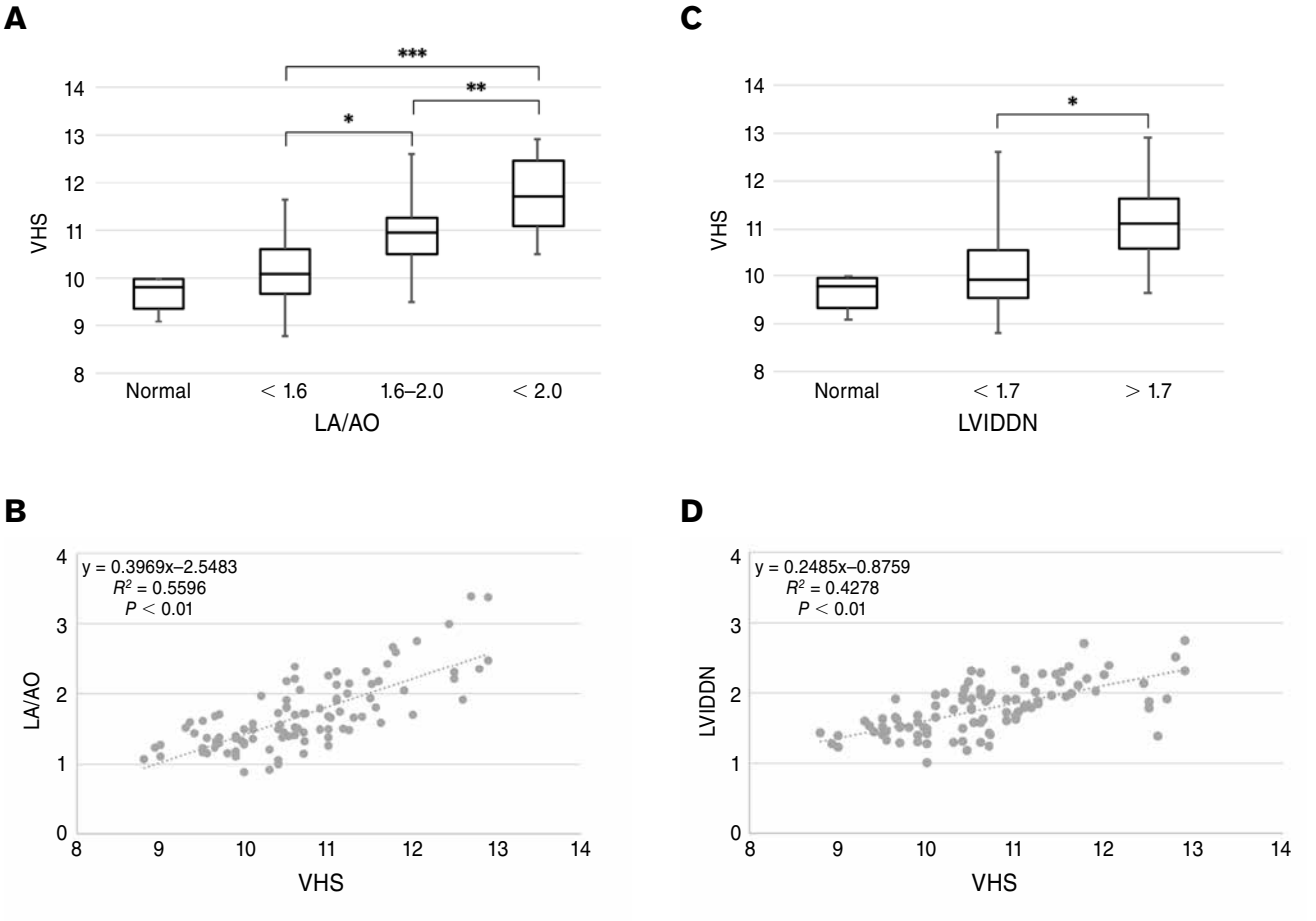

Figure 3. A – Box-and-whisker plot of the VHS in different LA/AO groups. B – Scatter plot and regression equation between VHS and LA/AO. C – Box-and-whisker plot of the VHS in different LVIDDN groups. D – Scatter plot and regression equation between VHS and LVIDDN. *, ** and *** indicate differences ($P < 0.01$). VHS – Vertebral heart size; LA/AO – Left atrium to aortic ratio; LVIDDN – Left ventricular internal dimension in diastole normalized.

positive relationships of VHS to LVIDDN, and the regression equation was:

$y = 0.2485x - 0.8759$ ($R^2 = 0.43$) (Figure 3 D).

The ROC for mild cardiac enlargement had an AUC of 0.87, with the best diagnostic accuracy at the VHS cutoff of 10.5 (sensitivity 0.64, specificity 0.93) (Figure 4 A). Similarly, the ROC for severe cardiac enlargement had an AUC of 0.89, with the best diagnostic accuracy at the VHS cutoff of 11.1 (sensitivity 0.82, specificity 0.78) (Figure 4 B). Therefore, VHS of 10.5 met LA/AO > 1.6 and LVIDDN > 1.7, which meant at least mild left-sided cardiomegaly, and VHS of 11.1 met LA/AO > 2.0 and LVIDDN > 1.7, which meant severe left-sided cardiomegaly.

Discussion

The relationship between VHS and various degrees of cardiac enlargement in Chihuahuas with MMVD was investigated herein. There were significant positive correlations between VHS and LA/AO and VHS and LVIDDN. In addition, VHS differed significantly among normal heart size, mild cardiomegaly, and severe cardiomegaly. Consequently, reference VHS values determined in the present study were useful for evaluating the extent of cardiac enlargement.

The original study investigating VHS of various dog breeds reported that VHS of normal dogs was 9.7 ± 0.5, and 98% of normal dogs were included in VHS ≤ 10.5 (2). Although the VHS for normal Chihuahuas was recently reported to be larger than in a previous study involving multiple breeds (14), the VHS for normal Chihuahuas reported here was similar to the previous study.

When the VHS of Chihuahuas was at least 10.5, the LA/AO and LVIDDN were > 1.6 and > 1.7 from the regression equations; these values met the criteria of mild left-sided cardiomegaly. When the VHS of a Chihuahua was 11.1, the LA/AO and LVIDDN were > 2.0 and > 1.7 from the regression equations, which suggested severe left-sided cardiomegaly. These VHS values may be useful in assessing the severity of MMVD and determining treatment in Chihuahuas with MMVD.

In addition to radiography, echocardiography was also required to diagnose the severity of MMVD (1). However, VHS-based heart size evaluation can be the second-best approach due to difficulties in conducting echocardiography, due to equipment, examination techniques, or animal conditions. In the guidelines

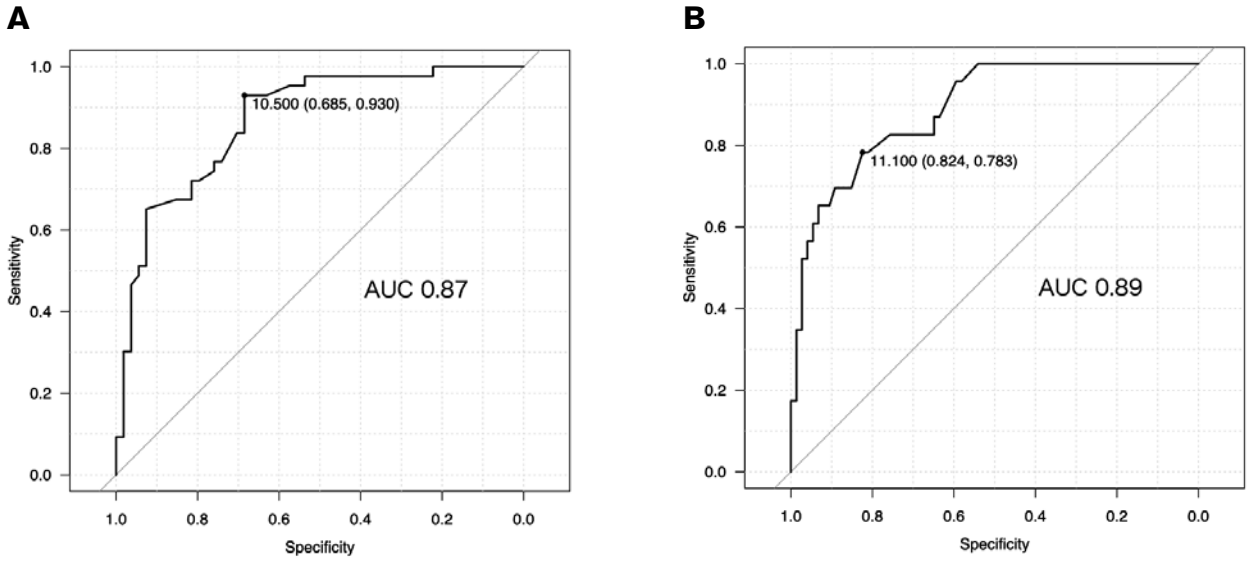

Figure 4. A – ROC curve of VHS and mild cardiac enlargement (LA/AO ≥ 1.6 and LVIDDN ≥ 1.7). The diagnostic cutpoint of VHS is indicated along the curve. AUC = 0.87. B – ROC curve of VHS and severe cardiac enlargement (LA/AO ≥ 2.0 and LVIDDN ≥ 1.7). The diagnostic cutpoint of VHS is indicated along the curve. AUC = 0.89. ROC – Receiver operating characteristic; VHS – Vertebral heart size; LA/AO – Left atrium to aortic ratio; LVIDDN – Left ventricular internal dimension in diastole normalized; AUC – Area under the curve.

for canine MMVD, VHS > 10.5, LA/AO ≥ 1.6, and LVIDDN ≥ 1.7 are proposed as diagnostic criteria for Stage B2 (1). Furthermore, in the absence of echocardiographic measurements, VHS > 11.5 in general breeds or breed-specific VHS reference values can substitute for echocardiographic measurements for the diagnosis of Stage B2. In this study, when the VHS of Chihuahuas was at least 10.5, the LA/AO and LVIDDN were > 1.6 and > 1.7 from the regression equations; these values were similar to the criteria of Stage B2 in canine MMVD guidelines. However, the coefficients of determination of the regression equations were 0.56 in VHS against LA/AO and 0.46 in VHS against LVIDDN, respectively, which meant that the estimation of echocardiographic parameters from regression equations could yield errors. Vertebral heart size can be affected by several factors: cardiac cycle, respiratory phases, vertebral shape, and animal position (19–21). Therefore, VHS is ideally used as an evaluation of heart size in conjunction with other testing and clinical findings. When diagnosing Stage B2 in Chihuahuas with MMVD without echocardiography, it may be safer to use VHS of 11.1, which suggests severe left heart enlargement.

This study had some limitations.

1. Only the VHSs of Chihuahuas were investigated; therefore, it was unknown if these data could be extrapolated to other breeds. Nakayama et al (22) reported the relationship between VHS and cardiac enlargement in large breed dogs with a rapid heart rate. The correlation between VHS and LA/AO was good, and VHS of 11.4 corresponded to LA/AO of 1.6, and VHS of 12.2 corresponded to LA/AO of 2.0. These VHS values were greater than those of the present study. Further studies in various breeds are also needed to apply VHS in general practice.
2. This study could not completely exclude cases with abnormalities that can affect VHS. Patients with factors that can affect VHS (e.g., heart disease except for valvular disease, hydration disorder, abnormal vertebra, and Addison's disease) were excluded from this study. However, screening tests were not conducted in all cases; therefore, cases with these factors could have been included.
3. Accuracy of VHS measurements. As mentioned, VHS measurement could be affected by several factors, such as cardiac cycle, respiratory phases, vertebral shape, and animal position (19–21). Despite efforts to minimize these confounding factors, some cases could have been affected. Previous reports had also described inter-observer variations with VHS measurements (23). However, this type of variation was avoided because the same person conducted all the VHS measurements.
4. Blinding. Since examinations were performed in the order of thoracic radiography and then echocardiography, the observer was aware of radiographic findings during the echocardiography, which could have affected the echocardiography findings.
5. Differences in medical equipment. Examinations were performed at 6 veterinary clinics, and multiple radiography and echo machines were used. Although all the equipment was of adequate performance, there could have been some differences in measurements.
6. The effect of treatment on measurements. Pimobendan and Loop diuretics, such as furosemide, can decrease cardiac size (24–26); perhaps these drugs reduced VHS, LA/AO, and LVIDDN in this study. However, theoretically, all of these indicators could have been reduced at the same time, and thus it may have had little impact on the relationship of the indicators, which was the purpose of this study.

Vertebral heart size was increased according to the degree of cardiac enlargement in Chihuahuas with MMVD. A VHS

of 10.5 corresponded to mild left-sided cardiomegaly, and VHS of 11.1 corresponded to severe left-sided cardiomegaly, as assessed by echocardiography. These breed-specific VHS reference ranges might be useful for evaluations of heart size in Chihuahuas with MMVD.

Acknowledgments

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Brief Communication Communication brève

Pedigree study of the heredity of copper-associated hepatitis in Dalmatians in Japan

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Abstract — The pedigrees of 3 Dalmatian dogs afflicted with copper-associated hepatitis were investigated to discover the mode of inheritance. A composite family pedigree showed that the 3 affected Dalmatians were related. None of the parents of the affected dogs showed clinical symptoms of liver disease, and the disease had no sex predisposition. The estimated segregation ratio was approximately 3:1 based on surviving littermates. These findings suggested that the copper-associated hepatitis in these Dalmatians was an autosomal recessive mode of inheritance. In addition, some male Dalmatians imported from abroad might have been involved in the occurrence of this disease in Japan.

Résumé — Étude généalogique de l'hérédité de l'hépatite associée au cuivre chez des Dalmatiens au Japon. Les pedigrees de trois chiens dalmatiens atteints d'hépatite associée au cuivre ont été étudiés pour découvrir le mode de transmission. Un pedigree familial composite a montré que les trois Dalmatiens affectés étaient apparentés. Aucun des parents des chiens affectés n'a présenté de symptômes cliniques de maladie du foie et la maladie n'avait aucune prédisposition associée au genre. Le ratio de ségrégation estimé était d'environ 3:1 sur la base des compagnons de portée survivants. Ces résultats suggèrent que l'hépatite associée au cuivre chez ces Dalmatiens était un mode de transmission autosomique récessif. De plus, certains dalmatiens mâles importés de l'étranger pourraient avoir été impliqués dans l'apparition de cette maladie au Japon.

(Traduit par Dr Serge Messier)

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Copper is an essential trace element in the body, but its excessive accumulation causes severe damage to various organs. Copper-associated hepatitis is a fatal disease caused by impaired copper metabolism, resulting in excessive accumulation of copper in the liver (1,2). This disease has been widely reported in some breeds of dogs (3–7), including Bedlington terriers, in which it was shown to be an autosomal recessive disorder; the causative gene has been identified (8–10). Among these, copper-associated hepatitis in Dalmatians (CHD) has been reported mainly in North America (11–14), and is characterized by early onset, gastrointestinal symptoms, and death. Some studies have reported a familial disposition, suggesting that CHD may be a genetic disease (11,14); however, the mode of inheritance and responsible gene have not yet been identified. We reported the first case of CHD in Japan in 2021 (15), and since then, our wide-ranging investigations have identified 2 other Dalmatians in Japan being treated as CHD. In this study, we performed a pedigree analysis of these 2 cases and the previously reported case (15) to investigate the hereditary nature of CHD.

The details of 2 Dalmatians with CHD were as follows: Case 1 was a male Dalmatian born in 2014, with 8 littermates at birth. At 2 y of age, he was taken to a veterinary hospital because of inappetence. Blood biochemical tests showed markedly increased liver values (Table 1). A subsequent liver biopsy showed that necrotic foci were scattered in the liver parenchyma, and many eosinophilic fine granules indicating copper were discovered in many hepatocytes throughout the sections. These histopathological features were consistent with those of copper-associated hepatitis. Quantitative analysis of the liver copper content showed excessive copper accumulation in the liver [11.2 mg/g dry mass (11 200 ppm)], confirming the diagnosis of copper-associated hepatitis. The dog was treated continuously with an oral chelating agent (penicillamine; Metalcaptase, Taisho Pharmaceutical, Tokyo, Japan), 200 mg (10 mg/kg) q12h, total

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Table 1. Blood biochemical test results for Case 1 (D1), Case 2 (D2), and for a littermate of Case 2 (D5).

		Case 2 (D2)			
	Case 1 (D1)	Before treatment	After treatment*	Littermate of Case 2 (D5)	Normal range
BUN (mmol/L)	17.7	13.5	23.5	22.1	9.2 to 29.2
Cre (μmol/L)	97	62	97	80	35 to 124
AST (IU/L)	> 1000	> 1000	138	> 1000	17 to 44
ALT (IU/L)	> 1000	> 1000	281	> 1000	17 to 78
ALP (IU/L)	1071	1071	92	> 3500	47 to 254
Alb (g/L)	41	ND	ND	38	26 to 40
T-Bil (μmol/L)	12.0	22.2	6.8	400.1	1.7 to 8.6
Glu (mmol/L)	5.8	4.8	5.0	6.2	4.1 to 7.1

Case — Case 2 (D2) and its littermate (D5): suspected case.
* Penicillamine, 200 mg (10 mg/kg) twice daily [total 400 mg (20 mg/kg)].
ND — No data.

400 mg (20 mg/kg) to promote copper excretion, and remained alive at 7 y of age. The owner of the dog reported that 1 female littermate developed severe jaundice at 2 y of age and died of hepatic failure, with no detailed examination. The other 6 littermates showed no clinical signs of liver disease at 7 y of age.

Case 2 was a male Dalmatian born in 2019, with 7 littermates at birth. At 18 mo old, the dog was taken to a veterinary hospital because of jaundice. Blood biochemical tests showed markedly increased liver values (Table 1). Copper-associated hepatitis was strongly suspected, based on the breed, age of onset, clinical symptoms, and blood test results; however, a definitive diagnosis was not obtained because the owner did not want the dog to have a liver biopsy. The owner chose symptomatic treatment for the hepatitis and empirical treatment for copper-associated hepatitis. Treatment was started with an oral chelating agent (penicillamine). The dog's clinical symptoms and blood test results improved within 2 mo of treatment initiation (Table 1). The dog remained alive at 22 mo of age. One male littermate died at 19 mo of age after showing gastrointestinal symptoms, severely elevated liver values, and jaundice. The blood biochemical examination results of the littermate during treatment suggested severe hepatic failure (Table 1), and CHD was suspected. The other 5 littermates showed no clinical signs at 22 mo of age.

The pedigrees of these 2 cases and the previously reported case (15) were kindly provided by the animals' owners and used for this pedigree analysis with their permission. In addition, the breeders provided 8 other pedigrees for ancestors of the affected cases. We conducted a detailed pedigree survey and obtained a composite family pedigree of the Dalmatians in this study (Figure 1). The identities of D1 and D2 are Cases 1 and 2 described herein, respectively, and D3 is the previously reported case. D4 and D5 indicate the littermates of D1 and D2, respectively, both of which died because of severe hepatic failure of unknown causes, as described. Cases D6–11 are the parents of the affected Dalmatians (D1–D3), at least 4 of which (D6, D7, D10, D11) were still alive at the time of writing, with no clinical hepatic-related symptoms according to their owners. The current and previous statuses of some of the Dalmatians in this pedigree were not available. However, according to several owners, none of the Dalmatians in this pedigree had a definite history of liver disease, other than the known affected cases.

Cases D12 and D13 were the ancestors of the affected cases (D1–D3). The maternal ancestors of D1 and the paternal ancestors of D3 shared a common sire and dam pair (D12 and D13, respectively). Similarly, D12 and D13 were also paternal ancestors of D2, but unlike D1 and D3, there was no direct mating of D12 and D13. Furthermore, this pedigree also showed that D14, the ancestor of D13, was an ancestor of the parents of D1 and D2 on the opposite side; D14 was a paternal ancestor of D1 and a maternal ancestor of D2. Case D14 was therefore related to at least 5 parents of the 3 affected Dalmatians, except for D9. No pedigree information was available for D9, as the maternal ancestor of D3.

In addition, it was determined from this study that the ancestors of the 3 affected cases included 7 male Dalmatians imported to Japan for breeding purposes. Cases D14–D18 were imported to Japan from the USA as individuals or *via* frozen sperm between 1991 and 2011, and D12 and D19 were imported from Australia to Japan in 2007 and 1996, respectively. No detailed information was available on the physical condition of these 7 imported Dalmatians, nor was there a record of liver disease. In addition, the ancestor of D12 (D20) was imported from Canada to Australia *via* frozen sperm.

Copper-associated hepatitis in Dalmatians has been considered a hereditary disease; however, there have been no detailed reports on the mode of inheritance of CHD, and no definitive conclusions have been reached to date. Pedigree analysis of affected Dalmatians may be key to elucidating the mode of inheritance of CHD; however, to the best of our knowledge, no such familial studies have been reported. In this study, we performed a pedigree analysis of affected Dalmatians, with the kind cooperation of the owners and breeders of the affected and related dogs. The composite pedigree that was obtained showed that the 3 affected Dalmatians in this study were related, suggesting that the disease is likely hereditary. Regarding the mode of inheritance of CHD, it is difficult to reach a definitive conclusion without identifying the responsible gene mutation; however, the apparent lack of sex predisposition in the development of the disease (14) indicates a low probability of an X-linked disease. In addition, given that the parents of D1 and D2 (D6, D7, D10, D11) had not developed the disease at the time of writing, it seems unlikely that CHD is inherited in an autosomal dominant manner, and is most likely an autosomal

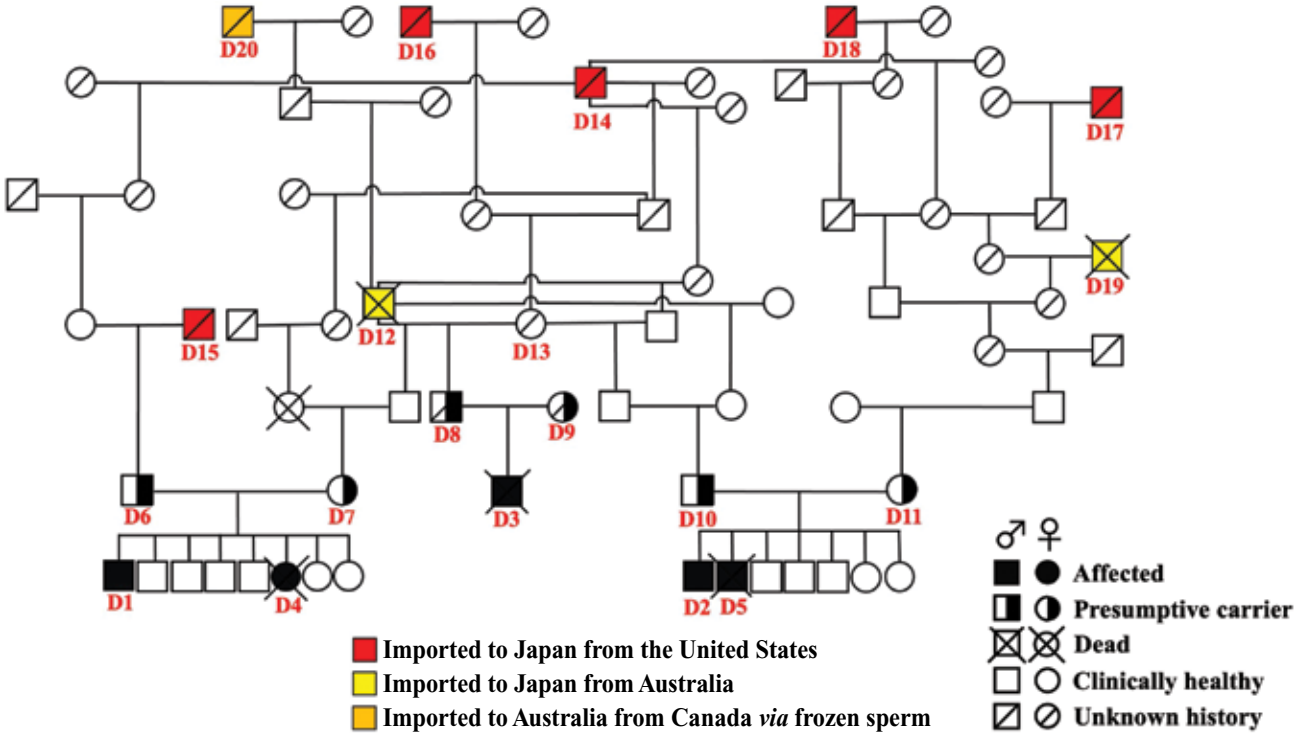

Figure 1. Composite pedigree containing multiple Dalmatians diagnosed as a copper-associated hepatitis, created based on multiple pedigrees of the affected cases and related dogs. D1–D3: affected Dalmatians; D1 and D2 represent Cases 1 and 2 in the text, respectively, and D3 represents the previous case. D4 and D5: dead littermates of D1 and D2, respectively. D6–11: parents of D1–D3 and presumptive carriers. D12–20: ancestors of D1–D3. D14–18: male Dalmatians imported from the United States for breeding (red squares). D12 and D19: male Dalmatians imported from Australia (yellow squares). D20: ancestor of D12 imported from Canada to Australia (orange square).

recessive trait. We were also provided with information on the survival of the littermates of D1 and D2, which allowed us to estimate the possible segregation ratio of the disease. The probability of having an affected dog in the D1 and D2 litters were 2/8 (25.0%, segregation ratio 3:1) and 2/7 (28.6%, segregation ratio 2.5:1), respectively. These findings may be consistent with an autosomal recessive inheritance pattern. However, the disease may have a more complex mode of inheritance, and further investigations are required to clarify this issue.

Assuming CHD demonstrates autosomal recessive inheritance, similar to copper-associated hepatitis in Bedlington terriers, the 3 affected cases (D1–D3) would be homozygous for the causative gene and their parents (D6–D11) would be heterozygous carriers, without clinical symptoms. Although the exact origin of the causative gene remains unknown, it might have been inherited by D1–D3 from common ancestors of D12 and D13, *via* D7, D8, and D10. Furthermore, this pedigree suggested that D14 might be a presumptive carrier, given that it corresponded to the ancestors of D12 and D13, although there was no clear evidence of this. Case D14, which was thought to be most closely related to the 3 affected cases in this study, was imported to Japan from the USA for breeding purposes. Information from breeders suggested that this male Dalmatian had been used extensively for breeding in Japan, producing many offspring. In addition to D14, the current pedigree included many other imported Dalmatians. Although these dogs were less frequently associated with the affected dogs and their parents than D14, they were predominantly imported from countries in which CHD has been reported, suggesting that they may also be potential carriers of CHD.

Copper-associated hepatitis in Dalmatians was first reported in Canada in 1996 (11), followed by sporadic clinical reports and a review of 10 cases in the United States (12–14). In contrast, the onset of CHD in Japan was after 2014, with no reported cases before that date. Considering that these Dalmatians were imported to Japan between 1991 and 2011, the recent familial onset of CHD in Japan might have been introduced in breeding dogs from abroad, specifically North America, where the disease has previously been reported, although there is no clear evidence for this. In addition, D12 and D19 were imported to Japan from Australia, and to the best of our knowledge, there have been no reports of CHD in Australia; however, the incidence of this disease in Australia is unknown. Our pedigree study indicated that D12's ancestors included a Dalmatian imported from Canada to Australia (D20). Given that CHD has been reported in Canada, D20 cannot be ruled out as a possible carrier, and the causative mutation may have been introduced into Japan *via* D12 from Australia.

Furthermore, the pedigree showed that numerous Dalmatians bred in Japan were involved in the affected cases, and the causative mutation might have occurred independently in these dogs. Although the involvement of imported Dalmatians in the recent familial development of CHD in Japan has not been clarified, it is possible that the causative mutation originated in Japan, or it

may have been introduced in Dalmatians imported from abroad for breeding purposes. Irrespective of the origin, this pedigree analysis strongly demonstrated the potential hereditary nature of CHD and revealed its familial occurrence in Dalmatians bred in Japan. Breeders and veterinarians should, therefore, be aware of this fact and take measures to prevent this disease.

Copper-associated hepatitis in Dalmatians is a life-threatening disease that can lead to death of affected dogs at an early age (11–15). The possible hereditary nature of CHD shown in this study highlights the need to avoid matings between carriers and to identify living carriers to help prevent the onset of this disease. Unplanned breeding programs should be discouraged, to prevent the use of possible carriers. However, genetic testing cannot currently be carried out because the gene responsible has not been identified. It is therefore realistic to identify potential carriers based on pedigree analysis of affected individuals, and to exclude these dogs from future breeding. The current pedigree analysis identified presumptive carriers and indicated the likely mode of inheritance, which were useful for elucidating the genetic aspects of CHD. It is also necessary to investigate the responsible gene mutations to clarify the cause of this disease and to enable genetic testing to be carried out.

This study had some limitations, as we only analyzed the pedigrees of a limited number of Dalmatians. More Dalmatians need to be investigated to reach a definitive conclusion regarding the mode of inheritance of CHD. In addition, the littermates in Case 2 may have been observed for too short a time to reliably calculate the segregation ratio. Although the current study suggests a recessive mode of inheritance of CHD, further similar pedigree analyses should be conducted in countries where CHD has been reported.

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Brief Communication Communication brève

First report of *Angiostrongylus vasorum* (French heartworm) in red foxes *(Vulpes vulpes)* on Prince Edward Island

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Abstract

Objective

To identify first-stage nematode larvae (L1) recovered from a red fox scat sample and adult female worms recovered from 2 red fox lungs at necropsy, using published molecular methods to confirm a morphological diagnosis of *Angiostrongylus vasorum* (French heartworm).

Animal

Red fox *(Vulpes vulpes).*

Procedure

Nematode larvae recovered from a Baermann examination survey of wild canid scats (n = 101) conducted from January 2017 to August 2020, were identified by size and morphology and subjected to PCR and DNA sequencing of the small subunit (SSU) rRNA gene, the large subunit (LSU) rRNA gene, or the second internal transcribed spacer (ITS2). In addition, these techniques were applied to adult female worms recovered from the heart/lungs of 2 red foxes (obtained from PEI trappers and stored frozen at −20°C since December of 2018 and 2020).

Results

Size and morphology of L1 recovered by Baermann examination from a wild canid scat sample (presumed to be red fox) collected near Montague, PEI and adult female worms recovered at necropsy from 2 red fox carcasses were identified as *A. vasorum.* Molecular analysis confirmed the larvae and adult worms were *A. vasorum.*

Conclusion

These findings indicated that *A. vasorum* has become endemic in the red fox population on PEI.

Clinical relevance

Angiostrongylus vasorum infection is potentially fatal in dogs. Veterinarians and regional diagnostic laboratories in the Maritime provinces should consider the possibility of *A. vasorum* infection in dogs with clinical signs of cardiopulmonary and/or central nervous system disease or bleeding disorders.

Résumé

Premier signalement d'*Angiostrongylus vasorum* (ver du cœur français) chez le renard roux (*Vulpes vulpes*) à l'Île-du-Prince-Édouard

Objectif

Identifier les larves de nématodes de premier stade (L1) récupérées à partir d'un échantillon d'excréments de renard roux et les vers femelles adultes récupérés à partir de deux poumons de renard roux à l'autopsie, en utilisant des méthodes moléculaires publiées pour confirmer un diagnostic morphologique d'*Angiostrongylus vasorum* (ver du cœur français).

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Animal
Renard roux (*Vulpis vulpis*).

Procédure
Les larves de nématodes récupérées lors d'une enquête sur des excréments de canidés sauvages (n = 101) par examen Baermann menée de janvier 2017 à août 2020, ont été identifiées par taille et morphologie et soumises à la PCR et au séquençage de DNA de la petite sous-unité (SSU) du gène de rRNA, de la grande sous-unité (LSU) du gène de rRNA ou du deuxième espaceur interne transcrit (ITS2). De plus, ces techniques ont été appliquées à des vers femelles adultes récupérés du cœur/poumons de deux renards roux (obtenus auprès de trappeurs de l'Î.-P.-É. et conservés congelés à −20 °C depuis décembre 2018 et 2020).

Résultats
La taille et la morphologie de L1 récupérées par examen Baermann à partir d'un échantillon d'excréments de canidés sauvages (présumé être du renard roux) prélevé près de Montague, Î.-P.-É. et des vers adultes femelles récupérés des carcasses lors de la nécropsie de deux renards roux ont été identifiés comme étant *A. vasorum*. L'analyse moléculaire a confirmé que les larves et les vers adultes étaient *A. vasorum*.

Conclusion
Ces résultats indiquent qu'*A. vasorum* est devenu endémique dans la population de renards roux de l'Î.-P.-É.

Pertinence clinique
L'infection à *A. vasorum* est potentiellement mortelle chez le chien. Les vétérinaires et les laboratoires de diagnostic régionaux des provinces maritimes devraient envisager la possibilité d'une infection à *A. vasorum* chez les chiens présentant des signes cliniques de maladie cardio-pulmonaire et/ou du système nerveux central ou de troubles de la coagulation.

(Traduit par Dr Serge Messier)

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Angiostrongylus vasorum (French heartworm) is a metastrongyloid nematode residing in the pulmonary artery and right ventricle of domestic and wild canids; the natural definitive hosts are the red fox *(Vulpes vulpes)* and various other species of foxes, which serve as reservoir hosts for dogs (1). Animals acquire infection by ingestion of infected intermediate hosts (land snails, slugs, frogs) or paratenic hosts (birds, frogs) (1,2). Recent studies have indicated that direct exposure to infective third-stage larvae (L3) released free into the environment from infected gastropods may be an additional transmission route (3,4). The epidemiological significance of paratenic hosts and environmental contamination in *A. vasorum* transmission has not been determined. The prepatent period is usually ~38 to 57 d, but ranges of 28 to 109 d have been reported (1,5). Infection in dogs can be subclinical or result in severe cardiopulmonary or other tissue damage and is potentially fatal. Clinical signs can be highly variable and the prodromol period can be months or years (1,5). The most common clinical sign reported in dogs infected with *A. vasorum* is a chronic cough, which may also be accompanied by dyspnea, exercise intolerance, and weight loss (5). Infection has also been associated with bleeding disorders and signs of ocular and central nervous system disease (1). Diagnosis occurs by detecting first-stage larvae (L1) shed in the feces of infected canids using the Baermann technique (5).

Angiostrongylus vasorum is considered endemic in parts of Africa, Europe, North America, and South America (1). Until the last decade, the single North American endemic focus had been on the island of Newfoundland. Computer modeling has suggested that conditions conducive to the spread of *A. vasorum* within North America (red fox, terrestrial gastropods) may occur throughout the eastern half of the continent and the states and province along the western coast (6). Due to the large red fox population, climatic conditions (high rainfall), and abundant terrestrial gastropod fauna, the threat of spread from Newfoundland to the Maritime provinces of New Brunswick (NB), Nova Scotia (NS), and Prince Edward Island (PEI) has been of particular concern (1). Recent research has indicated a spread of *A. vasorum* within North America, with infection in red foxes reported in West Virginia, USA, and in coyotes *(Canis latrans)* in Nova Scotia, Canada (7,8).

During a wild canid fecal scat survey (n = 101) conducted from January 2017 to August 2020, larvae identified as *A. vasorum* L1 based on size and morphology were recovered by Baermann examination from a scat sample presumed to be from a red fox collected near Montague, PEI (46 km east of Charlottetown in Kings County). The mean L1 length was 392 μm (range: 384 to 400 μm), and the caudal end terminated in a sinus wave-shaped kink with a dorsal spine (Figure 1). Larvae of *Uncinaria stenocephala* were also recovered from the sample. Confirmation of the morphological identification by molecular methods was attempted due to the possibility that the larvae were 1 of the species of *Angiostrongylus* infecting rodents in North America *(A. blarini, A. michiganensis,* and *A. schmidti)* (9). Larvae of these species could have been present in the scat sample due to fox predation of rodent hosts.

DNA was extracted on 3 subsamples (~10 L1) from the original mixed sample comprising 80% *U. stenocephala* and 20% *A. vasorum,* using a DNeasy Blood and Tissue kit (Qiagen, Toronto, Ontario) following the manufacturer's instructions, except that the proteinase K digestion was 18 h at 56°C. A ribosomal DNA (rDNA) Internal Transcribed Spacer 2 (ITS2)

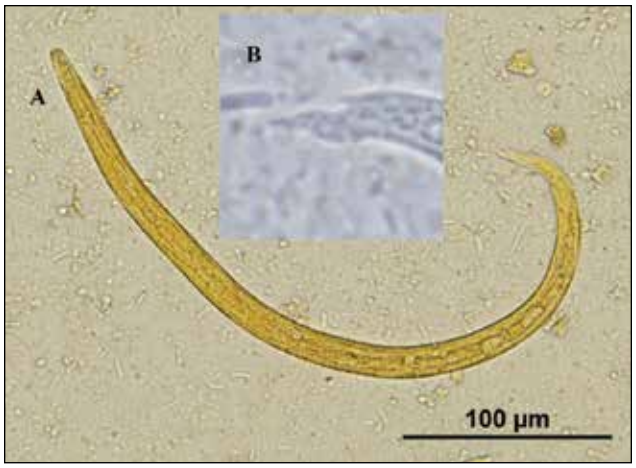

Figure 1. First stage larvae of *Angiostrongylus vasorum* (A) recovered from a canid scat sample collected near Montague, PEI. The caudal end (B) terminates in a sinus wave-shaped kink with a dorsal spine (inset – high magnification image of tail morphology). The mean L1 length was 392 µm (range: 384 to 400 µm).

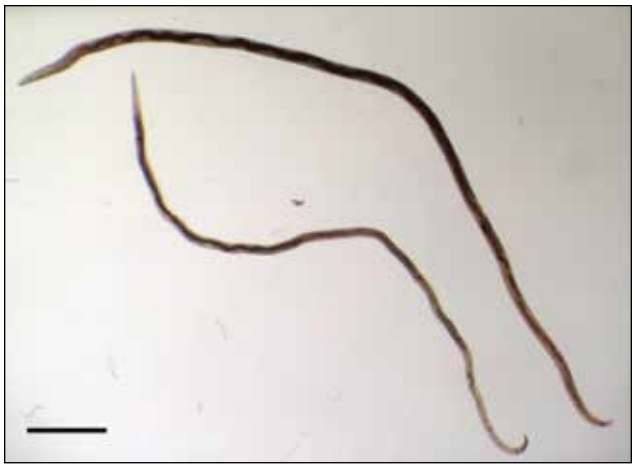

Figure 2. Adult female *Angiostrongylus vasorum* nematodes recovered from the heart/lungs of a red fox trapped in December of 2018. Size bar = 2 mm.

primer set AV5F (5′-CGATGACGGTAGCAATGACA-3′) and AV4R (5′-TTTGCGTGGTTCTTTACGTG-3′) specific for *A. vasorum* was used (10). In addition, 8 L1 of *A. vasorum* were isolated using the dissecting microscope from the mixed sample that contained *U. stenocephala,* DNA was extracted as before, and a partial fragment of the large subunit (LSU) rRNA gene sequence (~850 to 950 bp) was amplified using primers LSU537F (5′-GATCCGTAACTTCGGGAAAAGGAT-3′) and LSU531R (5′-CTTCGCAATGATAGGAAGAGCC-3′) (11).

The *A. vasorum* larval partial ITS 2 regions sequence (GenBank accession number: OK146880) shared 100% identity with *A. vasorum* from Europe (host: dog, *Canis familiaris* and red fox, *Vulpes vulpes;* MN178647, MN104952, GU045376, EU627593, EU627594, GU045374, EU627595, EU627592). The *A. vasorum* larval partial LSU rRNA gene region sequence (OK143439) isolated from a mixed infection with *U. stenocephala* shared 99.8% identity with *A. vasorum* (AM039758) from the red fox *(Vulpes vulpes)* from Canada. ITS2 and partial LSU rRNA gene were used successfully to confirm the presence of *A. vasorum* co-infected with *U. stenocephala* in a red fox scat sample.

Subsequently, during lung flushes of adult foxes (n = 76), 2 adult foxes contained 2 and 1 adult female nematodes, respectively. The 2 red foxes were trapped near Johnstons River (12 km east of Charlottetown, in Queens County) and near Larkens Pond (171 km east of Charlottetown, in Kings County). Both foxes had been frozen at −20°C between the time they were trapped in December 2018 and December 2020, respectively and the time of necropsy. Morphology of the adult worms was consistent with *A. vasorum* (~20 mm in length; lacked a buccal capsule and cuticular synlophe; vaginal opening located near the posterior-end of the worm). However, definitive identification of adult worms is primarily based on the morphology of the males (9). Adult worm tissue was treated as described previously for molecular identification of larvae and the DNA sequences were 100% identical to the larval isolate sequences.

Based on these results, the authors concluded that *A. vasorum* has spread to the red fox population of PEI and has been there since at least 2018. Currently, no data are available on the prevalence or geographic distribution within the red fox population on PEI. There was a 20-year interval in Newfoundland from the first report of *A. vasorum* infection in a red fox to the first diagnosis in a dog. Within 5 y after the first diagnosis in a dog, *A. vasorum* infection was reported in 24% of the cases of dogs with clinical signs of cardiopulmonary disease in Newfoundland (1). Although not definitively known, it is likely that the parasite slowly spread within the Newfoundland red fox population until reaching a sufficient level leading to exposure to dogs. Clinicians in NS, PEI, and NB should consider the possibility of *A. vasorum* infection in dogs presented with signs of chronic respiratory disease, bleeding disorders, or neurological disease. Dogs infected with French heartworm can be diagnosed by fecal examination using the Baermann technique. Due to the erratic fecal larval shedding pattern typical of most metastrongyloids, false-negative results can occur with a single Baermann examination. Therefore, multiple examinations (ideally 3) should be performed before ruling out *A. vasorum* infection (1). Collection of 3 consecutive day fecal samples in such cases may be advisable (5). Fenbendazole, milbemycin oxime, and moxidectin have all been used to treat cases of infection in dogs (1), whereas milbemycin oxime and moxidectin have been used as monthly preventative treatments (12,13). CVJ

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Answers to Quiz Corner
Corrigé du test éclair

1. B) Immune-mediated hemolytic anemia

This is the clinical picture of immune-mediated hemolytic anemia (IMHA). The slide description of autoagglutination of red blood cells (RBCs) is due to autoantibodies to RBC, causing red cell destruction by macrophages and complement.

Sometimes antibodies are directed against RBC precursors in bone marrow, which causes a nonregenerative anemia. Hematologic hallmarks of IMHA are spherocytosis, a positive Coombs test, and autoagglutination.

Thromboembolism and disseminated intravascular coagulation (DIC) are associated conditions to watch for in a dog with IMHA. Thrombocytopenia may occur in Evans syndrome (concurrent immune mediated hemolytic anemia and immune mediated thrombocytopenia) or if DIC is present.

Reference

Cohn L, Côté É. Clinical Veterinary Advisor-Dogs and Cats. 4th ed. Toronto, Ontario: Elsevier, 2020:60–63.

2. E) Surgical removal

Treatment for cystoliths is surgical removal (± lithotripsy to break it down first), either through a pelvic urethrotomy in males and *via* the urethra in mares or *via* ventral midline laparotomy.

A history of hematuria after exercise plus urinalysis results (red blood cells ± protein, white blood cells, calcium crys-

1. B) Anémie hémolytique à médiation immunitaire

Ceci est l'image clinique de l'anémie hémolytique à médiation immunitaire (AHMI). L'autoagglutination des globules rouges visible sur la lame est due à des autoanticorps ciblant les globules rouges et causant leur destruction par les macrophages et le complément.

Parfois les anticorps sont dirigés contre les précurseurs des globules rouges dans la moelle osseuse, causant une anémie non régénérative. Les caractéristiques hématologiques de l'AHMI sont la sphérocytose, un test de Coombs positif et l'autoagglutination.

La thromboembolie et la coagulation intravasculaire disséminée sont des affections associées à surveiller chez un chien souffrant d'AHMI. La thrombocytopénie peut se produire dans le syndrome d'Evans (anémie hémolytique à médiation immunitaire et thrombocytopénie à médiation immunitaire concomitantes) ou si une coagulation intravasculaire disséminée est présente.

Référence

Cohn L, Côté É. Clinical Veterinary Advisor-Dogs and Cats, 4th ed., Toronto, Ontario, Elsevier, 2020, pages 60-63.

2. E) Ablation chirurgicale

Le traitement des calculs vésicaux est l'ablation chirurgicale (avec ou sans lithotripsie pour les briser en premier), soit par

tals) make this a top differential. In this case, the transrectal palpation and ultrasound findings confirm the diagnosis (Figure 1).

Bladder stones can often readily be palpated per rectum. Transrectal ultrasound of the urinary bladder is easy and readily available to most practitioners in the field.

The normally alkaline pH of equine urine, especially combined with diets high in alfalfa (high in calcium) in certain parts of the USA (e.g., California, Texas) make this a not uncommon condition. Most common types of bladder stones in horses are calcium carbonate — either yellow with a spiculated, rough surface or smooth, white.

Secondary bladder infection or ascending pyelonephritis can occur. If a urolith passes into the urethra, the signs will be of straining to urinate, colic, extreme distress. Nephroliths and ureteroliths with secondary hydronephrosis or pyelonephritis are seen.

Reference

Smith BP, Van Metre DC, Pusterla N. Large Animal Internal Medicine. 6th ed. St. Louis, Missouri: Mosby, 2020:973–975.

The questions and answers are provided by The Zuku Review, online veterinary test prep.

Les questions et les réponses sont gracieusement fournies par le site de préparation aux examens vétérinaires Zuku Review.

urétrotomie pelvienne chez les mâles et par l'urètre chez les juments, soit par laparotomie sur la ligne médiane ventrale.

Une anamnèse d'hématurie après un exercice et des résultats de l'examen de l'urine (globules rouges ± protéines, globules blancs, cristaux de calcium) permettent un différentiel de choix. Dans ce cas, la palpation transrectale et les résultats de l'échographie confirment le diagnostic (figure 1).

Les calculs vésicaux peuvent souvent être palpés par le rectum. L'échographie transrectale de la vessie est facile et aisément accessible pour la majorité des praticiens dans le champ.

Le pH alcalin normal de l'urine du cheval, spécialement combiné à la diète riche en luzerne (élevée en calcium) dans certaines régions des États-Unis (Californie, Texas, par exemple), permet à cette affection de ne pas être rare. La plupart des calculs vésicaux communs chez le cheval sont des carbonates de calcium – soit jaunes à surface rugueuse avec spicules, soit à surface lisse et blanche.

Des infections secondaires de la vessie ou une pyélonéphrite ascendante peuvent se produire. Si un urolithe passe dans l'urètre, les signes seront des efforts pour uriner, des coliques et une détresse extrême. Des néphrolithes et des urétérolithes avec hydronéphrose secondaire ou une pyélonéphrite sont observés.

Référence

Smith BP, Van Metre DC, Pusteria N. Large Animal Internal Medicine, 6th ed., Saint-Louis, Missouri, Mosby, 2020, pages 973-975.

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Nature, nurture, and mental health. Part 2: The influence of life experience

Debbie L. Stoewen

The first article in this series (1) covered the nature-related factors that can influence mental health. This article will focus on the nurture-related factors. It is the interplay of the environmental conditions to which we are exposed along with our genetic, psychological, and biological constitution that gives rise to the unique attributes that make each human being different from another. These attributes influence the extent to which we may be challenged by mental health problems or develop a mental illness.

Whether we thrive (or not) in life depends on the environments in which we are conceived, born, grow, learn, build a career and family, and age (2). The conditions and contexts of our lives — both social and physical — can either protect mental health or put it at risk. They can enable us to reach our highest potential or challenge us in ways that can leave us with troubles that can take a lifetime to heal. They shape our appreciation of life and what it may offer, including our values, morals, and worldviews.

Our life experiences, however, are not definitive in their influence. People naturally respond to the same circumstances in different ways. What may be an experience of significance for one person may not be for another, related, at least in part, to the unique aspects of their genetic, psychological, and biological constitution, reflecting again the intersectionality of nature and nurture. Likewise, we each have a unique life story, woven with its own players, plots and subplots. Such novelty makes any response possible.

The designs of our lives are unique and infinitely complex. Each person has a one-of-a-kind life story with parts both enabling and challenging. Our childhood experiences, so formative; the ordinary and extraordinary experiences of our lives; and the universally influential realities of social media, climate change, and the pandemic all can influence mental health. Each will be discussed in turn.

Adverse childhood experiences

Our experiences in childhood, particularly the traumatic ones, can have great influence on our lives. Traumatic experiences that occur before the age of 18 are called adverse childhood experiences (ACEs) (3). ACEs fall into 3 domains (and 10 categories): *abuse* (physical, emotional, and sexual); *neglect* (emotional and physical); and *household dysfunction* (divorce, mental illness, substance abuse, violence, and incarceration among caregivers) (3,4). Although there is no national survey data on ACEs in Canada, the Centers for Disease Control and Prevention (CDC) report 61% of adults have at least one ACE and 16% have 4 or more types (categories) of ACEs (5). Women have higher overall ACE scores than men (5).

People who have experienced abuse, neglect, and household dysfunction during their childhood are at much greater risk of mental illness throughout life (4). There is a dose effect: the more categories of exposure a person experiences, the more likely he or she is to experience poor mental health (4,6), and alongside this, poor physical health, increased at-risk behaviors, and early death (7). These outcomes are thought to be associated with the effects of "toxic stress" on healthy brain development, affecting the development of socio-cognitive skills, which in turn, leads to poor choices in health habits and life decisions (3). Those with ACEs have an increased risk for, and incidence of, anxiety disorders, depression, substance abuse, and suicidality (8,9).

The ordinary to extraordinary experiences

The ordinary to extraordinary experiences of our lives that cause stress can impact us as well. It has long been recognized that stress plays a significant role in the development of mental disorders (10). A stressor can be thought of as a life event, or series of events, that disrupts psychological equilibrium, and in this, may catalyze a mental disorder (11).

Stressors can take the form of *discrete events,* such as relationship breakups, car accidents, complications during pregnancy, a death in the family, or the loss of a job. Stressors can also be more *chronic circumstances,* such as long-term illness, ongoing marital problems, perpetual workplace troubles, unending financial difficulties, or wider difficulties such as political strife and war (12). Stressors can also be the *daily hassles,* like keeping up with chores or meeting deadlines. Stressors — as discrete events, chronic circumstances, and daily hassles — can take their toll, causing stress that can culminate in a mental disorder.

Social media

Although social media can offer many benefits, with the ability to connect with anyone anywhere and with many people at the same time, building relationships and sharing information, it can also adversely affect mental health. It can incite "fear of missing out" (FOMO) and unhealthy social comparison (13).

Dr. Stoewen is an academic, entrepreneur, and facilitator committed to advancing the health and well-being of people and animals through speaking, writing, and education.

Many studies have found a strong link between heavy social media use and an increased risk for anxiety, depression, eating disorders, loneliness, self-harm, and even suicide ideation (13).

Cyberbullying is a real concern in the veterinary profession. A recent study by the American Veterinary Medical Association (AVMA) reported that 1 in 5 veterinarians has been a victim, or works with someone who has been a victim, of cyberbullying in the workplace (14). Incidents of bullying can range from the posting of negative reviews to threats of financial, physical, and/or emotional harm to veterinarians, their staff, and families. The stress of cyberbullying not only adds tension in the workplace, as a dark, hovering cloud, but can lead to depression and suicide.

Climate change

Climate change is one of the great challenges of our time. Since 2000, the frequency of climate change-related weather disasters has soared by 46% (15). Rising temperatures, heat waves, floods, tornadoes, hurricanes, droughts, fires, loss of forest, and melting glaciers, along with the disappearance of rivers and desertification, can impact mental as well as physical health (16). Climate change can cause stress and distress, provoke high-risk coping behaviors (such as increased alcohol use), and lead to anxiety, depression, post-traumatic stress, and suicidal thoughts (16–18). Climate change can also affect mental health through the loss of jobs, social and community resources, and through forcing people to move (18). Among other populations that are especially vulnerable, those with pre-existing mental health disorders are disproportionately affected by the consequences of climate change (17,18).

Importantly, climate change can be experienced not only as a *direct* threat, but as a global or existential threat to civilization and ways of life (19,20). Awareness of the looming threats and impacts of climate change on the current and future well-being of the earth and its inhabitants can negatively affect emotional and social well-being (20). Climate change can contribute to several recently coined *psychoterratic syndromes: ecoanxiety, ecoparalysis, solastalgia,* and *biospheric concern* (16,19).

Ecoanxiety refers to the anxiety people face from constantly being surrounded by the 'wicked' and threatening problems associated with a changing climate. *Ecoparalysis* refers to the complex feelings of not being able to take effective action to significantly mitigate climate change risks. *Solastalgia* refers to the distress and isolation caused by the gradual removal of solace from the present state of one's home environment (1). Lastly, *biospheric concern* refers to a type of stress that people feel when they see plants, animals and ecosystems that are vulnerable (16).

COVID-19 pandemic

The pandemic has profoundly affected people around the globe, causing high levels of stress, distress, fear, anxiety, and insomnia; especially with the uncertainties accompanying a new disease (21,22). Social distancing and widespread lockdowns; which constrained people's ability to access support from loved ones, learn, work, and engage in their communities; added to the stress. These measures also led to feelings of isolation, loneliness, and for some, despair. On top of all of this has been the suffering with COVID-related illness and deaths. To date, over 37 000 Canadians (and 6 million worldwide) have died due to COVID-19 (23).

According to a recent report by the World Health Organization (WHO), there has been a 25% increase in the prevalence of anxiety and depression worldwide (24). Women have been more impacted (than men), as well as those with pre-existing health conditions (such as asthma, cancer, and heart disease). Young people have especially been affected, with a rise in the risk of self-harming and suicidal behaviors. Across the globe, people are looking for hope and signs of brighter days ahead as they navigate the challenges in a now much more complicated world.

Although many faced job loss, others faced greater demands, including those in the veterinary profession. Veterinary clinics around the world needed to implement new policies and procedures in response to the pandemic, including shifting to curbside care, practicing social distancing, intensifying sanitation measures, wearing personal protective equipment, and adopting new technologies such as virtual check-ins, telemedicine, and contactless payment. Many clinics initially dealt with restrictions on elective services, and, at times, had to limit the range and volume of services due to staff shortages or supply chain issues. Although the new ways of working reduced efficiency (decreasing the number of appointments that could be handled in a day), the demand for care rose, with reports of higher client numbers (with new adoptions) and earlier detection of health problems (with working from home), along with the need to attend to a backlog of postponed care. According to the 2020 CVMA Workforce Study, the veterinary profession appears to be working at, or above, capacity, with a shortage of veterinarians and technicians identified as one of the key challenges faced by the profession (25). The stress of substantial workplace modifications, heavy demands, shortage of staff, and serving a stressed, anxious, and demanding clientele, can predispose to burnout and/or culminate in a mental disorder.

Taking it from here

So, who are you in your world? What is it about you, *meaning your genetic, psychological,* and *biological constitution,* and your world, *meaning your collective life experience,* that may be influencing your mental health? Your understanding of this is the pivotal first step to better mental health. Awareness, however, is not enough; it needs to be allied with acceptance. In any given moment, we can lean in and accept or deny and avoid. Acceptance requires open, full acknowledgment of *what is,* with courage and authenticity. When we see with *what is* clarity, we will be able to see what we can do about it.

As mental health is determined by the combination of, and interaction between, personal and environmental factors, you may presume that there are some things that we can't do anything about — like the hereditary predispositions that we are born with and the life experiences that have shaped us. These simply *are,* right? After all, you can't trade in your brain for a different model! You can't rewrite history! So, what *can* you do? The answer is simple.

"It's not just what you were born with or what you've experienced that determines your mental health. It's what you do

with these. It's *how you live your life.* And *how you live your life* is a matter of choice."

The choices we make

You may think it's the big decisions you've made over the course of your life that have shaped you into who you are today — what schools you went to, what vocation you chose, whether or who you married, whether you raised a family, how you grew your career, and the shifts you made to go in whole new directions. But in truth, it's just the opposite. It's all the thousands — if not tens of thousands — of microdecisions we make every day, which we are often unaware of, that most shape the course of our lives (26). These are the seemingly inconsequential decisions made all the time that, in fact, are of profound influence. Indeed, it's the millions of microdecisions that pave the way for the macrodecisions.

The decisions you make add up to define *how you live your life.* To optimize your mental health begins with accepting that *decisions matter,* even — and especially — the decisions that you make every moment of every day. *How do you live your life?* Do you *maximize* your health potential? What *can* you do to maximize it? The next and final article in this series will offer a range of strategies to do just that; especially those to counter the nature and nurture aspects that increase the risk of mental illness. Through awareness, acceptance, and then action — taking the right steps — we can each optimize our mental health.

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Veterinary leadership: Time for us to step into our own power

Jeff Wilson, Jocelyn Rivers, Michele Anholt, Dauda Onawola, Gabor Lantos, David J. Speicher, Sal De Monte, Hind Kasab-Bachi, Treasure Haines, Sanna Noor, Will Gillam, Erin Suganda, Jeff Aramini

The year 2020 will be forever carved in the minds of mankind as a year that many will label as "annus horribilis." It is the year that COVID-19 was declared a global pandemic (1). As the virus spread, it wreaked havoc on already weakened and fragile social and healthcare systems, in a manner that the modern world was not prepared to address. Yet all is not lost.

The pandemic has created something good from the chaos — the opportunity for the veterinary profession to break away from mainstream stereotypes and traditional roles and to show our contributions to society's well-being. Traditionally, we veterinarians have shied away from our fundamental mission: collaborative leadership in integrative health. It is now time to step up into our own power. We have toyed with the idea for decades while unintentionally portraying ourselves as weak cousins to 'real' medicine.

Having many years of collective experience in epidemiology, outbreak response and relevant subdisciplines, we noticed early in the pandemic that the approach to COVID was seriously off the rails (2). In fact, a few years before that, we began noticing that this was the case for many issues in our profession — including antimicrobial resistance (AMR), Lyme disease, honeybee health — and many others, nationally and globally.

What is the fundamental problem? That's easy — it's a lack of coherent leadership. We live in a profession — and broader world — that is highly siloed. In almost every case, there is no overarching logical and well-organized process to lead and manage the networks to create effective solutions. It is time for a paradigm shift.

Beginning with honeybee sustainability in 2014, we began aligning distributed network partners from academia, business, government, non-governmental organizations (NGOs), and the public at large, for coherent solutions to issues that appear intractable due to the lack of an effective overarching leadership and management framework. What emerged was a process now called Community Network Integration (CNI) (3). It has been described in detail (4). In brief, it consists of a combination of business process and social psychology designed to move distributed networks from a state of perpetual 'swirl' to coherent effective action to create solutions to 'wicked' problems.

Using CNI, we began establishing the required initial leadership teams in 2015 to support development, integration, and rollout of scalable projects to address issues of relevance to Veterinary Medicine across Canada. Much of this involves identifying, supporting, and integrating relevant initiatives already underway across the country — many of them initiated by scientists, professionals, and individual citizens frustrated by the incoherent and disorganized approach from the established institutions.

When COVID emerged in early 2020, it was obvious that there was no coherent leadership (5) or plan to deal with the pandemic locally, nationally, or globally, and that we were about to enter a state of chaos (6). To those of us with experience in outbreak response, it was particularly evident that the fundamental tenets of outbreak management were being systematically violated, with disastrous results.

We began connecting with multiple key players in communities across Canada who immediately began to see the benefit of a collaborative leadership framework to institute outbreak response under established best practices. Those best practices are also well-described (7), and we have simplified them to what we call The Pillars of Outbreak Response:

1. Establish inclusive, transparent, and accountable **leadership teams.**
2. **Validate tests** for infection and disease and social and economic health outcomes and determinants; create a transparent and complete **data framework** with proper **analysis** to drive effective actions.

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3. Institute evidence-based **treatments** (e.g., over-the-counter and generic products) and **preventive** strategies [e.g., air quality remediation, personal protective equipment (PPE), safe and effective vaccines that prevent transmission, etc.].
4. Establish complete, honest, transparent multi-directional **communication** with all required parties, stakeholders, public and politicians.

Some of our initiatives under the Pillars include:

1. Establishing leadership teams at the community level — and within communities of practice, including ones with direct veterinary applications such as food animal health, antimicrobial resistance (AMR), pet wellness, honeybee sustainability, and mental health.
2. Undertaking collaborative action meetings, including a regional consensus conference on effective outbreak response; acquiring initial resources to fund pilot projects.
3. Connecting with local politicians to discuss easy-to-implement improved COVID response strategies, and their role in doing so.
4. Building a multi-partner alliance for evaluation of COVID tests, prospective research on antibody and antigen levels, and amalgamation into a transparent data framework with proper analyses to allow for outbreak management.
5. Evaluating the literature on efficacy of COVID treatments and preventives — and working with partners in Australia to manufacture, in Canada, a safe and effective vaccine that blocks transmission, and undertaking scalable pilot projects for air remediation for viral transmission control.
6. Development and implementation of a comprehensive communications process that is truthful, complete, and that fosters dialogue on all relevant issues for collaborative decision-making on solutions.

What does this mean for those of us in veterinary practice?

Once again, the key is cultivating our own leadership. Leadership can be developed in many ways — don't be fooled by complex and intensive practices. Oftentimes we are required to do more and more; let's take a pause in the businesses of careers and life and create some space and ease. One of the easiest ways to do that is through personal reflection. Here are a few questions to ask yourself to get that started:

- ☐ *What is leadership to me?*
- ☐ *Where have I seen good leadership and bad*
  - ○ *At work?*
  - ○ *In COVID?*
  - ○ *In myself?*
- ☐ *What can I do to improve my own leadership and that of my profession, my community, and my country?*

Spend some time on this — and share it with your friends, family, and colleagues. After personal reflection, the next step in leadership development is generating dialogue. We'll have more on this in subsequent issues of the *CVJ* — including specific things you can do to make a demonstrable difference in your own life.

Guelph-Wellington has been established as the first community in Canada to develop comprehensive, integrated outbreak response according to The Pillars of Outbreak Response. Local politicians have been contacted to open initial dialogue and all have expressed a willingness to work collaboratively. Multiple citizens, businesses, professionals, government officials, NGOs and academics have been engaged and the initial overarching leadership team has been established. Subgroups are beginning intersecting pilot projects to address the elements indicated above. Media and social media have been engaged to spread the word and involve more people in the process. All of this is being done under a validated quality management system known as *The Box*. To our knowledge, this is the first community in Canada (and perhaps globally) to use principles of quality management to manage their affairs through direct citizen participation. We are actively scaling the approach now to communities across Ontario and Canada.

With the establishment of leadership teams in areas like agri-food, pet wellness, and mental health, we are reaching out to map the relevant networks, identify needs and solutions and the resources required to co-fund and enable them.

All this creates a platform in which, together, we can bring about effective solutions, not only for the issues of direct relevance to our profession, but to those of society as a whole — and even for future generations. No need to remain in the shadows any longer — time to step into our own leadership, and our own power.

For more information, check out the Novometrix website at https://www.novometrixinc.com/ and the Canada Collaboration website at https://novometrixr-ccc.com/ There you'll find information on how we're using CNI to create solutions for COVID and other issues, some more detailed information on leadership strategy — and ways to become more involved.

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