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Cruelty to Animals

Dear editor,
This letter is in regard to the ongoing cruelty and abuse that our food-producing animals and birds are undergoing across Canada on a daily basis.

The following are examples of undercover videos showing acts of cruelty and abuse that have been aired over the past 1 to 2 years on CTV.

- Horses — abused while being processed at slaughter houses (no longer slaughtered in Canada);
- Horses shipped in undersized crates overseas to Japan. Many horses cannot lift their heads and end up going down and dying in transport;
- Dairy calves — housed in poor conditions, wooden slatted floors, tied to chains, unable to move around, and not treated when sick;
- Dairy cows — Downer cows prodded with electric prods, dragged across floors and beaten;
- Swine — Sows kept in gestation crates approximately 90% of their lives, not able to walk or turn around. This results in extreme mental cruelty, stress, and greater susceptibility to disease;
- Chickens — In a large commercial enterprise, a video showing chickens being thrown against walls, and having their legs pulled off while alive to entertain the inhumane workers.

Cruelty and abuse can happen at any level of farm production, but it appears that there is a much higher incidence in large commercial operations with large numbers of employees. Small owner-operated farms are likely to have a lower incidence of animal abuse.

I would like to see a law requiring commercial livestock operations to install video cameras to monitor their operation on a 24-hour daily basis. This would allow owners, managers, supervisors to see any abuse or cruelty and take appropriate steps to correct it. The videotapes should also be checked by government inspectors to ensure any abuse or cruelty is dealt with appropriately. This system would replace undercover surveillance, which is difficult to undertake and is spotty, resulting in only a small percentage of abuse cases being identified.

In summary, our food-producing animals and birds are suffering cruelty and abuse across Canada on a daily basis with only a small percentage of cases being identified. A compulsory video system, along with government inspection of recordings, would identify the majority of cases and would also act as a strong deterrent to acts of cruelty, as abusers would risk loss of their jobs and prosecution with fines or a jail term.

If there was support for such a law, how would one go about getting it implemented? Perhaps petitions to the federal government by the Canadian Veterinary Medical Association, Saskatchewan Veterinary Medical Association, Society for the Prevention of Cruelty to Animals, Members of Parliament, at both the federal and provincial levels, veterinarians, and taxpayers might be helpful.

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Northeast Veterinary Services
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Animal Health Surveillance

Dear Editor,
We would like to recognize and thank Dr. Wayne Lees and Mr. Cameron Prince for preparing the special report on “Lessons learned from the evolution of terrestrial animal health surveillance in Canada and options for creating a new collaborative national structure,” found in the May issue of The CVJ (Can Vet J 2017;58:459–465).

The publishing of this report is very timely as the topics of animal health surveillance, how we derive intelligence from raw information, and how we collectively share this information are becoming increasingly important as new and emerging animal health risks and zoonoses are occurring more frequently. Formulating early advice in order to effectively deal with risks is essential in order to protect the public health of Canadians, and to support the animal health status of our country, thereby ultimately benefitting our trade negotiations with international partners.

The Canadian Food Inspection Agency (CFIA) is a strong supporter of the need for this type of collaboration as has been demonstrated by its ongoing support of Canadian Animal Health Surveillance Network (CAHSN) over the past decade. I would like to highlight that CAHSN has had ongoing progress...
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over the years towards data sharing and test development collaboration between animal health laboratories and networks across the country. While the surveillance component has not perhaps progressed to the degree envisioned originally by the federal and provincial partners when the project began over a decade ago, there have been significant accomplishments. CAHSN has an Information Sharing Agreement which is currently signed by 10 of 12 partners, has finalized both the privacy and data security frameworks and has ongoing data collations. Bovine spongiform encephalopathy (BSE) data are collected by automated daily uploads to the central database, as managed by the Canadian Network for Public Health Intelligence, from all 8 laboratories that test for this disease in Canada. Scrapie and Chronic Wasting Disease data are similarly collected. CAHSN has enabled daily uploads of clinical test results from the public sector animal health laboratories in western Canada and is developing and distributing case reports, syndromic surveillance, and other innovative products based upon this data. The combined efforts of CAHSN, the Community for Emerging and Zoonotic Diseases (CEZD) and the Canadian Animal Health Surveillance System (CAHSS) provide Canada with a unique opportunity to further develop this collaborative approach to surveillance and intelligence activities.

These surveillance activities align well with objectives of the Plant and Animal Health Strategy, which is bringing federal, provincial, and territorial governments as well as industry together to guide future collaborative work on plant and animal health. Once again we would like to thank the authors for their article and for their work in developing the systems discussed here.

Dr. Ian Alexander  
Executive Director, Animal Health Science  
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The medical case report
Le rapport de cas médical

The medical case report is a format whose origins have been traced to hundreds of years before records on Egyptian papyrus around 1600 BCE (1). This format remains an important part of the array of methods for education and continuing education of personnel in all medical fields, including veterinary medicine. The case report is popular because it tells a story (and people love to read stories), it provides information in a relevant real-life context, it usually does not require substantial expenditure on the part of the authors, and the time from beginning of the case to preparation of a manuscript may be relatively short. However, the case report format faces a number of challenges, not the least of which is the journal impact factor.

Case reports are generally cited less frequently than research papers. One reason for this is that the case report is viewed as a less reliable type of evidence compared with research studies. In the latter part of the 1900s there was a downgrading of the importance of this type of data as evidence-based approaches began to be emphasized and the case report was placed at the bottom of the evidence hierarchy in which the weight to be attached to knowledge is stratified with the randomized clinical trial at the top of the pyramid (1). The other reason for low frequency of citation is that case reports are often geared toward unusual cases, including rare diseases or rare forms of disease, which are not often the topic of research articles.

Infrequent citations of articles in a journal result in low impact scores that are often translated to mean low quality of the journal. However, the value of the case report cannot be measured by its citation in research publications. As an example, The Journal of Medical Case Reports (BMC) (https://jmedicalcasereports.biomedcentral.com/) has an impact factor of 0.69 — which is low; however, the journal reports that “throughout 2016, articles were accessed from the journal website more than 1.7 million times; an average of over 4600 accesses per day.” Professor Michael Kidd, editor-in-chief of the journal notes that “In the era of evidence-based practice,
we need practice-based evidence … detailed information from the case reports of individual people which informs both our clinical research and our daily clinical care.”

In the veterinary field, Veterinary Record Case Reports (http://veterinarycasereports.bmj.com/pages/authors/) states: “We want to publish cases with clinically valuable lessons… Articles may be about a single animal, herd, flock or other group of animals managed together. Common cases that present a diagnostic, ethical or management challenge, or that highlight aspects of mechanisms of injury, pharmacology or histopathology are deemed of particular educational value. We want to publish cases worthy of discussion particularly around aspects of differential diagnosis, decision-making, management, clinical guidelines and pathology. The advantage is that we learn from real cases… Cases will be judged on clinical interest and educational value NOT novelty or rarity.” This is a departure from the usual requirement for novelty and clearly recognizes the value of the case report as an educational tool not only a mechanism for reporting rarity.

The case report has its limitations. For example, reports of a single case are limited with respect to the conclusions that can be drawn regarding effectiveness of a novel therapy. However, a report of a single case may describe a new disease, a new variation of a well-known disease, an important rare adverse reaction to a drug, unusual drug interactions, or may alert practitioners to new diagnostic and therapeutic approaches. Furthermore, a case series or several independent reports of a particular disease may provide valuable information on diagnosis, case management, and therapy. These studies may point to successful and unsuccessful treatments and may be the basis for designing prospective studies to test hypotheses.

What can be done to improve the effectiveness of the case report as an educational tool? High quality color images can contribute much to the story that is told and should be used whenever they are needed. Because of costs, authors sometimes use black and white images or no images where color images would be more effective. Also, tests that could add to the understanding of the disease are sometimes not done because the client is unable or unwilling to pay. There should be funds in clinical departments to meet the costs of publication and the cost of tests, where such tests are not essential for patient care but could contribute to understanding the disease process.

I close with a quotation from the Dutch medical scientist, J.P. Vandebroucke (2): “Now that medical practitioners all over the world are firmly convinced that ‘evidence’ should guide their actions, is there still a role for the age-old cornerstone of the medical literature, the case report? The answer is an emphatic yes: The case report is as necessary as ever for the progress of medical science and the practice of medicine.”

Carlton Gyles

References


on a accédé aux articles sur le site Web de la revue plus de 1,7 million de fois, soit une moyenne de plus de 4600 accès par jour». Le professeur Michael Kidd, rédacteur en chef de la revue fait remarquer que : «En cette ère de pratique basée sur les preuves, nous avons besoin de preuves basées sur la pratique… des renseignements détaillés provenant de rapports de cas sur des personnes individuelles qui infirment notre recherche clinique et nos soins cliniques quotidiens.»

Dans le domaine vétérinaire, Veterinary Record Case Reports (http://veterinarycasereports.bmj.com/pages/authors/) déclare : «Nous désirons publier des cas présentant des leçons cliniques utiles… Les articles peuvent porter sur un seul animal ou troupeau ou sur un autre groupe d’animaux gérés ensemble. Les cas communs qui présentent des difficultés diagnostiques ou éthiques ou des problèmes de gestion ou qui soulignent les aspects des mécanismes de la blessure, de la pharmacologie ou de l’histopathologie sont jugés d’une valeur éducative particulière. Nous désirons publier des cas qui méritent d’être discutés, particulièrement sur les aspects du diagnostic différentiel, de la prise de décision, de la gestion, des lignes directrices cliniques et de la pathologie. L’avantage est que nous apprenons de cas réels… Les cas seront jugés selon leur intérêt clinique et leur valeur éducative et NON leur nouveauté ou raréité.» Il s’agit d’une nouvelle approche par rapport au critère habituel de nouveauté qui reconnait clairement la valeur du rapport de cas comme un outil éducatif et non seulement comme un mécanisme pour signaler la raréité.

Le rapport de cas possède ses limitations. Par exemple, les rapports sur un seul cas sont limités en ce qui a trait aux conclusions concernant l’efficacité d’une thérapie nouvelle. Cependant, le rapport d’un seul cas peut décrire une nouvelle maladie, une nouvelle variation d’une maladie bien connue, une réaction indésirable rare importante face à un médicament, des interactions inhabituelles de médicaments ou il peut informer les praticiens à l’égard de nouvelles approches diagnostiques et thérapeutiques. De plus, une série de cas ou plusieurs rapports indépendants sur une maladie particulière peuvent fournir de précieux renseignements sur le diagnostic, la gestion des cas et la thérapie. Ces études peuvent signaler le succès et l’échec de traitements et elles peuvent servir de fondement à la conception d’études prospectives pour tester des hypothèses.

Que peut-on faire pour améliorer l’efficacité du rapport de cas en tant qu’outil éducatif? Des images en couleur de haute qualité peuvent apporter une contribution importante à l’histoire racontée et elles devraient être utilisées au besoin. En raison des coûts, les auteurs utilisent parfois des images en noir et blanc là où des images en couleur seraient plus efficaces. De plus, les tests qui pourraient améliorer notre compréhension de la maladie ne sont parfois pas réalisés parce que le client ne peut pas ou ne veut pas payer. Il devrait y avoir des fonds dans les départements cliniques afin de financer les coûts de publication et des tests lorsque ces tests ne sont pas essentiels pour les soins du patient mais pourraient contribuer à la compréhension du processus pathogénique.

Je termine par une citation du scientifique médical hollandais J.P. Vandebroucke (2) : «Maintenant que les praticiens médicaux de toutes les régions du monde sont fermement

References

convaincus que les «preuves» devraient guider leurs actions, y a-t-il toujours une place pour l’éternel pilier de la littérature médicale, le rapport de cas? La réponse est un oui catégorique : Le rapport de cas est toujours aussi nécessaire pour les progrès de la science médicale et de la pratique de la médecine.»

Carlton Gyles

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Todd Donaldson
Ethical question of the month — October 2017

Stockpeople raise livestock with the intention of producing meat, milk, fiber, and a range of other products. When an animal develops a problem such as lameness, producers wrestle with a sense of failure together with the belief that it is wrong to “waste” the animal’s life, i.e., euthanize an animal that has not fulfilled its purpose. The belief that an animal’s life should have a purpose is one reason that less than perfectly fit animals are sometimes transported to slaughter. When such animals appear at abattoirs or sales barns, producers may be accused of trying to extract the last bit of profit from an animal, or that they didn’t recognize that the animal had a problem. The producer on the other hand feels it is wrong that an animal that he or she has cared for over months or years should be killed and disposed of on the farm because it was not perfectly fit to travel.

Is this belief that an animal should fulfill its intended purpose misguided? Is it wrong to “waste” an animal’s life?

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

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

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

Les propositions de questions déontologiques sont toujours bienvenues! Toutes les questions et situations présentées dans cette chronique s’inspirent d’événements réels dont nous modifions certains éléments, comme les noms, les endroits ou les espèces, pour protéger l’anonymat des personnes en cause.
Ethical question of the month — July 2017

In modern livestock farming a variety of metrics are used to measure animal productivity. Many of these production metrics are also considered indicators of animal welfare. Mortality rate is one metric used to judge both production efficiency and animal welfare on the farm. By extension, some use mortality rates during transport to judge the welfare of livestock during transport. Whereas livestock on a farm may die from a wide variety of causes including infectious disease, only fit and healthy animals are transported for sale. Therefore the reasons for transport deaths are seldom the same as the reasons for mortalities in the barn. Is transportation mortality an appropriate indicator for judging the welfare of livestock being transported?

Question de déontologie du mois — Juillet 2017

Dans l’agriculture d’élevage moderne, divers paramètres sont utilisés pour mesurer la productivité de l’animal. Beaucoup de ces paramètres de production sont aussi considérés des indicateurs du bien-être animal. Le taux de mortalité est l’un des paramètres utilisés pour évaluer l’efficacité de la production et le bien-être animal à la ferme. Par extension, certaines personnes utilisent les taux de mortalité durant le transport pour évaluer le bien-être du bétail durant le transport. Tandis que le bétail à la ferme peut mourir en raison d’une diversité de causes, dont les maladies infectieuses, seulement des animaux aptes et en santé sont transportés aux fins de vente. Par conséquent, les causes de décès durant le transport sont rarement les mêmes que celles des mortalités se produisant à la ferme. La mortalité lors du transport représente-t-elle un indicateur approprié pour évaluer le bien-être du bétail qui est transporté?

Is mortality the mark of welfare in transport? — Comments

Animal welfare assessment evaluates quality of life and a humane death. Following death, there are no health or behavioral parameters to measure. Therefore, transport mortality is not an appropriate welfare indicator of transported livestock. Rather, welfare indicators should be animal-based and reflect conditions of the transport environment.

Lindsay Nakonechny, M.Sc, Edmonton, Alberta

There are some very stringent regulations under the Canadian Food Inspection Agency (CFIA) Transport of Animals. Mortality is one of the parameters but probably not more common or important than downers, lameness, fractures, dehydration, stress or injuries from lacerations, bruising or trauma to the skin. Overcrowding is regulated by the animal transported, size, sex, cold or heat stress, type of truck/trailer, and square footage per animal. Time duration of transport without rest, feed, and water is regulated depending on the species of animal. Not only is the transport conveyance regulated, and the humane handling of the animals by personnel, but the loading and unloading facilities must be safe and humane for the type and size of animal.

The CFIA regulations are much more extensive and detailed than presented here. Don’t be misled to think that mortality is the only parameter in the animal welfare of transported animals, as your Ethical Question implies. There are severe penalties for the trucker, producer, or handlers for not following Best Management Practices for transport of animals.

Don Church, DVM, Red Deer, Alberta, dchurch@platinum.ca

An ethicist’s commentary on is mortality the mark of welfare in transport?

There is no question that if an animal dies as a result of transport, one can confidently assert that during the period of transport, it did not enjoy good welfare. In other words, not dying is a necessary condition for an attribution of good welfare. But in the same sense, so are the presence of oxygen, a temperature above absolute zero, and myriad other factors.

Asserting that if an animal did not die during transport, it enjoyed good welfare is absurd. In the bad old days when farmers, particularly dairy farmers, used to routinely ship downer cows to slaughter so as to realize some minimal profit from these miserable animals, no one with an ounce of common sense would have affirmed that those animals were well off, since the animals were often sick or seriously injured. Indeed, on some occasions, they arrived at the slaughterhouse with broken legs, unable to walk.

I have been told that horses are crated and shipped by air to Japan to be killed for food. Again, it is beyond disingenuous to suggest that if they arrive alive, they enjoyed good welfare during the trip. When cattle are crowded into double-decker trucks that are poorly ventilated and horrendously hot, and the ride is hellishly uncomfortable, it is absurd to suggest that these animals are well off if they do not die.

My son was and is an extremely tough guy. When he was four years old, he crashed a bicycle and broke his arm. He never cried. When we rushed him to the doctor, the pediatrician concluded that the arm could not be broken because the child was not crying. In fact, I only remember him crying twice when he was a small child. On one occasion, we stopped at a railroad crossing right next to a cattle truck. After peering at the truck, he began to cry silently and profoundly. I was very upset and
asked him what was wrong. He replied, “Those poor cows. It is very hot outside and even hotter in that two-level truck. And the ones on the top level are peeing and pooping on the others. That is wrong!”

To assume that animals are well-off in transport because they arrive at a destination not dead, but possibly weak, sick, sore, or dehydrated is a fantasy. On other occasions in this column, we have discussed the amount of time the animals are legally permitted in a truck without being fed and watered or off-loaded. To use an odious human analogy, one might as well affirm that people crammed into cattle cars in Nazi Germany for transport to a concentration camp were well-off when they arrived alive.

We have repeatedly stressed in this column that animal welfare is an extremely complex and value-laden notion, predicated on ethical positions articulating what we owe animals. Defining welfare by reference to a simple and patently observable single criterion makes a mockery of the concept. The Farm Animal Welfare Council in Britain was spot on when it affirmed that:

“The welfare of an animal includes its physical and mental state and we consider that good animal welfare implies both fitness and a sense of well-being. Any animal kept by man, must at least be protected from unnecessary suffering.”

Shame on anyone who dares to affirm that an animal enjoys good welfare if it is not dead! In fact, a thorough overhaul of all aspects of animal transportation from stress-promoting loading to heat and poor ventilation is long overdue.

Bernard E. Rollin, PhD
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1. Cavalier King Charles spaniels are predisposed to which of the following heart diseases?
   A. Dilated cardiomyopathy
   B. Subaortic stenosis
   C. Mitral valve endocardiosis
   D. Hypertrophic cardiomyopathy
   E. Chemodectoma

2. Which of the following is most correct concerning uroabdomen (uroperitoneum)?
   A. The measurement of abdominal fluid BUN is the definitive biochemical test for confirming the diagnosis.
   B. The measurement of abdominal fluid creatinine is the definitive biochemical test for confirming the diagnosis.
   C. The measurement of abdominal fluid sodium and potassium are the definitive biochemical tests for confirming the diagnosis.
   D. The observation of urination excludes the diagnosis of uroperitoneum.
   E. The retrieval of urine after the passage of a urinary catheter excludes the diagnosis of uroperitoneum.

3. Which of the following immunosuppressive drugs should NOT be administered to cats?
   A. Cyclosporine
   B. Prednisolone
   C. Chlorambucil
   D. Azathioprine
   E. Gold salts

4. An Egyptian Arabian foal is displaying neurologic signs at birth. Examination reveals tetany, paddling, and a dilute coat color. Which of the following is the most likely diagnosis for this foal?
   A. Hypopigmentation
   B. Albinism
   C. Lethal white foal syndrome
   D. Lethal lavender foal syndrome
   E. Vitiligo

1. Les Épagneuls cavalier King Charles sont prédisposés à laquelle des maladies cardiaques suivantes?
   A. cardiomyopathie dilatée;
   B. sténose subaortique;
   C. endocardiose de la valve mitrale;
   D. cardiomyopathie hypertrophique;
   E. chémodectome.

2. Lequel des énoncés suivants est le plus juste à propos de l’uroabdomen (uropéritoine)?
   A. La mesure du BUN du liquide abdominal est le test biochimique de référence pour confirmer le diagnostic.
   B. La mesure de la créatinine du liquide abdominal est le test biochimique de référence pour confirmer le diagnostic.
   C. La mesure du sodium et du potassium du liquide abdominal est le test biochimique de référence pour confirmer le diagnostic.
   D. La présence de miction exclut un diagnostic d’uropéritoine.
   E. La récupération de l’urine à la suite du passage d’un cathéter urinaire exclut un diagnostic d’uropéritoine.

3. Lequel des médicaments immunosuppresseurs suivants ne doit pas être administré aux chats?
   A. cyclosporine;
   B. prednisolone;
   C. chlorambucil;
   D. azathioprine;
   E. sels d’or.

4. Un poulain Égyptien de type arabe montre des signes neurologiques à la naissance. L’examen révèle de la tétanie, du pédalage et un pelage de couleur diluée. Lequel des diagnostics suivants est le plus probable?
   A. hypopigmentation;
   B. albinisme;
   C. syndrome létal du poulain blanc;
   D. syndrome létal du poulain lavande;
   E. vitiligo.
5. Which of the following options LEAST warrants investigation in an outbreak of papillomatous digital dermatitis in cattle?
A. Foot bath size
B. Alley scraping
C. Concrete age
D. Copper sulfate invoices
E. Stock invoices

(See p. 1122 for answers./Voir les réponses à la page 1122.)

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

Have Another Look at CJVR
Avez-vous consulté la RCRV dernièrement?

Members of the CVMA are entitled to receive the Canadian Journal of Veterinary Research (CJVR) at no additional charge. The CJVR, in the form of an interactive (portable document format) pdf, can be found on the CVMA member-only website (www.canadianveterinarians.net/publications-research-issue.aspx).

Published by the CVMA, this quarterly, peer-reviewed journal is Canada’s only national veterinary research publication.

Articles from the July 2017 issue of CJVR that might be of interest to practitioners include:

Direct repeat unit (dru) typing and antimicrobial resistance of methicillin-resistant Staphylococcus pseudintermedius isolated from dogs in Atlantic Canada on page 192

The impact of carboplatin and toceranib phosphate on serum vascular endothelial growth factor (VEGF) and metalloproteinase-9 (MMP-9) levels and survival in canine osteosarcoma on page 199

The CJVR, along with the monthly Canadian Veterinary Journal, is also archived on PubMed Central (www.pubmedcentral.com) 6 months after publication.

An interactive pdf of The CVJ is also available on the member-only section of the CVMA website.


Publiée par l’ACMV, cette revue trimestrielle évaluée par les pairs est la seule publication nationale de recherche vétérinaire au Canada.

Les articles suivants du numéro de juillet 2017 de la RCRV pourraient intéresser les praticiens :

Direct repeat unit (dru) typing and antimicrobial resistance of methicillin-resistant Staphylococcus pseudintermedius isolated from dogs in Atlantic Canada à la page 192

The impact of carboplatin and toceranib phosphate on serum vascular endothelial growth factor (VEGF) and metalloproteinase-9 (MMP-9) levels and survival in canine osteosarcoma à la page 199

La RCRV, avec La Revue vétérinaire canadienne qui est publiée mensuellement, est aussi archivée sur PubMed Central (www.pubmedcentral.com) six mois après la publication.

Un pdf interactif de La RVC est aussi disponible dans la section réservée aux membres du site Web de l’ACMV.
2017 CVMA Convention and Council Meeting

The Canadian Veterinary Medical Association (CVMA) held its 69th Annual Convention July 13th to 16th in Charlottetown, PEI. The program provided 105 concurrent sessions delivered by 42 speakers for the almost 1000 participants. Once again, the Program was RACE (Registry of Approved Continuing Education) approved.

The 2017 CVMA Convention enjoyed the valued partnership of the Registered Veterinary Technicians and Technologists of Canada (RVTTC) and the Atlantic Veterinary College (AVC).

CVMA Convention – Where Canada's veterinarians meet

In addition to continuing education (CE), the CVMA Convention provides an annual forum for discussion and meetings of veterinarians from across the country.

The CVMA Summit, chaired by Dr. Troye McPherson, featured the theme of “The Future of Veterinary Medicine: Embracing Change and Innovation,” followed by the National Issues Forum, moderated by Dr. Art Ortenburger under the

Congrès de l’ACMV et réunion du Conseil de l’ACMV 2017

L’Association canadienne des médecins vétérinaires (ACMV) a tenu son 69e congrès annuel du 13 au 16 juillet à Charlottetown, à l’Île-du-Prince-Édouard. Le programme comportait 105 ateliers parallèles présentés par 42 conférenciers pour les plus de 1000 participants. De nouveau, le programme était approuvé par RACE (Registry of Approved Continuing Education).

Le congrès 2017 de l’ACMV a profité du précieux partenariat de Technologues et techniciens vétérinaires agréés du Canada (TTVAC) et de l’Atlantic Veterinary College (AVC).

Le congrès de l’ACMV – Le lieu de rencontre des vétérinaires du Canada

En plus de la formation continue, le congrès de l’ACMV sert de forum annuel pour les discussions et les réunions des vétérinaires provenant de toutes les régions du pays.

Le Sommet de l’ACMV, qui a été présidé par la Dʳ Troye McPherson, présentait le thème «L’avenir de la médecine vétérinaire : Adopter les changements et l’innovation», suivi du Forum sur les enjeux nationaux, qui a été modéré par le

Les personnes ci-dessus sont assises en face du quai de Charlottetown où était accosté le grand voilier de la marine chilienne, l’Esmeralda.
theme “Is Alternative Medicine no Longer Alternative.” The lat-
ter presentations and plenary discussions will assist the CVMA
in its endeavor to renew its current position. Both initiatives,
together with further research, are meant to help explore the
“Uber” of veterinary medicine and how the CVMA can assist
its members with changes to come in the profession.

The annual CVMA Emerging Leaders Program allowed
37 individuals to participate in this highly interactive 8-hour
workshop facilitated by Dr. Rick DeBowes. Attendees sharpened
their skills and knowledge on how to manage various challenges
encountered in professional and personal life. This program is
graciously supported by VIROX Animal Health.

Approximately 260 individuals attended the Annual General
Meeting. Canada’s Minister of Health, the Honorable Jane
Philpott, sent a message to CVMA members. Excerpts of her
address include: “I want to commend the CVMA for the work
you are doing to tackle AMR. Your recent work on updating
guidelines for the prudent use of veterinary antimicrobial medi-
cations and developing a national veterinary prescription-based
antimicrobial use surveillance program are examples of our
shared commitment to reducing the burden of AMR.” “The
action that the CVMA is taking shows that you understand
the complex challenges of AMR. The Government of Canada
looks forward to continuing to work with our partners, such as
the CVMA, to find innovative solutions to this global health
problem.” The Mayor of Charlottetown, Mr. Clifford Lee,
also extended greetings to the CVMA members assembled.
International guests attending the AGM included: Dr. René
Carlson, president of the World Veterinary Association;
Dr. Walter Ingwersen, president of the World Small Veterinary
Animal Association; Dr. Rafael Laguens, president of the
Federation of Veterinarians of Europe; Dr. Tom Meyer, president

D’ Art Ortenburger sous la rubrique «La médecine parallèle
est-elle toujours parallèle?». Ces présentations et les discussions
plénières aideront l’ACMV à tenter d’améliorer sa position actuelle.
Les deux initiatives, conjointement à de nouvelles recherches,
visent à explorer l’“Uber” de la médecine vétérinaire et comment
l’ACMV peut appuyer ses membres à l’égard des changements à
venir dans la profession.

L’édition annuelle du Programme des futurs leaders de
l’ACMV a permis à 37 personnes de participer à un atelier
hautement interactif d’une durée de huit heures qui a été animé
par le D’ Rick DeBowes. Les participants ont perfectionné
leurs compétences et leurs connaissances en vue de gérer les
divers défis qui doivent être relevés dans la vie professionnelle
et personnelle. Ce programme est généreusement appuyé par
VIROX Animal Health.

Environ 260 personnes ont assisté à l’Assemblée générale
annuelle. La ministre de la Santé du Canada, l’honorable Jane
Philpott, a envoyé un message aux membres de l’ACMV. Voici
un extrait de son message : «Je désire féliciter l’ACMV pour
le travail que vous réalisez afin d’aborder la résistance aux
antimicrobiens. Votre travail récent en vue de mettre à jour les
lignes directrices sur l’administration judicieuse des antimicrobiens
vétérinaires et de créer un programme national de surveillance
de l’utilisation des antimicrobiens représentent des exemples
de notre engagement commun afin de réduire le fardeau de la
résistance aux antimicrobiens. Les mesures prises par l’ACMV
montrent que vous comprenez les défis complexes de l’utilisation
des antimicrobiens. Le gouvernement du Canada se réjouit à
l’avance de poursuivre le travail avec nos partenaires, comme
l’ACMV, afin de trouver des solutions innovatrices à ce problème
de santé mondial.» Le maire de Charlottetown, M. Clifford Lee,
aussi souhaité la bienvenue aux membres de l’ACMV réunis lors

Following the Chain of Office and Pinning Ceremony: Dr. Troy Bourque, CVMA out-going
President, Dr. Troye McPherson, CVMA in-coming President

Après la cérémonie de la remise de la chaîne de fonction et de l’épingle : D’ Troy Bourque,
président sortant de l’ACMV. D’troye McPherson, présidente désignée de l’ACMV
of the American Veterinary Medical Association; and Dr. Robert Johnson, president of the Australian Veterinary Association.

The new president and Executive of the CVMA were introduced: Dr. Troye McPherson, president; Dr. Terri Chotowetz, president-elect; Dr. Melanie Hicks, vice-president; Dr. Enid Stiles, executive member; Dr. Troy Bourque, immediate past-president; Dr. Barry Stemshorn, treasurer; and Mr. Jost am Rhyn, chief executive officer. The CVMA would like to extend sincere thanks to Dr. Nicole Gallant for her leadership and dedication through many years to the CVMA’s governing bodies as a Council member, Executive member, president, and immediate past-president.

A number of veterinary professionals were honored at the Annual Awards Ceremony held during the Convention:

• Small Animal Practitioner Award: Dr. David Condon (PEI), for his compassion towards the animals in his care and his dedication to the student veterinarians he mentors and supervises.

• Merck Veterinary Award: Dr. Stephen LeBlanc (ON), for his production of high quality applied clinical research in the diagnosis and control of metabolic, inflammatory, and reproductive diseases of dairy cattle.

• CVMA Humane Award: Dr. Anne McDonald (BC), for her role in the removing of, caring for, and re-homing of almost 600 parrots from the World Parrot Refuge on Vancouver Island.

• CVMA Practice of the Year Award: Mona Campbell Centre for Animal Cancer (ON), for creating a comprehensive veterinary cancer centre serving central Canada and beyond, while offering unique clinical trial research opportunities, facilitated by the University of Guelph’s Institute for Comparative Cancer Investigation.

• CVMA Life Membership: Dr. Jeanne Lofstedt (PEI), for her significant contributions to the veterinary profession worldwide.

• CVMA President’s Award: Dr. Bob Bellamy (SK), for his innovative approach to veterinary medicine communication and his dedication to the profession.

The president of the Students of the CVMA, Ms. Elizabeth Hartnett, was recognized for her work in promoting student interests in the Association. The Registered Veterinary Technologists and Technicians of Canada (RVTTCC) also joined the Awards Ceremony to present one of its members, Ms. Elise Wickett, with the 2017 Canadian Registered Veterinary Technologists/Technicians of the Year Award. Finally, Veterinarians without Borders presented its Canada Volunteer of the Year Award to Dr. Joseph Ansong-Danquah.

Numerous business meetings and collegial and social events took place during the Convention such as the Presidents’ Meeting (regulatory body, self-interest, species and specialties associations presidents), the Provincial Forum (registrars/executive directors, communications directors), the Canadian Council of Veterinary Registrars (CCVR), deans; the CVMA Past-Presidents’ Forum Luncheon meeting, and OVC and AVC alumni receptions.

Thank you to the Professional Development Committee, its chair, Dr. Natalie Reid; the 2017 local chair, Dr. Kathleen du congrès. Les invités internationaux présents incluaient notamment : Drs René Carlson, présidente de l’Association mondiale vétérinaire; Dr Walter Ingwersen, président de la World Small Animal Veterinary Association; Dr Rafael Laguens, président de la Fédération des vétérinaires d’Europe; Dr Tom Meyer, président de l’American Veterinary Medical Association; et Dr Robert Johnson, président de l’Australian Veterinary Association.

La nouvelle présidente et le nouvel exécutif de l’ACVM ont été présentés : Dr. Troye McPherson, présidente; Dr. Terri Chotowetz, présidente désignée; Dr. Melanie Hicks, vice-présidente; Dr. Enid Stiles, membre de l’exécutif; Dr. Troy Bourque, président sortant; Dr. Barry Stemshorn, trésorier; et M. Jost am Rhyn, président-directeur général. L’ACVM aimerait sincèrement remercier la Dr Nicole Gallant de son leadership et dévouement pendant de nombreuses années passées au sein des instances dirigeantes de l’ACVM en tant que membre du Conseil, membre de l’exécutif, présidente et présidente sortante.

Plusieurs professionnels vétérinaires ont été honorés lors de la Cérémonie annuelle de remise des prix qui s’est déroulée durant le congrès :

• Prix du praticien des petits animaux : Dr. David Condon (L.-P.-É.), pour sa compassion envers les animaux confiés à ses soins et son dévouement envers les étudiants en médecine vétérinaire qu’il supervise et appuie en tant que mentor.

• Prix vétérinaire Merck : Dr. Stephen LeBlanc (Ontario), pour sa production de recherche clinique appliquée de grande qualité pour le diagnostic et le contrôle des maladies métaboliques, inflammatoires et reproductrices des bovins laitiers.

• Prix humanitaire de l’ACVM : Dr. Anne McDonald (C.-B.), pour son rôle dans le retrait, les soins et l’adoption de près de 600 perroquets du World Parrot Refuge dans l’île de Vancouver.

• Prix de la pratique de l’année de l’ACVM : Mona Campbell Centre for Animal Cancer (Ontario), pour la création d’un centre vétérinaire complet pour le traitement du cancer desservant le centre du Canada et d’autres régions, tout en offrant des occasions uniques pour la recherche et les essais cliniques, facilitées par l’Institute for Comparative Cancer Investigation de l’Université de Guelph.

• Titre de membre à vie de l’ACVM : Dr. Jeanne Lofstedt (L.-P.-É.), pour ses contributions importantes à la profession vétérinaire à l’échelle mondiale.

• Prix du président de l’ACVM : Dr. Bob Bellamy (Saskatchewan), pour son approche innovatrice face à la communication en médecine vétérinaire et son dévouement envers la profession.

La présidente des Étudiants de l’ACVM, Mme Elizabeth Hartnett, a été reconnue pour son travail en vue de promouvoir l’intérêt des étudiants envers l’Association. L’organisme Technologues et techniciens vétérinaires agréés du Canada (TTVAC) a aussi participé à la Cérémonie de remise des prix afin de présenter à l’une de ses membres, Mme Elise Wickett, le Prix du technologue/technicien vétérinaire agréé 2017 pour le Canada. Enfin, Vétérinaires sans frontières a présenté son Prix du bénévole canadien de l’année au Dr Joseph Ansong-Danquah.

Plusieurs réunions d’affaires, réunions d’anciens et activités sociales se sont déroulées durant le congrès, comme la Réunion des présidentes (présidentes des organismes de réglementation, des groupes d’intérêt, des groupes d’espèces et des associations de...
MacMillan; Dr. Jeanne Lofstedt (CE Coordinator); the numerous volunteers and CVMA staff, both onsite and in the office, who made this Convention and the many corporate meetings happen. Thank you to all participants, exhibitors, and sponsors for choosing to be part of the 2017 CVMA Convention.

Strategic Planning: Under the theme “A Successful Career, a Balanced Life,” the CVMA has developed and delivered a number of member programs over the years, including its Business Management Program with the Suggested Provincial Fee Guides, a Mentorship Program, an Emerging Leaders Program, Member Wellness web content, Continuing Education and more. As a whole, career success and life balance is increasingly important as is the need for providing service. In this regard, Council has approved a Strategic Plan, developed during the March meeting, with input from about 140 selected veterinarians. The CVMA’s goal is to foster the personal and professional well-being of its members. Some examples of the strategic actions are to provide pertinent wellness resources; establish and promote mentorship services; promote and adapt Emerging Leaders Program; maintain and adapt career and financial tools; and provide pertinent practice management tools.

Antimicrobial Resistance (AMR): As part of the Government of Canada’s Federal Action Plan on Antimicrobial Resistance and Use, the final version of the Regulations Amending the Food and Drug Regulations (Veterinary Drugs — Antimicrobial Resistance) was published in the Canada Gazette, Part II. The new rules come into force between November 2017 and July 2019. Regulatory changes include 1) Increased oversight on importation of veterinary drugs (OUI) and APIs; 2) The facilitation of access to low-risk veterinary health products as additional tools for the maintenance of animal health and welfare; and 3) Mandatory reporting of sales volume from manufacturers and importers to support antimicrobial use surveillance. Policy changes include 1) Removing growth promotion claims from pre-2004 approved medically important antimicrobials (MIAs); and 2) Increasing veterinary oversight over all MIAs (pre-2004 approved).

• In conjunction with the CCVR and with broad stakeholder input, the CVMA developed the “Veterinary Oversight of Antimicrobial Use-Professional Standards for Veterinarians,” which serves veterinary regulatory bodies as a template for developing their own regulations addressing the upcoming policy and regulatory changes.

• On behalf of the Veterinary Pharmaceutical Stewardship Advisory Group (VPSAG), Dr. Duane Landals is developing preliminary guidelines for veterinary care of bees and will present this to the CCVR.

• With funding from Agriculture and Agri-Food Canada, the CVMA held its first workshop, chaired by Dr. Phil Buote, with approximately 40 stakeholders, to initiate the renewal of CVMA’s Antimicrobial Prudent Use Guidelines. The purpose of this project is to develop ready-for-delivery, practical tools to assist veterinarians in the prudent use of antimicrobials for 6 defined species groups (including food and companion animals). The purpose of the workshop was to engage stakeholders and obtain input into defining the pertinent guidelines, which serve as a template for developing their own regulations addressing the upcoming policy and regulatory changes.

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needs for future tools to assist veterinarians in the prudent use of antimicrobials. New Prudent Use Guidelines are scheduled to be available by April 2018.

- With funding from the CFIA, the CVMA initiated an Antimicrobial Use (AMU) Surveillance project for large and small animals and, in March, hosted a workshop chaired by Dr. Duane Landals including approximately 40 stakeholders. Directed by CFIA needs, the object of this workshop was to build buy-in from stakeholders and identify the most relevant type and level of data that should be collected as part of a prescription-based AMU surveillance program in support of Canadian commitments to the World Organisation for Animal Health (OIE) and the international community. Some of the outcomes included in a comprehensive report identified different means and needs for surveillance in different species groups. Questions also arose on the subject of data collection at the prescription versus dispensing level and whether different approaches should be chosen for different species groups. The CVMA is in discussions with the CFIA on a 2-year follow-up project to, first, put this AMU surveillance project into context with AM Stewardship and educate stakeholders on the need for this activity, and second, develop a surveillance concept that includes a dataset and options for the actual data-gathering.

- All veterinarians will be kept abreast of a communications campaign for the implementation of new regulations and policies that will be developed by the CVMA in conjunction with Veterinary Drugs Directorate (VDD).

- Since March, the CVMA has engaged in meetings on antimicrobial resistance and the implementation of the new regulations and policies with VDD, the Canadian Animal Health Products Regulatory Advisory Committee (CAHPRAC), and the new CAHPRAC Communications Sub-committee, Antimicrobial Stewardship Canada (AMS is a working group of approximately 25 human health NGOs) and as part of the Canadian Global Food Animal Residue Avoidance Databank (CgFarad) Advisory Board.

Engagement of early career DVMs: Helping early career DVMs is one of the CVMAs focal points. Some of the programs and resources being worked on include: raising awareness of the existing CVMA mentorship guidelines and mentor roster; adding resources to the early career DVM online Resource Hub; constantly adding online Wellness Resources; sharing of early career experience through The CVJ articles on “What Can’t Be Taught;” implementation of reduced recent graduates membership dues (complimentary membership during year of graduation; 75% reduction during year 1 after graduation, 50% reduction during year 2; 25% reduction during year 3).

Student Leadership Workshop: The second annual SCVMA Student Leadership Workshop (SLW) will be held at the Ontario Veterinary College (OVC) on November 18, 2017. This Workshop is designed to complement the CVMA’s Emerging Leaders program. Future rotations for the SLW are foreseen for 2019 at WCVM; 2020 at UCVM; 2021 at AVC; and 2022 at FMV.

Animal Health Technology/Veterinary Technician Program Accreditation: Council approved accreditation of the Ridgetown
Veterinary Technology program and the Vanier College Animal Health Technology Program.

**Housing systems for laying hens:** Council agreed to the Animal Welfare Committee’s proposal to draft a position statement on housing systems for laying hens.

**Humane Transportation:** On April 4, the CVMA appeared before the House of Commons Standing Committee on Agriculture and Agri-Food regarding the Amendment to the Health of Animals Regulations (Humane Transportation). As a follow-up, the CVMA was invited to a more informal meeting with the Liberal caucus working group on animal welfare, chaired by Alexandra Mendes, MP (Brossard-Saint-Lambert, QC). We plan to interact with this Liberal caucus working group more frequently to identify their needs and have them consider which of the CVMA’s animal welfare positions may be pertinent to them as legislators.

**Kennel Code:** The newest edition of the CVMA’s Kennel Code has been circulated among stakeholders for feedback and is scheduled to be presented for approval to Council in November 2017. In order to be aligned more closely with the National Farm Animal Care Council (NFACC) Codes of Practice, this Code varies greatly from the previous one. The Code is designed to assist breeders and kennel operators and to serve as a resource for the public, including prospective dog owners.

**Vaccination:** CVMA Council approved the joint position statement with the American Veterinary Medical Association and the Federation of Veterinarians of Europe on the benefits of animal vaccination programs in advancing animal and human health (see https://www.canadianveterinarians.net/policy-advocacy/international-relations). The 3 organizations intend to use this new position statement to advocate for federal and regional support for vaccine development and distribution and as a resource to educate the animal-owning public and other audiences on the benefits of animal vaccination programs as a means to counter anti-vaccination arguments. At the World Veterinary Association (WVA) General Assembly 2017, the 3 organizations will propose that the WVA develop a similar statement that would address this issue from a global perspective.

**OIE:** In March, the OIE’s site visit team evaluated Canada’s performance of veterinary services (PVS). The CVMA took part in the preparation of the PVS evaluation that was led by the CFIA and made a presentation to the site visit team on its involvement in the national exams, vet college accreditations, antibiotic resistance, and more.

In May, the CVMA president, Dr. Troy Bourque, attended the OIE General Assembly as part of the Federal Government’s delegation led by Canada’s Chief Veterinary Officer, Dr. Harpreet Kochhar.

**WSAVA:** The CVMA continues supporting the WSAVA campaign on the use of Ketamine and provided an update on the subject in its June e-newsletter. The CVMA continues its work in the planning of the WSAVA-CVMA joint Conference in Toronto in 2019.

**FVE-AVMA-CVMA:** As a member of this collaborative group, the CVMA currently provides input into joint statements on “Responsible and Judicious Use of Antimicrobials,” humaine) and dans le cadre du Conseil consultatif de la Canadian Global Food Animal Residue Avoidance Databank (CgFarad).

**Engagement des vétérinaires en début de carrière:** L’appui des vétérinaires en début de carrière est l’un des objectifs de l’ACMV. Voici quelques-uns des programmes et des ressources en voie de réalisation: rehausser la sensibilisation à l’égard des lignes directrices de mentorat actuelles de l’ACMV et de la liste de mentors; ajouter des ressources au Carrefour des ressources en ligne pour les vétérinaires en début de carrière; continuer d’ajouter à la page Web sur les ressources de bien-être; partager de l’expérience de début de carrière par l’entremise des articles de La RVC sur «Ce qui ne s’enseigne pas»; et instaurer des cotisations réduites pour les diplômés récents (cotisation gratuite durant l’année d’obtention du diplôme; réduction de 75 % durant la première année après l’obtention du diplôme, réduction de 50 % durant la deuxième année après l’obtention du diplôme; réduction de 25 % durant la troisième année après l’obtention du diplôme).

**Atelier de leadership étudiant:** La deuxième édition annuelle de l’Atelier de leadership étudiant (ALE) des ÉACMV se tiendra le 18 novembre 2017 à l’Ontario Veterinary College (OVC). Cet atelier est conçu afin de servir de complément au Programme des futurs leaders de l’ACMV. Les rotations futures de l’ALE sont prévues au WCVM en 2019; à l’UCVM en 2020; à l’AVC en 2021; et à la FMV en 2022.

**Agrément des programmes de technologie en santé animale et de techniques vétérinaires:** Le Conseil a approuvé l’agrément du Programme de technologie vétérinaire du Ridgetown Campus et le Programme de technologie en santé animale de Vanier College.

**Système de logement pour les poules pondesuses:** Le Conseil a accepté la proposition du Comité sur le bien-être animal de rédiger un énoncé de position sur les systèmes de logement pour les poules pondesuses.

**Transport sans cruauté:** Le 4 avril, l’ACMV a comparu devant le Comité permanent de la Chambre des communes sur l’agriculture et l’agroalimentaire concernant la modification du Règlement modifiant le Règlement sur la santé des animaux (transport sans cruauté). Comme suivi, l’ACMV a été invitée à une réunion plus informelle avec le groupe de travail du caucuses libéral sur le bien-être animal qui est présidé par Alexandra Mendes, députée fédérale (Brossard-Saint-Lambert, QC). Nous planifions une interaction plus fréquente avec ce groupe de travail du caucuses libéral afin d’identifier ses besoins et de l’interroger sur les énoncés de position de l’ACMV sur le bien-être animal qui pourraient être pertinents pour les membres en tant que législateurs.

**Code de pratiques recommandées aux chiens:** La plus récente édition du Code de pratiques recommandées aux chiens du Canada de l’ACMV a été distribuée aux intervenants aux fins de rétroaction et on prévoit qu’elle sera présentée pour approbation au Conseil en novembre 2017. Afin de s’aligner plus étroitement sur les Codes de pratiques du Conseil national pour les soins aux animaux d’élevage (CNSEA), ce code présente des modifications importantes par rapport à la version antérieure. Ce code est conçu afin d’assister les éleveurs et les exploitants de chiens et de servir de ressource pour le public, y compris les futurs propriétaires de chiens.
CVMA declared March as National Tick Awareness Month. The second year. In partnership with Merck Animal Health, the campaign is in its third year and targets public audiences on Facebook and Twitter. The National Tick Awareness campaign is in its second year for pick-up at the clinic at certain intervals. whereby the food will be delivered either at home or available for pick-up at the clinic at certain intervals.

Business Management: Annually, the CVMA, in collaboration with provincial veterinary medical associations, conducts a practice owners’ economic survey. The purpose of the survey is to gather data on revenue, expenses, income, number of current and new clients, fees, and DVM and non-DVM staff compensation. In addition to the CVMA’s investment, this survey is graciously supported by IDEXX Laboratories, Petsecure, Merck Animal Health, and Scotiabank. The 2016 report on the CVMA national Practice Owner survey can be found on www.canadianveterinarians.net/practice-economics/reports

The overall 2016 findings were that, on average, it was a good year for veterinarians in Canada. Net incomes were climbing for both small animal and mixed/large animal hospitals. Companion animal hospitals leaned on increasing revenues to outweigh climbing expenses, allowing net income to increase. The growth in revenue was likely partially driven by a return of current and new clients. In contrast, mixed and large animal hospitals employed prudent cost cutting measures to trim expenses in the face of declining revenues in order to grow net income.

WebStore: The CVMA WebStore provides member veterinarians with an easy to use online presence. A new initiative aims at improving compliance with diets using a subscription model, whereby the food will be delivered either at home or available for pick-up at the clinic at certain intervals.

Communications: The 2017 Animal Health Week is scheduled for October 1–7. The theme is “Animal Welfare: Safeguarding the Five Animal Freedoms.” The monthly #VetCareEverywhere Social Media Awareness Campaign is in its third year and targets public audiences on Facebook and Twitter. The National Tick Awareness campaign is in its second year. In partnership with Merck Animal Health, the CVMA declared March as National Tick Awareness Month. The 2017 National Tick Awareness materials included a webinar, Tick Talk poster, social media messages, and waiting and examination room posters. The CVMA deployed a Forward Booking Campaign. Forward booking simply means scheduling next appointments for patients during their current visit, before they leave the practice. The goals of forward booking are to advance patient care and strengthen the health of veterinary practice.

Canadian Veterinary Reserve: Through a recruitment campaign, we added 70 reservists, bringing the total to 288 reservists (minimum target number is 200). In late March, the CVR

Vaccination: Le Conseil de l’ACMV a approuvé un énoncé de position conjoint avec l’American Veterinary Medical Association et la Fédération des vétérinaires d’Europe sur les bienfaits des programmes de vaccination des animaux pour l’avancement de la santé animale et humaine (voir https://www.veterinairesaucanada.net/policy-advocacy/international-relations). Les trois organisations ont l’intention d’utiliser ce nouvel énoncé de position pour exercer des pressions en vue d’obtenir un soutien fédéral et régional pour le développement et la distribution de vaccins et en tant que ressource d’éducation pour le public propriétaire d’animaux et d’autres publics à l’égard des bienfaits des programmes de vaccination animale comme contrepoints aux arguments anti-vaccination. À l’Assemblée générale 2017 de l’Association mondiale vétérinaire (AMV), les trois organisations proposeront que l’AMV élaboré un énoncé semblable qui aborderait cette question d’un point de vue international.

OIE: En mars, l’équipe d’inspection de l’OIE a évalué la performance des services vétérinaires du Canada. L’ACMV a participé à la préparation de cette évaluation qui a été dirigée par l’ACIA et elle a fait une présentation devant l’équipe d’inspection sur sa participation aux examens nationaux, l’antibiotoxine et plus encore.

En mai, le président de l’ACMV, le Dr Troy Bourque, a assisté à l’Assemblée générale de l’OIE en tant que membre de la délégation du gouvernement fédéral dirigée par le vétérinaire en chef du Canada, le Dr Harpreet Kochhar.

WSAVA: L’ACMV continue d’appuyer la campagne de la WSAVA sur l’utilisation de la kétamine et elle a fourni une mise à jour sur ce sujet dans son cyberbulletin de juin. L’ACMV poursuit son travail pour la planification de la Conférence conjointe de la WSAVA-ACMV à Toronto en 2019.


Gestion commerciale: L’ACMV, en collaboration avec les associations provinciales de médecins vétérinaires, réalise un sondage économique annuel auprès des propriétaires de pratique. Le but de ce sondage consiste à recueillir des données sur les...
conducted its annual call-up drill, this time as a multi-wave and multi-scenario exercise. This call-up involved the CFIA and Emergency Management BC as first responders.

**Veterinary services for Indigenous communities:** The CVMA discussed the issue of availability of veterinary services, animal health, welfare, and public health and safety with the PHAC president and subsequently with Veterinarians without Borders (VwB). As a result, the CVMA provided VwB with a location to host a workshop during the 2017 CVMA Convention. The workshop, in which the CVMA participated, provided a forum to discuss animal and public health and safety issues within First Nations communities.

**Future CVMA Conventions:** The CVMA is looking forward to greeting all Canadian — and international — veterinarians and veterinary technicians at its Canadian — and international — veterinary conventions:

- **2018 Vancouver, BC:** 5–8 July.
- **2019 Toronto, ON:** July (exact days to be determined). This will be a unique opportunity for the CVMA to co-host the World Small Animal Veterinary Convention on Canadian soil.
- **2020 Quebec City, QC:** June 11–14 2020.

revenues, the dépenses, the bénéfices, the nombre de clients actuels et nouveaux, les tarifs ainsi que la rémunération des vétérinaires et des employés non-vétérinaires. En plus de l’investissement de l’ACMV, ce sondage est grâce à l’appui de IDEXX Laboratories, Petsecure, Merck Santé animale et la Banque Scotia. On peut consulter le rapport 2016 sur le sondage national de l’ACMV auprès des propriétaires de pratique au veterinairescaunada.net/practice-economics/reports

Les résultats 2016 ont constaté que, en général, l’année a été bonne pour les vétérinaires du Canada. Les bénéfices nets ont connu une hausse pour les pratiques pour petits animaux ainsi que pour les pratiques mixtes et pour grands animaux. Les cliniques pour animaux de compagnie ont compté sur la hausse des revenus afin de compenser une augmentation des dépenses, ce qui a permis au bénéfice net de croître. La croissance des revenus est probablement partiellement attribuable à un retour des clients actuels et à l’arrivée de nouveaux clients. Par contre, les cliniques mixtes et pour grands animaux ont employé des mesures de réduction des coûts pour sabrer dans les dépenses en raison d’une chute des recettes, ce qui leur permet d’accroître leur bénéfice net.

**MaVitrineVétérinaire:** MaVitrineVétérinaire de l’ACMV procure aux vétérinaires membres une présence en ligne facile d’utilisation. Une nouvelle initiative vise à améliorer l’observance des diètes en utilisant un modèle d’abonnement en vertu duquel les aliments sont livrés soit au domicile ou sont disponibles pour cueillette à la clinique à certains intervalles.

**Communications:** La **Semaine de la vie animale 2017** se tiendra du 1er au 7 octobre. Le thème de la campagne est «Protéger les cinq libertés afin d’assurer le bien-être animal». La campagne mensuelle de sensibilisation dans les médias sociaux #Vétérinairespartenaires en est maintenant à sa troisième année et elle vise des publics cibles sur Facebook et Twitter. La campagne de sensibilisation nationale aux tiques en est maintenant à sa deuxième année. En partenariat avec Merck Santé animale, l’ACMV a déclaré le mois de mars comme le Mois national de sensibilisation aux tiques. Le matériel de l’édition 2017 du Mois national de sensibilisation aux tiques comprenait un webinaire, une affiche, des messages dans les médias sociaux ainsi que des affiches pour la salle d’attente et la salle d’examen. L’ACMV a mis en œuvre une Campagne de prise de rendez-vous à l’avance. La prise de rendez-vous à l’avance signifie simplement la prise du prochain rendez-vous des patients pendant leur visite à la clinique, avant qu’ils ne quittent les lieux. La prise de rendez-vous à l’avance a pour objectif d’améliorer les soins aux patients et la santé de la pratique vétérinaire.

**Réserve vétérinaire canadienne:** Dans le cadre d’une campagne de recrutement, nous avons ajouté 70 réservistes, pour un total de 288 réservistes (le nombre cible minimum est de 200). À la fin mars, la RVC a effectué son exercice de mobilisation annuel et il s’agissait cette fois d’un exercice à plusieurs vagues qui comportait des scénarios multiples. L’ACIA et Emergency Management BC ont participé à l’exercice à titre de premiers répondants.

**Services vétérinaires pour les collectivités autochtones:** L’ACMV a discuté l’enjeu de la disponibilité des services vétérinaires, de la santé et du bien-être des animaux ainsi que de la santé et de la sécurité publiques avec la présidente de l’ASPC et successivement avec Vétérinaires sans frontières (VSF). À la suite de cette réunion, l’ACMV a fourni un local à VSF pour la tenue d’un atelier durant le congrès 2017 de l’ACMV. L’atelier, auquel l’ACMV a participé, a servi de forum pour discuter des enjeux liés à la santé animale et à la santé et sécurité du public au sein des collectivités des Premières nations.

**Futurs congrès de l’ACMV:** L’ACMV se réjouit à la penser d’accueillir tous les vétérinaires et techniciens vétérinaires canadiens et internationaux à ses futurs congrès :

- **2018 Vancouver (Colombie-Britannique):** du 5 au 8 juillet.
- **2019 Toronto (Ontario):** juillet (les dates exactes restent à déterminer). Il s’agira d’une occasion unique pour l’ACMV d’être co-organisateur des congrès de la World Small Animal Veterinary Association en sol canadien.
- **2020 Québec (Québec):** Du 11 au 14 juin 2020.
Animal Welfare: Safeguarding the Five Animal Freedoms
Happy Animal Health Week!

This month, we celebrate Animal Health Week from October 1 to 7, 2017. The Canadian Veterinary Medical Association (CVMA) is highlighting the importance of animal welfare through the campaign slogan, “Animal Welfare: Safeguarding the Five Animal Freedoms.”

The Five Freedoms include: adequate shelter, proper nutrition, appropriate veterinary care, proper socialization, and the ability to exhibit normal behaviors. This year’s theme provides us with an opportunity to remind animal owners of the fundamental elements they are required to provide the animals in their care to ensure them healthy and happy lives. It is our responsibility to ensure the animals we care for not only survive, but thrive.

We’re reminding animal owners they can protect the Five Animal Freedoms by:

• Providing proper nutrition
  – Freedom from hunger and thirst by ready access to fresh water and a diet to maintain full health and vigor.

• Ensuring proper socialization
  – Freedom to spend time with or away from members of their species as appropriate.

• Providing adequate shelter
  – Freedom from discomfort by providing an appropriate environment including shelter and a comfortable resting area.

• Providing appropriate veterinary care
  – Freedom from pain, injury or disease by prevention or rapid diagnosis and treatment.

• Allowing animals to exhibit normal behavior
  – Freedom to express normal behavior by providing sufficient space, proper facilities, and tools/accessories and not punishing animals for carrying out undesired behaviors.

Social media
The CVMA has promoted Animal Health Week for over 30 years. We invite you to share your celebrations on Facebook or tweet using the hashtag #AnimalHealthWeek.

Protéger les cinq libertés afin d’assurer le bien-être animal
Joyeuse Semaine de la vie animale!

Ce mois-ci, nous célébrons la Semaine de la vie animale du 1er au 7 octobre 2017. L’Association canadienne des médecins vétérinaires (ACMV) souligne l’importance du bien-être animal sous le thème du slogan de la campagne, «Protéger les cinq libertés afin d’assurer le bien-être animal».

Les cinq libertés comprennent : un hébergement adéquat, une alimentation appropriée, des soins vétérinaires appropriés, une socialisation appropriée et la capacité de manifester un comportement normal. Le thème de cette année nous fournit l’occasion de rappeler aux propriétaires d’animaux les éléments fondamentaux qui sont requis pour que les animaux confiés à leurs soins mènent une vie heureuse et en santé. C’est notre responsabilité de veiller à ce que les animaux ne fassent pas seulement survivre, mais qu’ils s’épanouissent.

Nous rappelons aux propriétaires d’animaux qu’ils peuvent protéger les cinq libertés animales en :

• Fournissant une alimentation appropriée
  – Prévenir la faim et la soif en fournissant de l’eau fraîche et des aliments afin d’assurer une santé vigoureuse.

• Offrant une socialisation appropriée
  – Donner la possibilité de passer du temps avec ou sans les membres de leur espèce en fonction de leurs besoins.

• Procurant un hébergement adéquat
  – Fournir un environnement approprié qui comprend un abri et une aire de repos confortables afin d’éviter l’inconfort.

• Fournissant des soins vétérinaires appropriés
  – Favoriser l’absence de douleur, de blessures ou de maladies par la prévention ou un diagnostic et un traitement rapides.

• Permettant aux animaux de manifester un comportement normal
  – Promouvoir la possibilité d’exprimer un comportement normal en fournissant suffisamment d’espace, des installations adéquates ainsi que les outils et les accessoires nécessaires et en ne punissant pas les animaux lorsqu’ils manifestent des comportements indésirables.
Our sponsors

Generous support of the 2017 Animal Health Week campaign is provided by Principal Plus Sponsor, Boehringer Ingelheim, Principal Sponsor, Petsecure, and Program Sponsors, Elanco and iFinance Canada (Petcard).

The CVMA would not be able to carry out the important educational campaign that Animal Health Week is without the generous support of our sponsors and the dedication of veterinary teams throughout the country. Thank you.

During this week-long campaign many veterinary clinics and hospitals host open houses, plan dog washes, organize pet poetry or photo contests, and clinic tours. Some veterinarians visit school children or appear on television to talk about animal health care.

Médias sociaux

L’ACMV fait la promotion de la Semaine de la vie animale depuis plus de 30 ans. Nous vous invitons à partager vos célébrations sur Facebook ou à gazouiller en utilisant le mot-clé #célébromasla.

Nos commanditaires

Le commanditaire principal Plus, Boehringer Ingelheim, le commanditaire principal, Petsecure, et les commanditaires de programme, Elanco et iFinance Canada (Petcard), ont fourni un généreux soutien à la Semaine de la vie animale 2017.

L’ACMV ne pourrait pas mettre en œuvre l’importante campagne éducative de la Semaine de la vie animale sans le généreux soutien de nos commanditaires et le dévouement des équipes vétérinaires partout au pays. Merci.

Durant cette campagne d’une semaine, beaucoup de pratiques et de cliniques vétérinaires organiseront des journées portes ouvertes, planifieront des lave-chien, organiseront des concours de poésie sur les animaux de compagnie ou des concours de photos ainsi que des visites de la clinique. Certains vétérinaires visiteront des enfants dans les écoles ou se présenteront à la télévision pour parler à propos de la santé animale.

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Move Over National Vet Tech Week, it’s Time to Celebrate RVT Month!
La Semaine nationale des techniciens vétérinaires est terminée, célébrons le Mois des TVA!

It is with great pleasure that the Registered Veterinary Technologists and Technicians of Canada (RVTTC) will be celebrating the first annual “RVT Month” this October. The Ontario Association of Veterinary Technicians, with the support of all our provincial associations, has been instrumental in developing this national campaign. Because one week just wasn’t enough, RVT Month will feature professional recognition for registered veterinary technologists and technicians. Emphasis will be placed on the value and importance of RVTs within veterinary healthcare. Two teaser videos and one feature video were launched in August and September that highlight the many roles that RVTs play towards animal healthcare. See them at (http://rvttcanada.ca/october2017/).

RVT Month kits are available on our website for workplaces to highlight their RVT team members and educate colleagues and members of the public on these skilled members of the team. Each veterinary team is encouraged to utilize the kit materials to launch their own activities and join in on social media with the hashtags #HugAnRVT #RVTMonth, #oneweekjustwasntenough. Check out our website (http://rvttcanada.ca/october2017/) or social media @RVTTC for more activities and ideas to share. Join together to celebrate RVT Month!

The RVTTC would like to thank the Ontario Association of Veterinary Technicians, British Columbia Veterinary Technologists Association, Alberta Association of Animal Health Technologists, Saskatchewan Association of Veterinary Technologists, Manitoba Veterinary Technologists Association and Eastern Veterinary Technicians Association in working together for this truly national campaign in support of our members. It is a testament that we accomplish great things when we work toward a common goal.

(by Heather Quilty, RVT)
16th Annual CAHLN-RCTLSA Meeting in Guelph a Success!

Over 160 delegates attended the annual scientific meeting of the Canadian Animal Health Laboratorians Network — Réseau canadien des travailleurs des laboratoires de santé animale (CAHLN-RCTLSA), June 4–7, 2017, hosted by the Animal Health Laboratory, University of Guelph, in Guelph, Ontario. The theme was “Laboratory based disease intelligence in 2017: New and practical approaches,” and attendees were informed through 76 oral and 13 poster presentations of the opportunities in deriving disease surveillance information from a variety of sources, including social media and multi-stakeholder networks, coupled with enhanced sharing of laboratory data. The program also included updates on technology advances and research findings in veterinary diagnostics.

The CAHLN-RCTLSA meeting was followed on June 7 by the annual meeting of the Canadian Association of Veterinary Pathologists — L’Association Canadienne des Pathologistes Vétérinaires (CAVP-ACPV), which included presentations on lymphoproliferative and histiocytic disorders, mucosal immunity, and swine diagnostic pathology, followed by case reports and provincial updates.

Selected for the 2017 Laboratorian of the Year Award for his meritorious service to veterinary laboratory medicine was Dr. Doug Campbell, who has worked as a wildlife pathologist for the Canadian Wildlife Health Cooperative (CWHC) since 1993. During this period, Doug has made substantial contributions, not only to wildlife health and disease diagnostics and surveillance, but also to human and production animal health.

Succès de la 16e réunion annuelle du RCTLSA-CAHLN à Guelph!

Plus de 160 délégués ont assisté à la réunion scientifique annuelle du Réseau canadien des travailleurs des laboratoires de santé animale-Canadian Animal Health Laboratorians Network — (RCTLSA-CAHLN), du 4 au 7 juin, qui a été organisée par le Laboratoire de santé animale de l’Université de Guelph, à Guelph, en Ontario. Le thème était «Données de laboratoire pour le renseignement sur les maladies en 2017 : approches nouvelles et pratiques» et les participants ont été informés dans le cadre de 76 présentations orales et de 13 présentations d’affiches sur les possibilités de puiser des données de surveillance des maladies d’une diversité de sources, dont les médias sociaux et les réseaux d’intervenants multiples, jumelées à un partage amélioré des données de laboratoire. Le programme incluait aussi des mises à jour sur les avancées technologiques et des résultats de recherches sur les diagnostics vétérinaires.

La réunion du CAHLN-RCTLSA a été suivie le 7 juin par l’assemblée annuelle de L’Association canadienne des pathologistes vétérinaires – Canadian Association of Veterinary Pathologists — (ACPV-CAVP), qui incluait des présentations sur les troubles lymphoprolifératifs et histiocytaires, l’immunité des muqueuses et la pathologie diagnostique chez les porcs, suivie de rapports de cas et de mises à jour provinciales.

Le Dr Doug Campbell a été choisi comme récipiendaire du Prix du travailleur de laboratoire de l’année 2017 pour son service méritoire en médecine vétérinaire de laboratoire et il travaille en tant que pathologiste de la faune pour le Réseau canadien de la santé de la faune (RCSF) depuis 1993. Durant cette période,
Doug a apporté des contributions considérables, non seulement pour la santé de la faune ainsi que le diagnostic et la surveillance des maladies, mais aussi pour la santé humaine et la santé des animaux de production. Doug a participé au dépistage initial et au diagnostic de nouvelles maladies de la faune en Ontario, dont le syndrome du museau blanc chez les chauves-souris, les maladies fongiques des serpents et le virus du Nil occidental, et il a contribué à l’élaboration de définitions de cas utilisées en Amérique du Nord pour le suivi des maladies et la propagation des pathogènes. L’une des nombreuses forces de Doug est sa capacité à communiquer des renseignements compliqués, oralement et par écrit, d’une manière qui est accessible à un vaste public, dont les scientifiques, les étudiants et le public. Les vastes connaissances du Dr Campbell sont souvent sollicitées pour les cas de diagnostic inusités chez les espèces sauvages et domestiques et il est aussi très en demande pour ses connaissances sur les maladies de la faune au Canada. Il donne généreusement de son temps et de son expertise et il est toujours disposé à partager ses vastes connaissances avec ses collègues.

Des prix ont aussi été décernés pour les présentations des étudiants diplômés. Le prix de la meilleure présentation orale a été jugé à égalité et décerné à Jamie Rothenburger, du Département de Pathobiologie, University of Guelph et à Ellie Milnes du Zoo de Toronto, pour leurs présentations respectives, “Pathology of wild urban rats” et “Mycobacterium epizootic in a zoo population of Chinese gliding frogs (Rhacophorus dennysi): Investigation, management, and public health response.” The best poster presentation award went to Corrine Schut, for her poster “Salmonella shedding and antibody response to Salmonella in pigs from weaning to marketing.”

The 2018 meeting will be held in Winnipeg, Manitoba, with the 2019 meeting to be held in Sainte Hyacinthe, Quebec, and the 2020 meeting in Calgary, Alberta. Updates will be posted on the website (www.cahln-rctlsa.com).
Epidemiology of gastrointestinal nematode infections in grazing yearling beef cattle in Saskatchewan

Murray Jelinski, John Gilleard, Lisa Rocheleau, Grant Royan, Cheryl Waldner

Abstract — The objective of this study was to provide contemporary data on the epidemiology of gastrointestinal nematode parasite infections of grazing yearling beef cattle in the province of Saskatchewan. Fecal samples \((n = 1290)\) were collected over 4 time periods during the summer grazing season from 21 separately managed groups of cattle. Fecal egg counts (FEC) were estimated using generalized estimating equations with a negative binomial distribution with log link function, adjusting for clustering of samples within each herd for each time period. *Nematodirus* spp. and *Trichuris* spp. eggs were enumerated separately and were detected in 5.7\% (73/1290) and 1.7\% (22/1290) of samples, respectively. One or more strongyle-type eggs were detected in 79.5\% (1025/1290) of the samples and FEC increased by 2.8 times over the summer grazing season. Interestingly, FEC were \(~3.4\) times higher on pastures located in dark brown versus brown soil zones, a finding that warrants further investigation.

Résumé — Épidémiologie des infections aux nématodes gastro-intestinaux chez les bovins d’un an en pâturage en Saskatchewan. L’objectif de cette étude consistait à fournir des données contemporaines sur l’épidémiologie des infections aux parasites nématodes gastro-intestinaux des bovins de boucherie âgés d’un an en pâturage dans la province de la Saskatchewan. Des échantillons fécaux \((n = 1290)\) ont été prélevés pendant quatre périodes durant la saison de pâturage estival auprès de 21 groupes de bovins gérés séparément. Les œufs dans les fèces (CŒF) ont été estimés en utilisant des équations d’estimation généralisées ayant une distribution binomiale négative en lien avec la fonction log, en ajustant pour le regroupement des échantillons au sein de chaque troupeau pour chaque période. Les œufs de *Nematodirus* spp. et de *Trichuris* spp. ont été énumérés séparément et ont été détectés dans 5,7\% (73/1290) et 1,7\% (22/1290) des échantillons, respectivement. Un ou plusieurs œufs de type strongyle ont été détectés dans 79,5\% (1025/1290) des échantillons et les CŒF ont augmenté de 2,8 fois pendant la saison de pâturage estival. Fait intéressant, les CŒF étaient de ~3,4 fois supérieurs dans les pâturages situés dans des zones de sol brun foncé comparativement à du sol brun, une constatation qui justifie de nouvelles investigations.

Can Vet J 2017;58:1044–1050

Introduction

The most economically important gastrointestinal nematodes (GIN) of cattle belong to the superfamily Trichostrongyloidea, colloquially known as strongyles (1). While studies on GIN have been conducted on beef cattle in western Canada, most were conducted decades ago and only a small number involved pastured yearling beef (2–4) or dairy (5) cattle. Therefore, much of the information used to design parasite control programs in western Canadian beef cattle has been extrapolated from American data. This extrapolation is problematic because infection intensities and strongyle species vary dramatically among regions and by climatic zones.

Based on studies in Quebec (6) and the United States (7), infective trichostrongyloid nematode larvae can survive severe winter conditions; however, survivability is often low, resulting in a dramatic decline in the population of free-living larvae on pasture (6,7). Therefore, most pastures are relatively free of...
infective larvae when cattle are placed on pasture. These low infection pressures may explain, in part, why overt clinical parasitism occurs infrequently in the northern temperate regions. Although overt parasitism is uncommon, sub-clinical parasitism has been shown to impact production performance in western Canadian beef cattle on pasture (2,3).

There are several excellent reviews relating to the myriad of factors that determine the prevalence and transmission of GIN within cattle populations (1,7–9), with the main determinants of transmission being ambient temperature and moisture within cattle populations (1,7–9), with the main determinants of transmission being ambient temperature and moisture (1,7,10,11). A recent study involving pastured beef cattle in the province of Alberta confirmed that parasite transmission was reduced in the hot dry southeastern and cool dry northwestern regions of the province (12). While environmental factors are important, host factors such as host genetics and acquired immunity also influence parasite transmission. A recent study of beef cow-calf pairs on pasture in the province of Saskatchewan found the cows’ fecal egg counts (FEC) were very low at the time of pasture turnout and remained low throughout the grazing period, whereas the calves’ FEC increased 9-fold over the same grazing period (13). These differences in FEC were likely related, at least in part, to acquired host immunity (9,14,15).

The most common method of monitoring GIN parasitism at the herd level is to perform fecal egg counts (16). However, FEC are only a proxy for infection intensity and must be interpreted with some caution, particularly when performed in the fall and winter months (17). Extrapolating FEC from an individual animal to the herd level can also be problematic because shedding of GIN eggs is not normally distributed within a group of animals; 15% to 25% of animals are generally responsible for shedding the majority of eggs (18,19). It is generally recommended to obtain 15 to 20 fecal samples from each group of animals, which provides a 95% probability that one or more samples will have come from a high shedding animal (20).

The purpose of this study was two-fold: i) to monitor fecal egg counts in pastured yearling beef cattle over the summer grazing season, and ii) to assess how environmental conditions (temperature and rainfall) and soil zone types in the province of Saskatchewan influence fecal egg counts.

**Materials and methods**

**Sample collection and processing**

Sixteen beef cattle producers, managing 21 separate cohorts (herds) of commercial yearling steers (n = 9) and heifers (n = 12), located in southern and central Saskatchewan were purposively chosen for this study. The cattle were distributed over a geographical area of ~230 km (East–West) by 460 km (North–South). The inclusion criteria for the study included geographical location, number of animals, producers’ willingness to participate in the study, and the producers’ ability to provide information relating to both anthelmintic usage and when their cattle were placed on pasture (‘turnout’). The number of cattle per management group ranged from ~30 to ~200.

The objective was to collect 20 samples from each group of animals at 4 time points, ~1 month apart, over the 2015 summer grazing season. Sample collection involved monitoring the cattle until they defecated at which time a golf ball sized fecal sample was collected using a plastic palpation sleeve. Samples were labeled (herd ID), placed on ice, and transported to the laboratory where they were refrigerated at 4°C until shipped on ice by overnight courier to a commercial testing laboratory (BioCheck Veterinary Diagnostics and Technologies, Lethbridge, Alberta). The laboratory processed 3 g aliquots of fecal material as per the Modified Wisconsin Sugar Flotation Technique (21). All results were reported as the numbers of eggs per 1 g of fecal material (EPG). Most parasites from the superfamily Trichostrongylidea shed smooth oval-shaped eggs, which are morphologically indistinguishable from each other. The exceptions are Nematodirus spp. and Trichuris spp., both of which have unique appearances. Therefore, these latter parasites were enumerated separately, while all other eggs were grouped together and classified as strongyle-type eggs.

**Table 1.** Percentage of individual samples having at least 1 Trichostrongyloidea egg and the percentage of management groups (herds) having at least 1 or at least 2 samples test positive for Trichostrongyloidea eggs (n = 1290 samples, N = 21 management groups)

<table>
<thead>
<tr>
<th>Period in 2015</th>
<th>1 (22 May to 15 June)</th>
<th>2 (June 16 to July 15)</th>
<th>3 (July 16 to August 19)</th>
<th>4 (September 9 to October 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strongyle-like</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Individual samples</td>
<td>74.4% (293/394)</td>
<td>74.6% (282/378)</td>
<td>87.8% (244/278)</td>
<td>85.8% (206/240)</td>
</tr>
<tr>
<td>Herds ≥ 1 positive sample</td>
<td>100% (21/21)</td>
<td>90.5% (19/21)</td>
<td>66.7% (14/21)</td>
<td>57.1% (12/21)</td>
</tr>
<tr>
<td>Herds ≥ 2 positive samples</td>
<td>90.5% (19/21)</td>
<td>90.5% (19/21)</td>
<td>66.7% (14/21)</td>
<td>57.1% (12/21)</td>
</tr>
<tr>
<td><strong>Nematodirus spp.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Individual samples</td>
<td>6.6% (26/394)</td>
<td>5.0% (19/378)</td>
<td>3.6% (10/278)</td>
<td>7.5% (18/240)</td>
</tr>
<tr>
<td>Herds ≥ 1 positive sample</td>
<td>52.4% (11/21)</td>
<td>47.6% (10/21)</td>
<td>33.3% (7/21)</td>
<td>33.3% (7/21)</td>
</tr>
<tr>
<td>Herds ≥ 2 positive samples</td>
<td>38.1% (8/21)</td>
<td>28.6% (6/21)</td>
<td>9.5% (2/21)</td>
<td>28.6% (6/21)</td>
</tr>
<tr>
<td><strong>Trichuris spp.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Individual samples</td>
<td>2.5% (10/394)</td>
<td>1.3% (5/378)</td>
<td>0.0% (0/278)</td>
<td>2.9% (7/240)</td>
</tr>
<tr>
<td>Herds ≥ 1 positive sample</td>
<td>1.9% (4/21)</td>
<td>19.1% (4/21)</td>
<td>0.0% (0/21)</td>
<td>19.1% (4/21)</td>
</tr>
<tr>
<td>Herds ≥ 2 positive samples</td>
<td>9.5% (2/21)</td>
<td>9.5% (2/21)</td>
<td>0.0% (0/21)</td>
<td>14.3% (3/21)</td>
</tr>
</tbody>
</table>
Data analyses were completed in a statistical software program (Stata/SE 14.0 for Windows; StataCorp LP, College Station, Texas, USA). Population-average differences in observed FEC across sampling periods were estimated using generalized estimating equations (GEE) with a negative binomial distribution with log link function adjusting for clustering of samples within each cohort for each time period. The only workable option for the correlation matrix was exchangeable as the same animals were not sampled over time; therefore, estimating the time ordered correlation of individual observations was not feasible. Adjustment for clustering of time period within herd was chosen based on QIC as the best fit when compared to adjustment for clustering within herd only. For all final models, variance estimation was completed using bootstrapping with a minimum of 5000 completed repetitions based on previously published recommendations for analysis of egg counts (25). This approach was used for the strongyle-type eggs, *Nematodirus* spp., and the total of all observed eggs regardless of species. The same GEE model would not run for *Trichuris* spp. because the number of positive samples was too small. Therefore, the best fitting negative binomial regression model with a log link function that converged included a robust variance option with adjustment for clustering within cohort.

Differences in the total observed FEC counts across soil types, levels of precipitation, GDD, and ecoregions, adjusted for sample period, were then estimated using GEE with a negative binomial distribution, log link function, adjusting for clustering within each herd for each time period, and using bootstrap variance estimation with a minimum of 5000 completed repetitions. All variables were screened using unconditional or bivariate analysis and only those with *P* < 0.20 were considered in building the final model. A final multivariable model was built using manual stepwise backwards removal and variables with *P* < 0.05 were retained. Variables removed from the model were checked to see if they confounded other effect estimates of interest and were considered a confounder if adding the variable back into the model changed other effect estimates by more
than 20%. Effect estimates were reported as relative differences in counts with 95% confidence interval (CI).

**Results**

All cattle were placed on pasture between April 18 and June 9, 2015, and no sampling was performed at this time. There were 66 separate herd samplings out of a potential 84; wet weather conditions and a shortage of personnel precluded all the herds from being sampled at all time points. Table 1 provides the date ranges of the 4 collection time periods. The 66 sample collections yielded 1290 individual fecal samples. The number of samples collected/group ranged from 10 to 20 (median = 20). Most (59/66; 89.3%) collections met the target of 20 samples/group, while 2 herd level collections yielded 10 samples, 1 yielded 16, 2 yielded 18, and 2 yielded 19 samples.

Fifteen (71.4%) groups of cattle were treated with an ivermectin product, at or prior to, the time of turnout, 1 (4.8%) group was treated with fenbendazole at or before turnout, and 4 (19.0%) had received ivermectin the previous fall. Of the 20 (95.2%) producers who administered an anthelmintic, 6 (30%) administered both ivermectin and fenbendazole products the previous fall.

At least 1 strongyle-type egg was detected in 79.5% (1025/1290) of the samples (Table 1). *Nematodirus* spp. and *Trichuris* spp. eggs were detected in 5.7% (73/1290) and 1.7% (22/1290) of samples, respectively. All groups had at least 1 strongyle-type egg in the first sample period; however, only 52% of groups had at least 1 *Nematodirus* egg and only 1.9% (4/21) groups had at least 1 *Trichuris* egg (Table 1).

The box-and-whisker plots in Figure 1 (a–c) show the dispersion of FEC by herd and sampling period. Overall, there was a wide variation of FEC between herds, within herds, and between collection periods. The highest mean strongyle-type FEC for a single sample period was 48 EPG for herd #1 and the lowest was 0.02 EPG for herd #6. Furthermore, herds #1 and #2 had individual animals with FEC of ~180 EPG, while none of the animals in herds #3 and #14 had a FEC above 15 EPG. Extreme intra-herd FEC variability is evident in the 1st collection in herd #1, which had a mean FEC of 19 EPG and a range of 0 to 181 EPG. Herd #1 consistently had the highest FEC of all groups; these animals had not received an anthelmintic treatment since being administered ivermectin the previous fall.

The strongyle-type FEC were significantly higher (*P* = 0.021) in the last (September–October) sampling period compared to the first (May–June) (Figure 2). *Nematodirus* spp. fecal egg counts were steady for the first 2 sampling periods, but significantly lower (*P*, 0.05) in the July–August versus September–October collection periods (Figure 3). A similar trend occurred with *Trichuris* spp. (not shown), with the FEC for the 3rd collection period being significantly lower (*P* < 0.05) compared to the other 3 collection periods.

Total predicted mean strongyle-type FEC varied from 4.4 EPG (95% CI: 1.6 to 7.1) in the May–June period to 11.6 (95% CI: 4.6 to 18.7) in the September–October period, after accounting for clustering. Risk factors screened using unconditional or bivariate analysis and considered to be potentially associated (*P* < 0.20) with total FEC included: total accumulated precipitation from May to August (*P* = 0.008), total accumulated precipitation from June to September (*P* = 0.01), total GDD from April to July (*P* = 0.009), and soil type (*P* = 0.06). These simple associations were adjusted only for differences across sample collection periods and clustering within management group and sample collection period.

There was no association between FEC and the following factors adjusted only for differences across sample collection

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**Table 1.** Collection date ranges and number of samples collected for each herd sampling period.

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Number of samples (n)</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

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**Figure 2.** Predicted mean (± standard error) of strongyle-like egg counts for fecal samples collected from May 22 to October 7, 2015 (n = 1290, 21 management groups). *a, b* — Different superscripts indicate significant differences between sample periods (*P* < 0.05).
periods and clustering within management group: total accumulated precipitation from May to June \( (P = 0.30) \), total accumulated precipitation from May to July \( (P = 0.96) \), ecoregion \( (P = 0.78) \), and total GDD from April to June \( (P = 0.79) \), April to August \( (P = 0.47) \), and April to September \( (P = 0.47) \).

The final multivariable model for total FEC included sample period \( (P = 0.06) \), total GDD from April to July \( (P = 0.0003) \), and soil type \( (P = 0.047) \) (Table 2). Total accumulated precipitation from May to August \( (P = 0.19) \) was included as it confounded the associations between both soil type and total GDD and total egg counts.

Total FEC were \( \approx 2.8 \) times higher in September–October than in May–June after accounting for other risk factors in the final multivariable model (Table 2). Total strongyle-like FEC were also \( \approx 3.4 \) times higher on pastures located on dark brown versus brown soil types (Table 2). Total FEC were significantly lower in the cattle in areas of mid-range GDD for the period April to July compared to areas with lower GDD (Table 2). After accounting for other risk factors there was no south to north \( (P = 0.85) \) or east to west \( (P = 0.89) \) trend in total egg counts and therefore northing and easting were not included in the final model.

### Discussion

Overall, there was a relatively high prevalence of strongyle nematode infections, with \( \approx 80\% \) of samples having 1 or more strongyle-like eggs. However, only a small number of samples had *Nematodirus* spp. and *Trichuris* spp. eggs, which is consistent with previous studies involving pastured beef cattle in western Canada (4,13). In the case of *Nematodirus* spp., the low prevalence is consistent with the view that these parasites are mainly a problem of younger calves.

All herds had cattle shedding strongyle-like eggs; however, of greater interest was the marked intra- and inter-herd variability in FEC. This finding is salient because most beef herds in western Canada currently use a standard “one size fits all” approach to parasite control. The findings, however, underscore that some herds will have very low levels of parasitism, even at the end of the grazing season and hence may not benefit from anthelmintic therapy. The extreme variability also extended to within the managed groups of cattle, in which some animals had very low levels of internal parasites and as such, anthelmintic treatment would be unwarranted. The challenge of course is coming up with a parasite testing method that is inexpensive, rapid, accurate, and logistically practicable for cattle producers. And while this may seem incomprehensible at this time, targeted anthelmintic treatment strategies have been introduced in recent years into the sheep sector (26). Not only can targeted approaches be cost-effective, but this strategy should mitigate the development of anthelmintic resistance.

The epidemiological pattern of rising FEC over the summer grazing season is typical of cattle raised in temperate zones; this finding was expected. However, the last peer-reviewed studies involving GIN infections of pastured yearling cattle in western Canada were published over 25 years ago (2,3). Given that most

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### Table 2. Final multivariable model describing the differences in total strongyle-like fecal egg counts among soil types, growing degree days (GDD), and sampling period adjusted for precipitation and clustering within management group for each sample collection \( (n = 1290, N = 66 \text{ sample collections from 21 management groups}) \)

<table>
<thead>
<tr>
<th>Sample period</th>
<th>Relative increase in egg count</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>May to June</td>
<td>1.77</td>
<td>0.87</td>
<td>3.59</td>
<td>0.11</td>
</tr>
<tr>
<td>June to July</td>
<td>2.71</td>
<td>1.09</td>
<td>6.68</td>
<td>0.031</td>
</tr>
<tr>
<td>July to August</td>
<td>2.82</td>
<td>1.17</td>
<td>6.79</td>
<td>0.021</td>
</tr>
<tr>
<td>September to October</td>
<td>2.82</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Soil type</th>
<th>Total strongyle-like FEC</th>
<th>Reference category</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black and dark gray</td>
<td>2.14</td>
<td>0.41</td>
<td>11.3</td>
<td>0.37</td>
<td></td>
</tr>
<tr>
<td>Brown</td>
<td></td>
<td>1.22</td>
<td>9.29</td>
<td>0.019</td>
<td></td>
</tr>
<tr>
<td>Dark brown</td>
<td>3.36</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| GDD (Base 0°C)    |                                  |                    |              |              |               |
| June to July      |                                 |                    |              |              |               |
| 713° to ≤ 879°    | 0.10                            | 0.02               | 0.42         | 0.002        |
| 880° to ≤ 1045°   | 0.44                            | 0.07               | 2.79         | 0.38         |
| 1046° to ≤ 1211°  |                                  |                    |              |              |               |

| Total accumulated precipitation (mm) |                                  |                    |              |              |               |
| June to September |                                 |                    |              |              |               |
| 175 to ≤ 200 mm   |                                  |                    |              |              |               |
| 201 to ≤ 225 mm   | 0.65                            | 0.29               | 1.44         | 0.29         |
| 226 to ≤ 250 mm   | 2.12                            | 0.85               | 5.32         | 0.11         |
| 251 to ≤ 275 mm   | 1.44                            | 0.27               | 7.77         | 0.67         |
| 276 to ≤ 300 mm   | 3.18                            | 0.96               | 10.5         | 0.06         |
of Canada’s beef cattle are located in the provinces of Alberta and Saskatchewan, it is important to have data that are both contemporary and unique to the environmental conditions of the Prairie Provinces. The need for these data is highlighted when comparing the results of the current study to those conducted years earlier. Specifically, FEC increased nearly 3-fold in the current study, whereas in the earlier studies FEC only increased marginally from 10 to 13 EPG and 16.3 to 24.1 EPG over a 90 or 120 d grazing period, respectively (2,3). Multiple factors may account for the differences in the epidemiological patterns of these earlier studies compared to the current study. The species composition of the parasite communities may have been different; the climatic conditions between the studies may have influenced parasite transmission rates; and differences in the type and amount of anthelmintic usage may also explain the differences in the FEC patterns. Paradoxically, most anthelmintics are very efficacious in reducing parasite burdens; however, prolonged exposure to a threshold level of parasites is required for the host to mount a protective immunological response (27). Therefore, anthelmintic usage may in some instances result in suboptimal immunity, leaving the animals prone to GIN infections when placed on pasture for the second grazing season (28,29). Regardless of the reason for the differences in the past and current studies, the current study provides a contemporary view of what is occurring in grazing yearling cattle in Saskatchewan.

There was nearly a 3.5-fold increase in FEC in cattle grazing pastures located in the dark brown versus brown soil zones. The association between FEC and soil type may have been confounded by cattle management practices. Saskatchewan cow-calf producers located in brown versus gray or dark brown soil zones are more likely to have larger herds, to pregnancy check, semen test, and to test their feedstuffs for nutritional content (32). Therefore, the higher FEC may be related to some uncharacterized management practices that influence FEC. Lastly, dark brown soils tend to be associated with wetter and cooler environmental conditions, which may have confounded the relationship between soil type and FEC.

There were several limitations to this study. An untreated control group would have provided insight into how anthelmintics administered the previous fall and at turnout influenced FEC. It would have also been useful to have determined the species composition of the eggs either by larval culture and morphology or molecular genotyping (33); the fecundity of Cooperia spp. is much higher than that of Ostertagia spp. Only 8 groups of cattle were sampled at all 4 time points and precipitation data were obtained from the closest Environment Canada reporting station as opposed to being collected at the level of the pasture.

Despite the limitations, this is the first study of a cross-section of cattle spanning a broad geographical area within the province of Saskatchewan in over 25 y. The rise in FEC over the summer grazing period appears to be quite different from what was reported decades ago. The extreme variability in FEC both within and between groups of cattle underscores the need to take a representative number of samples when assessing GIN burdens at the herd level. There is also a need for research into a targeted approach for anthelmintic use in pastured beef cattle. Lastly, the association between FEC and soil type was an interesting finding and deserves more attention.
Acknowledgments
We acknowledge Dr. Janice Berg and Glen Cartwright of Merck Animal Health (Canada) for their support of this project.

References
Evaluation of long-acting oxytetracycline and a commercial monovalent vaccine for the control of Campylobacter fetus subsp. venerealis infection in beef bulls

Nathan E.N. Erickson, Emily Lanigan, Taryn Waugh, Karen Gesy, Cheryl Waldner

Abstract — A blinded randomized controlled trial was used to evaluate a multi-modal therapeutic regime for treatment of beef bulls infected with Campylobacter fetus subsp. venerealis (Cfv). Treatment included 2 doses of a commercially available monovalent vaccine and long-acting oxytetracycline applied twice at a 2-week interval with treatment completed 2 weeks before post-treatment observation. Fifteen confirmed Cfv infected bulls were randomly allocated to control (n = 8) or treatment groups (n = 7). Preputial scrapings were collected each week from before infection to 11 weeks following the last treatment. When the polymerase chain reaction (PCR) results for both culture and preputial scrapings were interpreted in parallel, there were no significant differences between treated and untreated bulls. Regardless of the type of diagnostic testing considered, treatment with 2 label doses of this regime did not stop shedding of Cfv in all treated bulls and is, therefore, not recommended as an effective management strategy.

Introduction

Embryonic deaths and abortions in the North American cow-calf herd result in substantial production losses and economic hardship for producers (1). Venereal pathogens, such as bovine genital campylobacterosis (BGC), are an important cause of reproductive loss (2). The impact of BGC among western Canadian cow-calf herds was thought to be limited; however, recent studies suggest that BGC is present and an important cause of reproductive failure (3,4).

The causative agent of BGC, Campylobacter fetus subsp. venerealis (Cfv), also referred to as “vibrio” stemming from previous nomenclature (2,5–9), has been conclusively linked to fetal losses. The economic losses are often compounded since the full extent of the problem is not recognized until the herd is pregnancy checked in the fall or until the subsequent calving season (10–13). Campylobacter fetus subsp. venerealis is primarily maintained and transmitted by chronically infected bulls that serve as asymptomatic carriers which harbor the bacteria within folds or crypts in the prepuce (11,13,14).
effectiveness (15). As vaccination alone is often not considered sufficient to manage an outbreak, testing and culling of infected bulls is routinely recommended. Test and cull procedures, however, have a substantial cost associated with premature loss of high value animals; especially, considering the price of breeding bulls. The effectiveness of testing and removal of infected bulls is also limited by the clinical sensitivity and specificity of the diagnostic tests suitable for use under field conditions (16).

Some researchers have reported the potential for treating carrier bulls using either vaccination with a monovalent oil-based vaccine or repeated antibiotic therapy (17–22). To date, many of the published antimicrobial treatment protocols use antimicrobial products that are not commercially available in Canada and the USA, its limited use in human health care, and a report from research in Argentina (23). The authors hypothesize that the combination of antimicrobial treatment and vaccination will not result in the clearance of Campylobacter fetus subsp. venerealis from the prepuce of carrier bulls.

### Materials and methods

#### Experimental infection

All animal procedures were performed in accordance with the Canadian Council on Animal Care and approved by the University of Saskatchewan Animal Research Ethics Board (Protocol # 20150025). Twenty (n = 20) cull beef bulls were obtained either by purchase from a local auction or from a local community pasture bull battery (Table 1). Preputial scrapings were collected from all bulls before the start of the experiment and tested by culture and direct real-time polymerase chain reaction (RT-PCR) to confirm that the bulls were test negative for Cfv.

Three previously infected (PI) bulls, owned by the Western College of Veterinary Medicine (Saskatoon, Canada), were used as a source of organisms to infect the naïve bulls (16). Preputial scrapings were collected from the 3 PI bulls followed by isolation and recovery of Cfv isolates. Pure cultures of Cfv from the 3 previously infected bulls were expanded on Skirrow agar plates to generate sufficient inoculum to infect the naïve bulls. Pure Cfv cultures grown from the PI bulls were harvested into warmed phosphate buffered saline (PBS; 20 mM phosphate, 150 mM NaCl) and diluted to an optical density (OD$_{600}$) of 0.4. Immediately before transfer, 2.5 mL of this inoculum was loaded into a series of 10-mL sterile plastic syringes with

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Table 1. Outline of the timeline for infection, treatment and post-treatment monitoring of Campylobacter fetus subsp. venerealis in beef bulls

<table>
<thead>
<tr>
<th>Week</th>
<th>Infection period</th>
<th>Treatment period</th>
<th>Post-treatment monitoring period</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Preputial scraping and infection protocol</td>
<td>Preputial scraping</td>
<td>Preputial scraping</td>
</tr>
<tr>
<td>1</td>
<td>Preputial scraping protocol</td>
<td>Preputial scraping</td>
<td>Preputial scraping</td>
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<tr>
<td>2</td>
<td>Preputial scraping protocol</td>
<td>Preputial scraping</td>
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<tr>
<td>3</td>
<td>Preputial scraping protocol</td>
<td>Preputial scraping</td>
<td>Preputial scraping</td>
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<tr>
<td>4</td>
<td>Preputial scraping protocol</td>
<td>Preputial scraping</td>
<td>Preputial scraping</td>
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<tr>
<td>5</td>
<td>Preputial scraping protocol</td>
<td>Preputial scraping</td>
<td>Preputial scraping</td>
</tr>
<tr>
<td>6</td>
<td>Preputial scraping protocol</td>
<td>Preputial scraping</td>
<td>Preputial scraping</td>
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<tr>
<td>7</td>
<td>Preputial scraping protocol</td>
<td>Preputial scraping</td>
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<td>8</td>
<td>Preputial scraping protocol</td>
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<td>9</td>
<td>Preputial scraping protocol</td>
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<tr>
<td>10</td>
<td>Preputial scraping protocol</td>
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<tr>
<td>11</td>
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<tr>
<td>12</td>
<td>Preputial scraping protocol</td>
<td>Preputial scraping</td>
<td>Preputial scraping</td>
</tr>
<tr>
<td>13</td>
<td>Preputial scraping protocol</td>
<td>Preputial scraping</td>
<td>Preputial scraping</td>
</tr>
</tbody>
</table>

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1 syringe for each bull. Each of the 20 naïve bulls were infected by placing the inoculum directly into the prepuce using an AI pipette, then 6 mL of air was used to flush the remaining inoculum through the AI pipette. This technique was modified from Bier et al (24). The procedure was repeated 1 wk later, so each of the 20 naïve bulls was inoculated twice (Table 1). At the end of the infection protocol, 12 of the 20 bulls were determined by culture and PCR to be positive for Cfv. Together with the 3 PI bulls, a cohort of 15 infected bulls was available at the start of treatment.

The 15 infected bulls were randomized into either the control (n = 8) or treatment (n = 7) group within blocks based on source (auction, community pasture, or previously infected). The bulls were confirmed positive based on laboratory testing immediately before their second infective dose of Cfv at week 1 and their positive status was re-evaluated with a sample collected immediately before treatment at week 0. The treatment group was vaccinated with a monovalent oil-based Cfv commercial vaccine (Vibrin; Zoetis Canada, Kirkland, Quebec), 2 mL and injected with long-acting oxytetracycline (Iquamycin LA-200; Zoetis Canada), 1 mL/10 kg body weight (BW), after collection of a preputial sample. Both the vaccine and antibiotic were administered subcutaneously twice at a 2-wk interval (Table 1). The vaccine and antibiotic were placed on contralateral sides of each bull’s neck at each treatment.

The person who collected the preputial scrapings and the laboratory personnel were blinded to the treatment status of the bulls. Vaccination and injection with long-acting oxytetracycline were administered by other researchers and veterinarians from the WCVM teaching hospital. All treatment records were maintained by a research assistant.

Preputial samples were collected from all bulls each week of the study both before and during treatment and for 11 wk following the last treatment (Table 1). One aliquot from the sample was designated for culture and a second was tested using direct RT-PCR.

Preputial sample collection

The procedure for collecting preputial scrapings was adapted from Guerra et al (16). The sample was obtained from the prepuce of each bull using a 63.5-cm plastic uterine infusion pipette attached to a 20-mL syringe. The pipette was repeatedly inserted its full length into the prepuce in a back and forth fashion such that the preputial lining was scraped at least 10 times while at the same time approximately 15 mL of suction was applied by the syringe. The resulting sample was immediately transferred into a screw top vial containing 2 mL of PBS. The sample was maintained at 20°C for transport to the laboratory (25). A new sterile syringe and pipette and new latex gloves were used for each sample (Table 1).

Culture and PCR diagnostics

The culture protocol was adapted from Chaban et al (25). Fresh preputial scrapings were transported to the laboratory within 2 h of collection. Upon arrival, 300 µL aliquots were spread onto a sterile 0.65 µm mixed cellulose ester membrane filter (Millipore; Billerica, Massachusetts, USA) and placed on Skirrow (Campylobacter-selective) agar plates (Oxoid, Nepean, Ontario). After incubation of the plates for 30 min at 37°C, filter-side up, the membranes were removed and the plates were incubated for 48 h in microaerophilic conditions using GasPak EZ Campy Pouch System (BO Diagnostics, Mississauga, Ontario). Colonies with the morphology consistent with Campylobacter spp. were Gram-stained for verification then sub-cultured for 48 h under the same conditions to produce pure Campylobacter colonies for DNA extraction and PCR analysis.

Real-time PCR was completed weekly on both direct preputial DNA samples and DNA from pure Cfv colonies. The DNA was released from 200 µL prepuce scraping in PBS solution using direct heat lysis with minor alterations (4). The preputial samples were centrifuged for 5 min at 12 000 × g and the supernatant discarded (26). The preputial pellet was then re-suspended in 100 µL sterile water before heat lysis at 95°C for 10 min. Finally, samples were diluted 1:10 in sterile water before analysis using both conventional and real-time quantitative PCR (27).

The RT-PCR mixture was created using SYBR green (iQ SYBR green supermix; Bio-Rad, Mississauga, Ontario), 400 nM of each primer, and 2 µL of dilute lysate in a final volume of 25 µL. All samples were run in duplicate on a thermocycler (iCycler/MyIQ; Bio-Rad) as previously described (4) with a primer set targeting Cfv (VenSF and VenSR) (4). Each test included 1 template and positive controls, also in duplicate. Melt-curve analysis was used to indicate infection status; the lower detection limit was 103 copies. The resulting data were analyzed using commercial software (iQ5 Optical System Software, Bio-Rad). Samples with a melt curvature signature comparable to the positive control, peak signal of 78.5°C ± 0.5°C [mean ± standard deviation (SD)], and threshold cycle (Ct) value < 35 were considered positive.

Identification of the Cfv organisms and pure Cfv colonies at both the species and subspecies levels was confirmed with a series of conventional PCR tests of pure sub-cultured colony DNA lysate. In the first step, the highly conserved insertion gene, iscF1, was used for subspecies identification (28). A second multiplex PCR was used to confirm the species (i.e. Campylobacter fetus) and provide additional evidence to differentiate between subspecies (i.e., C. fetus fetus versus C. fetus venerealis) as per Hum et al. (29). The carbon starvation gene (cstA) identifies the species level, while the plasmid stabilization protein gene (para) provides additional information to differentiate the subspecies. The PCR products were resolved by gel electrophoresis (110 V, 40 min) on a 1.5% agarose gel stained with ethidium bromide (Fisher Scientific, Ottawa, Ontario) and visualised under UV light. Positively identified PCR products were purified using QIAquick PCR Purification Kit (Qiagen, Valencia, California, USA), and sequenced through Macrogen Inc. (Seoul, Korea). Sequence results were aligned using the Staden Software Package 2.1.0.0b9. A BLAST search was completed for consensus sequences on the National Center for Biotechnology Information (NCBI) website: (http://www.ncbi.nlm.nih.gov) for verification of identity.

Conventional PCR and PCR product sequence analysis was performed 4 times throughout the trial.
Whole genome sequencing

Due to some controversy in the literature regarding the specificity of the available PCR primers (14), we definitively verified the identity of the isolates used in the infection trial by submitting DNA from the Cfv isolates for whole genome sequencing (WGS) through Macrogen (South Korea) at the conclusion of the study. Isolates were selected and expanded in triplicate on Skirrow plates as described. Each plate was washed with 1.5 mL PBS then pelleted by centrifugation for 10 min at 21 000 × g. The DNA was extracted using a modified salting out procedure (30) then combined in various quantities until the desired concentration of 1 μg per sample was achieved. Quality and quantity were rechecked using a Nanodrop 2000 and a Qubit Fluorometer 3.0 (Thermofisher Scientific). Additional quality tests included running 10 μL DNA on 1% agarose gel at 90 V for 1 h to monitor for shearing and assure high quality samples were submitted.

Campylobacter fetus DNA of adequate quality was sequenced from isolates from 4 of the artificially infected bulls. The FASTA sequences resulting from the analysis were uploaded to the NCBI nucleotide site and a BLAST search was undertaken for highly similar sequences (megablast) using default settings to confirm the identity of isolates as Cfv (Appendix 1 — available on request from the corresponding author).

Statistical analysis

All data were entered into a spreadsheet and analyzed using Stata 13 for Windows (StataCorp LP, College Station, Texas, USA). Criteria for whether bulls were positive or negative were adapted from Guerra et al (16). All bulls were considered positive before treatment if they had at least 2 positive weekly tests at the time of treatment. A bull was considered negative if it had 4 consecutive negative tests (16).

Sampling times and results in the observation period following treatment were summarized into three 21-day periods representative of three 21-day estrous cycle periods which constitute an industry recommended 63-day breeding season (Table 1). The first 21-day cycle, which was also the first observation period, began on Week 4 or 2 wk after the final treatment (Week 2). The start of the post-treatment observation period (OP) was set assuming the final treatment would require at least 2 wk to be effective and, therefore, if recommended for field use the series of treatments would be completed at least 2 wk before commencement of a breeding season.

The sample collected on Day 21 of Period 1 (or Week 7) represented the status of the bull at the end of Period 1. The sample collected on Day 21 of Period 1 was also considered to represent the bull’s status for Day 1 of Period 2. An outline of the treatment and subsequent sampling periods is shown in Table 1. For a bull to have been considered test negative at the end of a complete 21-day OP, it needed to have a negative test on all 4 test days linked to the period (Days 1, 7, 14, and 21). If the bull was positive on any 1 test day during the respective period, it was considered test positive for that period.

A Wilcoxon rank-sum test was used to evaluate the differences in weight between the bulls in the treatment and control groups. The differences in Cfv infection between the treated and untreated groups were estimated for each period using exact logistic regression. Odds ratios and exact 95% confidence intervals (CI) were calculated to compare the odds of control bulls being positive for Cfv compared with the treated bulls. A P-value < 0.05 was considered statistically significant. The differences for control versus treated bulls were determined for 21-day cycle results summarized from weekly culture results confirmed with PCR, direct RT-PCR of preputial aspirates, and combined results for culture and prepuce RT-PCR. The joint interpretation of both culture and direct RT-PCR represented parallel interpretation of the 2 tests and was evaluated to optimize the sensitivity of the analysis.

Results

Of the 15 Cfv infected bulls used in the project, 5 were 3 y old and 2 were 5 y old. Age records were not available for the remaining 8 bulls, but physical appearance and size suggested they were at least 3 y of age. The bulls ranged in weight from 827 kg to 1102 kg with an average weight of 953 kg and a median weight of 939 kg. There was no difference in weights (P = 0.5) between the bulls assigned to the treatment and control groups. The 15 bulls included 8 Black Angus, 3 Simmental, 2 Red Angus, and 2 Charolais. None of the bulls required antibiotic treatment for other reasons during the study.

All 15 bulls were culture and PCR-positive on at least 2 weekly samples after inoculation of the naïve bulls with Cfv and before the 2 treatment sets were complete. Whole genome sequences of Campylobacter isolates from 4 of the artificially infected bulls provided definitive confirmation that the organisms used for artificial infections were Cfv (Appendix 1). The best match was to Cfv str. 84-112, complete genome GenBank: HG004426.1 (29,30).

Individual bull test results during the post-treatment observation period (OP) differed between the preputial scrapings cultured and verified with PCR (Figure 1) compared with scrapings analyzed by direct RT-PCR (Figure 2). The results of the 2 tests were then combined to facilitate parallel interpretation (Figure 3) and optimize sensitivity. One control bull was negative based on preputial scraping culture PCR throughout the three 21-day post-treatment OP (Figure 1); however, the bull did test positive once in the final of the three 21-day periods with the direct RT-PCR test (Figure 2).

Only 2 of the 7 treated bulls had at least 1 culture positive preputial scraping confirmed by PCR during the OP (Figure 1). One bull’s preputial scraping culture tested PCR positive once on Day 14 of the first 21-day period and then never tested positive again. The second bull’s preputial scraping culture tested PCR positive on Day 14 of the second 21-day period and Day 21 of the third 21-day period.

For the direct RT-PCR on the preputial scraping only 2 of the 7 treated bulls remained negative throughout the three 21-day post-treatment observation periods (Figure 2). In the first 21-day period there was only 1 direct RT-PCR test positive bull; however, it was not the same bull that had a positive culture result. Three bulls had a positive direct RT-PCR result during the second 21-day period and 4 of 7 bulls had a positive RT-PCR result during the third 21-day OP.
When the results of both culture and direct preputial RT-PCR were considered in parallel [i.e., the bulls that were positive in either of the 2 tests were considered test-positive (Figure 3)] all untreated, control bulls were positive at least once during the OP and all but 1 of the treated bulls were also positive at least once.

If only the preputial cultures confirmed with PCR were considered (Figure 1), the odds that control bulls would test positive for \textit{Campylobacter fetus} were 27.2 times higher than for the treated bulls \((P = 0.02)\) in all three 21-day post-treatment observation periods (Table 2). When only the results of the direct RT-PCR test were evaluated (Figure 2), control bulls were 27.2 times more likely to be positive for \textit{Cf} \((P = 0.02)\), but only in the first 21-day period (Table 2).

When the results of both culture and the direct PCR test were considered in parallel, there was no significant difference in the odds of a positive test result for any of the 21-day post-treatment OP, although the difference between treated and untreated bulls in the first 21-day period \((P = 0.07)\) (Table 2).

No serious side effects were observed in any of the 7 treated bulls. However, 5 bulls developed injection site swellings from either the vaccine (2 bulls) or long-acting oxytetracycline (3 bulls). The swellings were small and resolved with no long-term complications.

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**Figure 1.** Culture PCR results summarized for individual bulls beginning 2 wk after the second of 2 treatments with injectable oxytetracycline and 2 doses of monovalent \textit{Campylobacter fetus} vaccine. Bulls were reported as positive if they had at least 1 positive test result on day 1, 7, 14, or 21 for each of the subsequent three 21-day observation periods. A bull was reported as negative for a period if he was test negative on all 4 samples considered part of that period.

* Results were negative for direct prepuce PCR for 2 of 4 samples and 2 samples were undetermined due to fungal overgrowth.

**Figure 2.** Direct prepuce PCR results summarized for individual bulls beginning 2 wk after the second of 2 treatments with injectable oxytetracycline and 2 doses of monovalent \textit{Campylobacter fetus} vaccine. Bulls were reported as positive if they had at least 1 positive test result on day 1, 7, 14, or 21 for each of the subsequent three 21-day observation periods. A bull was reported as negative for a period if he was test negative on all 4 samples considered part of that period.
Discussion

The main objective of this study was to determine if a multimodal treatment approach, using a combination of vaccination and long-acting antimicrobial therapy, would reduce or eliminate shedding of \( C.\) fetus in chronically infected carrier bulls. Two treatments with long-acting oxytetracycline at label doses and a commercial monovalent bacterin did not eliminate BGC in all study bulls. There was also no significant difference between the proportion of treated and untreated bulls that tested positive when the results of both culture and direct RT-PCR were considered. The 2 test results were combined to optimize the sensitivity of the testing protocol detection of BGC post-treatment because of the severe consequences of false negatives.

When the results of each diagnostic test were observed separately, there was a significant reduction in the likelihood that a treated bull would test positive based on culture for all 3 post-treatment 21-day observation periods and for direct RT-PCR of the preputial samples for the first 21-day OP (Table 2). One potential argument for considering the results of culture alone would be that culture definitively identifies bulls shedding live organisms; whereas direct RT-PCR could potentially identify DNA from nonviable organisms that would not be a risk for transmission. However, in the current study the observed frequency of RT-PCR positive bulls increased throughout the trial which is consistent with what we would expect with increasing time after treatment. If the RT-PCR results are correct and the preputial cultures were less sensitive than RT-PCR during the post-treatment monitoring phase, the lower sensitivity may have been due to death of \( C.\) fetus during transport to the laboratory and decreasing environmental temperature during collection in September and October.

The clinical specificity of bacterial culture (100%) is higher than that of RT-PCR (85%) under field conditions in western Canada (16), suggesting the potential for false positive RT-PCR tests. However, recent field data suggest that the difference in the risk of false positives might not be as large as previously reported especially in situations with high pretest probability of infection (31). Previous studies reported similar sensitivities for bacterial culture using the methods described herein and RT-PCR (82.3% and 85.4%, respectively) (16). The published estimates of clinical sensitivity for culture, however, were based on samples delivered to the laboratory substantially faster than in the present study (< 30 min). Also, all samples for that study were collected in June and July in an insulated barn, potentially leading to higher culture sensitivity than that in the present study. Previous studies have shown that the sensitivity of the RT-PCR is resilient to the time delays and transport conditions seen herein (32).

Another argument for considering the treatment as potentially successful would be the tendency for a difference between treatments in the first 21-day post-treatment OP when the results of both culture and RT-PCR were considered. The failure to detect a significant result was very likely a reflection of limited study power. The precision of the estimates of effect for all testing methods was affected by the small number of bulls in this study. However, regardless of the statistical significance and precision of effect estimates, treatment success was not considered adequate in the present study given that 29% (first cycle), 43% (second cycle), and 71% (third cycle) of treated bulls were positive on either culture or direct PCR during post-treatment OP designed to simulate a typical breeding season. There was no complete cycle when all of the treated bulls were negative by culture or direct RT-PCR. The high potential cost of having even 1 bull remain infectious warrants a conservative interpretation of the findings.

There is relatively little good published evidence against which to compare the results of the present study; despite historical
use of topical streptomycin ointments for the treatment of vibrio-infected cattle (33). Vasquez et al (18) reported on the therapeutic efficacy of the Cfv bacterin used in the present study. Of the 10 bulls used in their 1983 study, 6 were initially vaccinated twice at a 4-week interval and 4 were kept as controls. The 6 original vaccinates tested negative by week 8 post-vaccination and the 4 controls were positive. The 4 controls were then vaccinated and 2 of these bulls infected heifers with Cfv. The authors determined that 2 of 10 vaccinated bulls remained chronically infected with Cfv and therefore did not recommend vaccination alone for treatment of Cfv. Based on this finding, we chose combination therapy with both vaccination and antimicrobials for the current study. The bulls in the present study were followed for 11 wk after vaccination compared with 8 wk in the earlier study. Other limitations of the Vasquez et al (18) study were the smaller sample size and lack of blinding.

The remaining identified published studies of vaccine trials in bulls used autogenous or experimental rather than commercial vaccines (18,19,22,34,35). Most previous studies did not use a negative control, and therefore the infections may have resolved spontaneously. Anecdotally, spontaneous recovery occurs in young bulls infected with Cfv (17). One bull in the control group for the present study tested positive twice before treatment but only once by PCR after treatment at the very end of the OP. Either this bull failed to completely spontaneously clear the experimental infection (likely) or the experimental infection did not establish in this bull and it was re-exposed later through bull-to-bull contact (less likely) (13).

Although a recent review reported that antimicrobial treatments for Cfv are impractical and of limited efficacy (14), 2 previous studies suggested some potential for antimicrobial use in management of positive bulls. The first study observed bulls that were infected by both Cfv and Tritrichomonas foetus and were treated with subcutaneous and intramuscular dimetridazole chloride (DCL) (21). Ten naturally infected bulls were confirmed positive by fluorescent antibody technique (FAT) and culture. Of the 10 bulls, 4 were infected by Cfv alone, 3 were infected by Cfv and Campylobacter fetus subsp. fetus (Cff), and 3 were infected by Cff alone. All 10 bulls were negative for Cfv and Cff by FAT and culture at each of 4 bi-weekly samplings after treatment. However, the authors acknowledged that the negative test results could be biased by sporadic resolution as no control animals were used. This previous study also used DCL, which is not allowed for use in food producing animals in Canada.

In addition to DCL, treatment with long-acting oxytetracycline and fluoroquinolone has been reported for bulls naturally infected with Cff in Argentina (23). While this paper did not directly address Cfv infection, it was the motivation for the choice of antibiotic in the present study. The Argentinian study reported 5 of 5 of bulls were negative for Cff by culture and FAME and PCR techniques directly on preputial culture and PCR. Of the 10 bulls, 4 were infected by Cfv alone, 3 were infected by Cfv and Campylobacter fetus subsp. fetus (Cff), and 3 were infected by Cff alone. All 10 bulls were negative for Cfv and Cff by FAT and culture at each of 4 bi-weekly samplings after treatment. However, the authors acknowledged that the negative test results could be biased by sporadic resolution as no control animals were used. This previous study also used DCL, which is not allowed for use in food producing animals in Canada.

A review (14) of published studies of vaccine trials in bulls with Cfv infection confirmed that prior unsuccessful attempts included long-acting oxytetracycline (0.10 mL/kg, ½ IM and ½ SC) (23). Only 1 of 7 bulls treated with fluoroquinolone was negative at 30 d. There was no negative control group. The preferred antibiotic for the present study was long-acting oxytetracycline because of its cost relative to other options, limited use in human health, wide availability in Canada, and due to its performance in the previous study. The authors acknowledged that the negative test results could be biased by sporadic resolution as no control animals were used. This previous study also used DCL, which is not allowed for use in food producing animals in Canada.

In addition to DCL, treatment with long-acting oxytetracycline and fluoroquinolone has been reported for bulls naturally infected with Cff in Argentina (23). While this paper did not directly address Cfv infection, it was the motivation for the choice of antibiotic in the present study. The Argentinian study reported 5 of 5 of bulls were negative for Cff by culture and FAME and PCR techniques directly on preputial culture and PCR. Of the 10 bulls, 4 were infected by Cfv alone, 3 were infected by Cfv and Campylobacter fetus subsp. fetus (Cff), and 3 were infected by Cff alone. All 10 bulls were negative for Cfv and Cff by FAT and culture at each of 4 bi-weekly samplings after treatment. However, the authors acknowledged that the negative test results could be biased by sporadic resolution as no control animals were used. This previous study also used DCL, which is not allowed for use in food producing animals in Canada.
or to moderate temperature changes (32). The sensitivity of the direct PCR also improves with repeated sampling employed in this study (16). The specificity of diagnosis for the agent used in the experimental infection and the isolates recovered during the trial was assured with conventional PCR using multiple primers followed by whole genome sequencing for a subset of isolates.

The differences in results between the RT-PCR of the direct prepuce samples and culture results observed in this study might be attributed to the limited sensitivity of culture under field conditions (14,25) or the limited sensitivity and specificity of the direct RT-PCR (16). While samples were collected as quickly as possible and efforts were made to hold the samples at a constant temperature and then deliver them directly to the laboratory, there is the potential for loss of viability due to the time lag and temperature fluctuations between collection and plating for culture, given the susceptibility of Cfv to adverse environmental conditions (25).

While this study does provide the first randomized, controlled, and blinded trial on combined therapy with commercially licensed products, increasing the number of animals in this study would have resulted in more precise estimates of the effect of combined vaccination and treatment on Cfv status in mature beef bulls. Subsequent studies should consider other commercially licensed long-acting antimicrobials or emerging alternatives to antimicrobial therapy.

Acknowledgments

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Retrospective evaluation of toceranib (Palladia) treatment for canine metastatic appendicular osteosarcoma

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

Abstract — This retrospective study evaluated the outcomes of dogs with macroscopic pulmonary metastasis of appendicular osteosarcoma (OSA) treated with toceranib. Medical records of 20 dogs with macroscopic pulmonary metastasis of OSA that received toceranib were reviewed. The median dose and duration of toceranib administration were 2.52 mg/kg (range: 2.12 to 2.72 mg/kg) and 60 days (range: 17 to 231 days). The median progression free survival (PFS) and overall survival (OS) were 36 days (range: 17 to 231 days) and 90 days (range: 17 to 433 days), respectively. The clinical benefit rate was 10% (2/20; 1 partial response and 1 stable disease). The longest length of initial pulmonary nodules had significant impact on both PFS (\( P = 0.01 \)) and OS (\( P = 0.02 \)). The prognosis for dogs with metastatic OSA was poor with only 10% of dogs showing clinical benefit from toceranib. These results suggest that toceranib may not improve outcome in dogs with macroscopic pulmonary metastasis of OSA.

Résumé — Évaluation rétrospective du traitement avec tocéranib (Palladia) pour l’ostéosarcome appendiculaire métastatique canin. Cette étude rétrospective a évalué les résultats des chiens souffrant de métastase pulmonaire macroscopique de l’ostéosarcome appendiculaire (OSE) traité avec tocéranib. Les dossiers médicaux de 20 chiens atteints de métastase pulmonaire macroscopique d’OSE qui ont reçu tocéranib ont été évalués. La dose médiane et la durée de l’administration de tocéranib étaient de 2,52 mg/kg (étendue de 2,12 à 2,72 mg/kg) et de 60 jours (étendue de 17 à 231 jours). La progression de survie libre (PSL) médiane et la survie totale (ST) étaient de 36 jours (étendue de 17 à 231 jours) et de 90 jours (étendue de 17 à 433 jours), respectivement. Le taux de bienfaits cliniques étaient de 10 % (2/20 ; 1 réponse partielle et 1 maladie stable). Le plus long intervalle avant l’apparition des nodules pulmonaires initiaux avait un impact important sur la PSL (\( P = 0.01 \)) et la ST (\( P = 0.02 \)). Le pronostic pour les chiens atteints d’OSE métastatique était mauvais et seulement 10 % des chiens ont manifesté des bienfaits cliniques lors de l’usage de tocéranib. Ces résultats suggèrent que le tocéranib pourraient ne pas améliorer les résultats cliniques chez les chiens souffrant de métastase pulmonaire macroscopique causée par OSE.


Introduction

Osteosarcoma (OSA), the most common primary bone tumor in dogs, can occur at various locations on the body. Appendicular OSA is the most prevalent type, however, comprising up to 85% of cases (1). The reported median survival time for dogs with appendicular OSA is 4 to 5 mo with amputation alone; the addition of adjuvant chemotherapy improves median survival times to 8 to 12 mo (2). Despite the improved overall outcome of this disease with chemotherapy, a positive response to conventional chemotherapy has not been observed in dogs with macroscopic pulmonary metastasis of OSA (3–5). Therefore, a new focus of treatment is shifting from standard cytotoxic approaches to targeted therapeutics in an attempt to suppress the growth of metastatic tumor cells (6–13). Among the various mechanisms associated with the process of tumor metastasis, tumor angiogenesis is known to play an important role in the metastatic process and has been a validated therapeutic target for various tumors (14).

The involvement of vascular endothelial growth factor (VEGF) and its receptor (VEGFR) in tumor angiogenesis has been reported in many studies (15–17). Tumor cells can drive the migration of VEGFR2 expressing circulating endothelial precursors (CEPs) from the bone marrow to the tumor microenvironment through the production of VEGF (18–20). Anti-VEGF/VEGFR therapy has been shown to decrease survival signaling and mobilization of CEPs to the site of tumor growth (21). These findings led to further studies with small molecule receptor tyrosine kinase (RTK) inhibitors such as sunitinib and sorafenib in preclinical settings. Both drugs were found to inhibit the proliferation of OSA cell lines in vitro and sunitinib...
treatment significantly reduced tumor burden, microvessel density, and pulmonary metastasis in a human xenograft OSA mouse model. These results suggested potential use of these drugs for OSA treatment (22,23).

Vascular endothelial growth factor is detectable in both human and canine OSA, and has been associated with increased malignancy and poor prognosis (24–29). Toceranib, a small molecule RTK inhibitor, has generated interest in veterinary medicine as a potential treatment option for metastatic OSA. Toceranib targets several members of the split-kinase family such as VEGFR, platelet-derived growth factor receptor (PDGFR), Kit, colony stimulating factor-1 receptor (CSF-1R), and Fms Related Tyrosine Kinase 3 (Flt-3) (30–32). A previous study revealed that a 2.4 to 2.9 mg/kg body weight (BW), q48h dose of toceranib significantly increased plasma VEGF, indicating VEGFR2 inhibition, suggesting that this concentration of toceranib may be considered for the treatment of VEGF-driven metastatic tumor (33).

In the setting of metastatic canine OSA, a retrospective multi-institutional study showed that 11/23 (47.8%) dogs experienced clinical benefit including 1 partial response and 10 stable disease (no progression nor new lesion for at least 10 wk) with toceranib treatment (13). The reported median duration of treatment for the 11 dogs that experienced clinical benefit was 24 wk, which suggested potential use of toceranib for the treatment of macroscopic metastatic OSA. In a recent randomized prospective clinical trial (12), however, the addition of toceranib to metronomic piroxicam/cyclophosphamide chemotherapy following limb amputation and adjuvant carboplatin chemotherapy failed to show any improvement in the outcome of dogs with appendicular OSA. This study raised a question regarding the benefit of toceranib treatment for microscopic metastatic OSA. The efficacy of toceranib treatment, however, is difficult to evaluate solely based on these studies because standardization of treatment and recheck protocols were lacking in the retrospective study while most dogs were removed from the prospective study once metastasis was present.

Conclusive data to support the use of toceranib for metastatic canine OSA has not been established. Therefore, the purpose of the current study was to evaluate the efficacy of toceranib treatment for macroscopic pulmonary metastasis of appendicular OSA in dogs. A secondary goal was to identify prognostic factors in this subset of the population.

Materials and methods

Case selection

Electronic and hard copy medical records from the Ontario Veterinary College from October 2011 to June 2016 were reviewed. Dogs that were cytologically or histologically diagnosed with appendicular OSA, had pulmonary metastasis confirmed by thoracic radiographs, and received toceranib treatment were included. For response evaluation, only dogs with follow-up thoracic radiographs were included.

Treatment protocol

Following confirmation of pulmonary nodules by 3-view thoracic radiographs, dogs were prescribed toceranib at a target dose of 2.5 mg/kg BW, PO, 3 times per week on Monday, Wednesday, and Friday (MWF). Monthly 3-view thoracic radiographs were recommended to monitor tumor response. The primary endpoint of toceranib treatment was the time when evidence of disease progression was observed. All dogs had baseline complete blood (cell) counts (CBC) and biochemistry before toceranib treatment. To monitor for toxicity during toceranib treatment, CBCs were performed every 2 wk for the first month and repeated monthly; serial biochemistry panels were performed monthly.

Medical records review. Information recorded included signalment, thoracic radiography results, histology or cytology results, primary tumor location, date of diagnosis of pulmonary metastasis, number and size (recorded as longest length) of pulmonary metastases, previous treatments, dose and duration of toceranib treatment, and adverse effects. Follow-up information was documented including monitoring pulmonary metastases via radiographs to determine progression-free survival (PFS) and overall survival (OS) (Table 1). Progression-free survival was defined as the time from the first toceranib treatment to progression of the disease or death from any cause. Overall survival was defined as the time from the first toceranib treatment to death from any cause. Progression-free survival and OS were obtained from the medical records or by contacting the referring veterinarians and/or the owners. Toxicities were graded according to the Veterinary Cooperative Oncology Group-Common Terminology Criteria for Adverse Events criteria (34).

Response to therapy. Modified response evaluation criteria in solid tumor (RECIST) was used for assessment of response to toceranib treatment (35). Response to therapy was defined as: complete response (CR), resolution of all target and non-target lesions and no new lesions; partial response (PR), at least 30% decrease in the longest diameter of the target lesions, no

<table>
<thead>
<tr>
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<th>P-values</th>
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progression of non-target lesions and no new lesions; stable disease (SD), decrease in the longest diameter of target lesions of < 30% or increase of target lesions < 20%, no progression of non-target lesions and no new lesions for at least 10 wk; or progressive disease (PD), > 20% increase in the longest diameter of target lesions, progression of non-target lesions and identification of new lesions. Clinical benefit (CB) was defined as CR, PR, or SD.

Statistical analysis. Kaplan-Meier survival curves were generated for median PFS and OS. All 20 dogs were included in PFS analysis while 1 dog still alive at the end of the study was censored from OS analysis. A Cox proportional hazards univariate analysis was used on variables including signalment, body weight, primary tumor location, previous treatment, dose and duration of toceranib treatment, longest length and number of pulmonary nodules, and concurrent metronomic treatment. In order to evaluate the impact of previous treatments, dogs were assigned to 1 of 4 treatment groups for analysis; surgery alone (n = 4), surgery and carboplatin (n = 10), surgery and carboplatin followed by metronomic treatment (n = 3), and others [radiation (n = 1); surgery and doxorubicin (n = 1); no therapy (n = 1)]. For further analysis of the number of initial pulmonary nodules, dogs were assigned to one of 3 groups based on the number of pulmonary nodules (low < 3, intermediate > 3 to ≤ 5, high > 5). For all analyses, a P-value < 0.05 was deemed significant. Statistical software (IBM SPSS Statistics version 23 software for Windows; SPSS, Chicago, Illinois, USA) was used for statistical analysis.

Results

A total of 29 dogs received toceranib treatment for macroscopic pulmonary metastasis of appendicular OSA during the study period. Nine dogs were excluded due to absence of follow-up thoracic radiographs (n = 6) or non-confirmation of diagnosis by cytology or histology (n = 3). The 20 remaining dogs consisted of 14 breeds including Rottweiler (n = 3), Labrador retriever (n = 2), doberman pinscher (n = 2), golden retriever (n = 2), mixed-breed (n = 2), and 1 each of American pit bull terrier, Australian shepherd, border collie, cocker spaniel, Scottish deerhound, Dogue de Bordeaux, English bulldog, great Dane, and mastiff. The median body weight was 31.6 kg (range: 13.4 to 61.2 kg), and the median age was 6.8 y (range: 1.7 to 13.2 y). There were 11 spayed females, 1 intact female, and 8 castrated males. The primary tumor was located in the humerus (n = 5), tibia (n = 5), femur (n = 4), radius (n = 2), scapula (n = 2), ulna (n = 1), and radius/ulna (n = 1).

The median dose and duration of toceranib were 2.52 mg/kg BW (range: 2.12 to 2.72 mg/kg) and 60 d (range: 17 to 231 d), respectively. During the course of treatment, all dogs received toceranib 3 times/week on MWF. Nineteen of the 20 dogs received other treatments prior to toceranib treatment: surgery (limb amputation, n = 15; scapulectomy, n = 1; acetabulectomy, n = 1; ulnar ostectomy, n = 1), chemotherapy (carboplatin, n = 13; doxorubicin, n = 1; metronomic cyclophosphamide, n = 3), and/or radiation therapy (n = 2). Of the 13 dogs receiving carboplatin, 3 dogs also received metronomic cyclophosphamide following carboplatin before starting the toceranib treatment. Six dogs were treated with toceranib and concurrent metronomic treatments (chlorambucil, n = 2; cyclophosphamide, n = 4), while 2 dogs received concurrent radiation therapy. Two dogs received follow-up chemotherapy after the toceranib treatment was discontinued (doxorubicin, n = 1; metronomic cyclophosphamide, n = 1). Other medications used include pamidronate (n = 1 before toceranib; n = 4 with toceranib), non-steroidal anti-inflammatory drugs (n = 6 with toceranib), and prednisone (n = 2 with toceranib; n = 4 after toceranib).

The most common adverse effects (AE) were gastrointestinal (GI), consisting of grade 3 GI AE in 3 dogs and grade 1 or 2 GI AE in 4 dogs. Three dogs had changes in the dose of toceranib during the treatment; the dose of toceranib was

Figure 1. Kaplan-Meier progression free survival (PFS) curve for dogs with macroscopic pulmonary metastasis of appendicular OSA treated with toceranib (n = 20). The median PFS was 36 days.

Figure 2. Kaplan-Meier overall survival (OS) curve for dogs with macroscopic pulmonary metastasis of appendicular OSA treated with toceranib (n = 20). One dog alive at the end of study was censored (+ mark). The median OS was 90 days.
reduced in 2 dogs (2.61 to 2.24 mg/kg BW and 2.61 mg/kg BW to 2.23 mg/kg BW) with grade 3 GI AE; the dose was increased in 1 dog (2.29 mg/kg BW to 2.72 mg/kg BW) due to the progression of pulmonary metastasis. Grade 1 alanine aminotransferase (ALT) and alkaline phosphatase (ALP) elevations were found in 1 and 5 dogs, respectively. Only 1 dog had grade 3 neutropenia during the course of toceranib treatment. However, no clinical signs were associated with the neutropenia and the neutrophil count returned to normal in 2 wk without any supportive treatment or delay of toceranib treatment. This dog received a 2.6 mg/kg BW dose of toceranib for 27 d. The reasons for discontinuation of toceranib were GI AEs (n = 7), death (n = 6), progression of pulmonary metastasis (n = 4), or lameness (n = 3).

All dogs had pulmonary metastasis confirmed by thoracic radiographs that were reviewed by a radiologist. The median time from the diagnosis of OSA to development of pulmonary metastasis was 113 d (range: 0 to 691 d). Three dogs had pulmonary metastasis at the time of OSA diagnosis. The median longest length of pulmonary nodules was 12 mm (range: 5 to 99 mm). Based on the number of initial pulmonary nodules on radiographs, there were 9, 6, and 5 dogs in low, intermediate, and high groups, respectively.

Four dogs had postmortem evaluation, which confirmed the presence of metastatic OSA in the lungs. Three of these dogs also had metastasis in multiple organs including kidney, pleura, pericardium, myocardium, small intestine, subcutaneous tissue, and skeletal muscle.

The median PFS and OS for toceranib treatment were 36 d (range: 17 to 231 d) and 90 d (range: 17 to 433 d), respectively (Figures 1 and 2). One dog still alive at the time of analysis was censored from the OS analysis (day 380). There was 1 PR and 2 CR in the 2 dogs that experienced CB. A possible explanation for this difference might be more frequent toceranib treatment in the previous study. In that study, 10/23 dogs received the drug every other day, whereas all dogs in the present study were treated on MWF schedule. Another potential difference between the 2 studies could be the schedule of the follow-up radiographs. The schedule of rechecks was not clearly defined in the previous study and unlikely standardized due to the nature of a multi-institutional retrospective study. Thus, it is possible that less frequent rechecks with thoracic radiographs might delay the detection of progression, which might have falsely increased the median PFS. It is also important to note that the previous study solicited the cases by the e-mail-based forum (American College of Veterinary Internal Medicine Oncology Listserve). This method might have caused a selection bias in the process by highlighting the minority of cases that had good responses to the toceranib treatment.

The longest length of initial pulmonary nodules was a prognostic factor identified for both PFS (P = 0.01, HR = 1.041) and OS (P = 0.02, HR = 1.087) (Tables 2, 3). Body weight had a significant impact on PFS (P = 0.01, HR = 0.998) (Table 2). The duration of toceranib treatment had a significant impact on OS (P = 0.03, HR = 0.985) (Table 3). No statistical significance was found in the other analyzed variables.

**Discussion**

The improvement in median survival times of dogs with appendicular OSA by the use of adjuvant chemotherapy has demonstrated that this is a chemosensitive disease in its early stages. However, the proportion of dogs cured or with long-term survival (> 2-year survival) remains intractably low at ~20% in spite of the adjuvant use of diverse approaches of chemotherapy (36,37). Furthermore, most OSA patients die of pulmonary metastasis, and chemotherapy has not been proven effective to delay progression of macroscopic metastases after their development. Ogilvie et al (3) evaluated single agent chemotherapy for macroscopic metastatic OSA in 45 dogs and found 1 dog achieved partial response for 21 d and the remaining dogs had a median survival time of 61 d without an objective response (3). They concluded that the chemotherapy agents used in the study were ineffective for the treatment of measurable metastatic OSA in the dog. A similar poor prognosis was shown in retrospective studies by Boston et al (4) and Batschinski et al (5) in which median survival time was reported as 76 d and 95 d, respectively. The latter studies corroborated the lack of efficacy of conventional chemotherapy against macroscopic pulmonary metastasis of OSA. These outcomes are comparable with the outcome herein, which suggests that macroscopic metastatic OSA is resistant to chemotherapy, including the kinase inhibitor toceranib in this study.

The poor outcome of the present study with 36 d of PFS contrasts with the previous study by London et al (13), which had a CB rate of 47.8% and a median PFS of 24 wk in the dogs that experienced CB. A possible explanation for this difference might be more frequent toceranib treatment in the previous study. In that study, 10/23 dogs received the drug every other day, whereas all dogs in the present study were treated on MWF schedule. Another potential difference between the 2 studies could be the schedule of the follow-up radiographs. The schedule of rechecks was not clearly defined in the previous study and unlikely standardized due to the nature of a multi-institutional retrospective study. Thus, it is possible that less frequent rechecks with thoracic radiographs might delay the detection of progression, which might have falsely increased the median PFS. It is also important to note that the previous study solicited the cases by the e-mail-based forum (American College of Veterinary Internal Medicine Oncology Listserve). This method might have caused a selection bias in the process by highlighting the minority of cases that had good responses to the toceranib treatment.
nODULES is high. However, the number of initial pulmonary nodules did not have an impact on either PFS or OS in the present study, which suggests that the longest length of pulmonary nodules might be a better representation of the overall tumor burden in the lungs. However, the lack of correlation between the number of pulmonary nodules and the outcome of this study might be the result of type II error due to the small sample size. The magnitude of the pulmonary metastatic burden in the dogs from the 2 studies could also have affected the results. This hypothesis could not be verified at this time since the information used to compare the magnitude of pulmonary metastasis, such as measurements and numbers of pulmonary nodules, was absent in the previous study. However, given that the addition of toceranib to metronomic chemotherapy/piroxicam adjuvant treatment in a previous study did not improve the outcome in microscopic metastatic OSA, it is possible that the magnitude of pulmonary metastatic burden might not impact the outcome with toceranib treatment. In the present study, 6/20 dogs received concurrent metronomic treatments during the toceranib treatment; however, it was not found to have a significant impact in the evaluation of prognostic factors.

There were other factors affecting PFS or OS in this study. Body weight was found to impact PFS ($P = 0.01$, HR = 0.951). The reason for this finding is not clear. It is possible that the dogs' body condition scores (BCS) affected the toceranib doses for each patient, as weight-based prescriptions tend to overexpose obese patients (38). This speculation could not be confirmed because BCS was not consistently recorded. The duration of toceranib treatment also had a positive impact on OS ($P = 0.03$, HR = 0.985). This result should be interpreted with caution, as dogs with longer survival were likely to have received toceranib for longer periods of time.

The most common toxicity was GI AE (7/20, 35%), characterized by inappetence, vomiting, diarrhea, or a combination of these. However, due to the presence of systemic OSA and the retrospective nature of the study, it is not possible to differentiate these adverse events from signs related to disease progression although OSA is less likely the cause of the GI signs given the usual metastatic pattern of OSA (39). Hematologic toxicity was rare. Grade 3 neutropenia occurred in 1 dog (1/20) and it was resolved in 2 wk without any further supportive treatments or drug holidays. No other hematologic toxicities were observed. This AE profile of common GI and rare hematologic toxicities is consistent with the previous report of the study evaluating the efficacy of toceranib in dogs with solid malignancies. In that study, GI toxicity was commonly seen (diarrhea 51.8%; anorexia 35.3%; vomiting 18.8%); neutropenia was only seen in 10.6% of patients (13). This similarity in toxicity profiles might be explained by the similar toceranib doses that were used between the previous (median doses between 2.67 to 2.87 mg/kg BW) and present studies (median dose: 2.52 mg/kg BW). Alterations in biochemical parameters were noted in 5 dogs (5/20). The most common biochemical toxicity was grade 1 ALP elevation (4/20) followed by ALT elevation (1/20). The clinical relevance of these abnormalities was not investigated. Transient liver enzyme elevations are consistent with the results of a study in which transient grade 1 ALT elevation was noted in 7 dogs (7/40) and grade 1 and grade 3 ALP elevations were observed in 10 dogs (10/40) and 1 dog (1/40), respectively (33). No dogs in that study were reported to have developed clinical evidence of hepatotoxicity. Three dogs had their toceranib treatment discontinued due to progression or new development of lameness. The lameness might be associated with an adverse effect of the toceranib treatment as lameness has been reported to be an adverse effect in previous studies (30,31,33). However, the lameness in 2 of the dogs was suspected to be due to the progression of OSA because the lameness occurred in the same limb that had been previously diagnosed with primary OSA. The other dog might have had the lameness as a true adverse effect from the toceranib treatment, but other possibilities such as metastasis cannot be ruled out as no further evaluation was performed at that time.

Some limitations exist in the present study because of its retrospective design with a relatively small number of patients and absence of standardization of treatments. The statistical power for this study is weak because each group in the Cox analysis had limited sample sizes, which increases the chance of type II error. Due to the small number of patients some valuable analyses could not be performed. For example, the effects of follow-up chemotherapy could not be evaluated because only 2 dogs received follow-up chemotherapy after the toceranib treatment failed. However, positive effects of follow-up chemotherapy are not expected given that no study has demonstrated chemosensitizer effects of toceranib and the general prognosis of this disease with conventional chemotherapy is poor. Similarly, the prognostic value of ALP elevation was not analyzed since only 2 dogs had ALP elevation before the toceranib treatment. The lack of complete information in this study also caused limitations; possible adverse effects including proteinuria and hypertension might have been overlooked because urinalysis and blood pressure measurement were not routinely conducted during the toceranib treatment. A lack of full staging tests before toceranib treatment and a lack of antemortem biopsy or postmortem evaluation meant that some of the pulmonary nodules might not have been due to OSA. Another limitation is that thoracic radiographs were used to measure the pulmonary nodules. According to the recommendation from the RECIST working group, thoracic radiograph measurement of lesions surrounded by pulmonary parenchyma is acceptable, but not preferable as the measurement represents a summation of densities. In conjunction with poor identification of new lesions within the thorax on radiograph as compared with CT, CT is a preferable modality for detection or measurement of pulmonary nodules. However, availability and cost of CT scan pose limitations in use of this modality for regular staging tests and recheck evaluations. The findings with radiographs in this study might be practical and relevant in many clinical settings. The other limitation was the various toceranib doses that were used in this study and the fact that 6/20 dogs received < 2.4 mg/kg BW on the MWF schedule. A previous study showed dogs dosed with > 2.4 mg/kg BW toceranib achieved a plasma concentration predicted to produce effective target inhibition (33). Given the study result, it is possible that the 6 dogs might not have achieved sufficient plasma concentrations to show efficacy of...
the treatment. This limitation could be addressed by setting up a minimum required dose of toceranib of 2.4 mg/kg BW in future studies.

In conclusion, the outcome of dogs with pulmonary metastasis from appendicular OSA treated with toceranib was similar to that of dogs treated with conventional chemotherapy, with short response duration and low CB rate. The prognosis for dogs with metastatic OSA was guarded in the present study with a median OS 90 d. This result suggests that single-agent toceranib treatment might not be an effective treatment for macroscopic pulmonary metastasis of appendicular OSA. The longest length of initial pulmonary nodules was a prognostic factor identified for both PFS and MST. Prospective studies using standardized criteria are warranted to evaluate the efficacy of toceranib for the treatment of macroscopic pulmonary metastasis in dogs with appendicular OSA.

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Evaluation of the effect of umbilical hernias on play behaviors in growing pigs

Melissa Atkinson, Rocio Amezcua, Josepha DeLay, Tina Widowski, Robert Friendship

Abstract — Umbilical hernias (UH) are common in pigs and are an animal welfare concern. This study used an assessment of play behavior to evaluate the welfare of pigs with UH. Twenty-one grower pigs with UH and 17 without hernias (WUH) were assigned to 16 playing groups (PG) of 2 or 3 pigs (with at least 1 UH pig per PG). The time each animal was engaged in any of the defined playing behaviors for locomotor/social or toy play behaviors was recorded. Mixed Poisson or negative binomial and linear models were used to determine the effect of UH and day of session, accounting for the cluster of pigs within groups, on the frequency of each play behavior, and playing times. Pigs with UH had the same frequency of most play behaviors and playing times as pigs without hernias. There was no indication that the presence of UH-affected play behavior or performance in pigs.

Résumé — Évaluation de l’effet des hernies ombilicales sur les comportements de jeu chez les porcs en croissance. Les hernies ombilicales (HO) sont communes chez les porcs et elles représentent une préoccupation liée au bien-être animal. Cette étude a utilisé une évaluation du comportement de jeu afin d’évaluer le bien-être des porcs ayant une HO. Vingt-et-un porcs en croissance ayant une HO et 17 sans hernies (SHO) ont été assignés à 16 groupes de jeu (GJ) de 2 ou 3 porcs (avec au moins 1 porc HO par GJ). Le temps consacré par chaque animal pour participer à l’un des comportements de jeu définis pour les comportements de jeu de locomotion/social ou de jouet a été consigné. Des modèles mixtes de Poisson ou binomiaux et linéaires négatifs ont été utilisés pour déterminer l’effet de HO et le jour de la séance, en tenant compte des regroupements de porcs au sein des groupes, de la fréquence de chaque comportement de jeu et des moments de jeu. Les porcs avec une HO avaient la même fréquence pour la plupart des comportements de jeu et des moments de jeu que les porcs SHO. Il n’y avait aucune indication que la présence d’une HO affectait le comportement de jeu ou la performance des porcs.

Introduction

A hernia is an abnormal protrusion of an organ or tissue through a defect or natural opening in skin or muscle (1). In pigs, umbilical and inguinal hernias are common, affecting anywhere from 1.7% to 6.7% of the animals in a herd (2–5). Inguinal hernias are typically identified in the first week of life at the time of castration and affected pigs are generally culled early, whereas pigs with umbilical hernias (UH) tend to enter the grower-finisher barn before the umbilical outpouchings are noticed (5). Umbilical hernias result in economic loss because they can affect pig performance and market value (2,6,7). If an umbilical hernia is detected early, the pig is typically culled or sold at a low price (6,7), but umbilical hernias are often not detected until the pig is close to market weight.

Raising pigs with UH may pose a welfare problem. Studies in humans and calves conclude that hernias cause abdominal pain and discomfort, particularly when complications such as strangulation, incarcerations, nerve compression, and/or infection are present (1). Large hernias may affect an animal’s mobility and growth performance and cause an increased risk of mortality (5,6). Canadian regulations prohibit the transportation of pigs with UH if the hernia impedes movement, touches the ground when the animal stands naturally, or has any open wound or infection (8,9). Certain abattoirs may not accept herniated pigs for processing because special handling and precautions are required (6).

Although the economic aspect of hernias has been widely reported in the literature, there are few publications on how the welfare of the animals is affected by the presence of moderate-sized umbilical hernias. However, Schild et al (10,11) recently examined the behavior of pigs during the day of slaughter and concluded that there was no significant difference between pigs with umbilical outpouchings and controls for any of the measures considered relevant for fitness for transport. They did,
however, find behavioral differences during the 6 h pre-transport holding that suggested pigs with hernias may be less fit for mixing and housing in the crowded and barren environments of the holding pens. These studies did not determine the welfare of pigs with hernias under the less challenging environment of a grower-finisher barn. There are various methods available to measure animal welfare and recently play behavior has been proposed as a potential technique for this purpose (12–15). Animals play only if they are healthy, and not stressed (12). The main types of play evaluated in animal studies are locomotor-rotational (alone or in company), social play (involving 2 or more animals), object play, and vocalization (12–16). The occurrence of a jump, spring, hop, sprint, scamper, trot, head-tossing or lever, are play markers defined as locomotor and social play in swine (15,17). The provision of enrichment objects, like plastic dog toys or hanging rope, can increase both social and solitary play, and the play behavior can be used as an indicator of welfare (17). In addition, pigs produce various vocalizations: grunts, squeals, and barks that can vary in duration, frequency, and amplitude (18), which may show emotional states in pigs. Juvenile pigs seem to bark at a broad range of stimuli such as the sudden appearance of humans and non-threatening stimuli, but in particular pigs utter barks within playing bouts (18,19). Although tail wagging has not been reported as a play marker or welfare indicator in pigs, these behaviors commonly occur during locomotor play in this species (20).

Play behavior may be a good indicator of the welfare of pigs, and may be useful in assessing whether pigs with hernias are experiencing pain. The objective of this study was to determine whether umbilical hernias reduce play behavior in pigs.

**Materials and methods**

This study was approved by the University of Guelph Animal Care Committee following the guidelines of the Canadian Council on Animal Care.

**Animals and housing**

A total of 21 pigs with UH (UH pigs) from 1 commercial farm and 17 healthy pigs without umbilical hernias (WUH pigs) from the Arkell Swine Research Station at the University of Guelph were transported to the Ponsonby General Animal Facility, University of Guelph. The pigs with UH were chosen on the basis that they were all the animals detected with umbilical outpouchings in a 2000-head grower-finisher barn that had been filled 1 mo previously with feeder pigs. Although the owner of the commercial farm was willing to sell the pigs with UH, he would not sell pigs WUH. Therefore, these control pigs were obtained from a second source and matched by weight with the UH pigs. Because pigs were from 2 sources the animals were allowed to acclimate for 3 wk before the play study was undertaken. At the time of arrival, pigs were ear tagged and weighed. The mean weight at entry for UH pigs was 53.0 kg (± standard deviation (SD) = 13.3) kg and for WUH pigs was 54.3 kg (± SD) = 11.1 kg. Pigs of similar size and weights were assigned to 1 of 11 pens. Five pens each housed 3 pigs and 6 pens each housed 4 pigs (all pens had at least 1 WUH pig and 1 UH pig). Pens were all identical, measuring 3.2 m² with solid cement flooring. No bedding was used, there was 1 water nipple per pen, and feed was provided *ad libitum*. Umbilical hernias were measured at the beginning and end of the trial. The circumference (measured at the midpoint between the base and apex), depth (from the base of the hernia to the tip/apex of the hernia), and consistency/firmness of the hernias were recorded. Firmness was determined by palpation and the umbilical outpouchings were categorized as either “soft” if the hernia was reducible or “hard” if the contents of the pouch could not be readily determined by palpation and the hernia could not be manually reduced.

**Experimental design**

Pigs were assigned to 16 play groups (PGs) in order to assess locomotor play. The pens housing 3 pigs were tested as a group and pens with 4 pigs were divided into 2 PGs with 1 pig with UH and 1 pig WUH. It was determined that PGs with 3 pigs were able to be monitored by video, whereas PGs of 4 proved to be too difficult to keep track of each individual animal’s behavior. Moreover, testing in small groups was preferred over individual testing, because social interaction encourages the display of play behavior (14). Pigs were tested with the same partners every time to avoid aggression during the testing time.

Two different experiments using the same PGs were run on different days of the week to determine the incentive/motivation to exhibit specific locomotor and social play behaviors or playing behavior with a toy. In each experiment, pigs were videotaped using a HD camcorder (CX405 Handyman; Sony, Tokyo, Japan). In order to easily identify the pigs in the videos, pigs within the playing groups were sprayed on their backs with different colors. One pig was identified with a blue marker; 1 pen mate was identified with a red marker, and in the case of PGs with 3 pigs, the third pig was not marked. The observer evaluating the videos was not blinded to the status of the hernias due to the obvious outpouched bellies of most of the herniated pigs.

**Locomotor play trial**

In this experiment, each PG was videotaped to determine the frequency of locomotor behaviors (scamper, pivot, head-toss, flop, and paw); social play behaviors (lever and pushover), vocalization (barks), and tail wagging in one 7-minute session per wk for 3 wk. Table 1a includes the definitions of each of the play markers evaluated in the locomotor play trial. Two video cameras were used in this experiment. An overhead camera was centrally located in the play area at approximately 4 m from the ground. The other camera was placed at one end of the play area at a height of 0.75 m to achieve a lateral view of the pigs. Time of recordings was initiated when the door was closed behind the last pig entering the playing area.

Prior to the start of the trial, the playing groups were each introduced to the play area. This was done on 3 separate occasions and each time cookies were left on the ground in the play area as a reward. The purpose of this pre-trial exposure to the play area was to familiarize the pigs with the trial conditions, so the behaviors would not be affected by the stress of a novel environment. The play area was rectangular, about 5 m wide and 10 m long. The flooring was cement with a roughened surfaced
designed to minimize the risk of livestock slipping but easy to clean. The play area was adjacent to the room housing the pigs on trial. The play area did not have provision for feed or water. It was well lit with a high ceiling, solid walls on 2 sides, and spindle penning along the other 2 sides.

In this experiment, 1 observer evaluated the videos of all PGs of days 1, 2, and 3. In order to evaluate the agreement between 2 observers on the evaluation of each behavior, an additional observer evaluated a subset of videos: day 1 and the first 8 PGs of day 3. An ethogram (Table 1a) and recording sheets were used to tally the frequency of the playing behavior of each piglet (13–16). The frequency of barks was recorded by 1 person at the time the pigs were in the playing area, because of the difficulty of identifying which animal was vocalizing on the videos. Tail wagging was recorded as present or not present. Pigs were considered to wag their tails if they exhibited this behavior at least once during each 7-minute session. The total time spent playing (the time each animal was engaged in any of the defined playing behaviors) was recorded using a cellular timer. The time spent playing was reported in seconds.

Object play trial
In the second trial, the PGs were videotaped in their home pen to determine the frequency of bite and shake of a dog toy (0.6 m length and ~ 4 cm in circumference, a soft cotton knotted rope designed for large dog breeds) in one 5-minute session per wk for 2 wk. The toy was suspended by a cotton rope attached to the toy’s center so that it hung somewhat horizontal to the ground and was lowered into the pen using a shepherd’s crook until it was within easy reach of the pigs. We chose a knotted rope as a toy because “pigs prefer to play with pliable objects compared to tough ones (like chains) when given the chance” (21). Similar to the first trial, a total of 16 PGs of 2 or 3 pigs at a time were tested. When 4 pigs were housed in 1 pen, PGs with 2 pigs were left in the home pen, the other PGs of 2 pigs were moved into an alternate pen until their turn to be exposed to the play object, then they were moved back to their home pen. Prior to the trial, the rope toy was lowered into each pen on 2 separate occasions for about 2 min each time, to allow the pigs to become familiar with the toy.

One video-camera held by a researcher was used to videotape the PGs in their home pens. The video was not started until all the pigs were standing. The videos were watched by 1 observer. An ethogram (Table 1b) and recording sheets were used to tally/record the frequency of bite and shake of the object by pigs (13–16). The total time spent playing (the time each animal was engaged playing with the toy) was recorded using a cellular timer. The time spent playing was reported in seconds.

<table>
<thead>
<tr>
<th>Table 1. Ethograms for evaluating playing criteria</th>
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<tr>
<td>a — Ethogram used to evaluate playing criteria in “locomotor” play trial (13–16)</td>
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<tr>
<td>Playing criteria</td>
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<tr>
<td>Locomotor play</td>
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<tr>
<td>Scamper</td>
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<tr>
<td>Pivot</td>
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<td>Head toss</td>
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<td>Flop</td>
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<td>Paw</td>
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<td>Tail wagging</td>
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<tr>
<td>Social play</td>
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<tr>
<td>Lever</td>
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<td>Push-over</td>
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<td>Play vocalization</td>
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<tr>
<td>Bark</td>
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<td>Play time</td>
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<tr>
<td>b — Ethogram used to evaluate playing criteria in “object” play trial (13–16)</td>
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<tr>
<td>Playing criteria</td>
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<tr>
<td>Shake object</td>
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<tr>
<td>Bite object</td>
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<tr>
<td>Play time</td>
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</tbody>
</table>
Tissue samples

At the end of the trial, all pigs were slaughtered at the University of Guelph abattoir. Hernias were excised en bloc and gross examination was conducted by 1 pathologist at the Animal Health Laboratory, University of Guelph. The size and consistency of the hernia, hernia content, and presence or absence and dimensions of a hernial ring were recorded. The external and transversely sectioned appearance of each sample was recorded by digital photography.

Statistical analysis

STATA 13 (Stata Corp. College Station, Texas, USA) was used for statistical analyses of the data. Agreement of the subset of videos that were watched by 2 observers in the locomotor trial was analyzed using a Kappa coefficient. Normality of all data was analyzed by the Shapiro-Wilk test. The simple association between pigs with UH and WUH pigs with the frequency of locomotor, social, vocal, and object play behaviors was determined using a Wilcoxon rank-sum test. The simple association of the size of PGs with the locomotor, social, vocal, and object play behaviors was determined using a Wilcoxon rank-sum test. The simple association between UH pigs and WUH pigs with weight at the beginning and the end of the trial and with average daily gain was determined using Student’s t-test. The simple association of the size of PGs with playing times was determined using Student’s t-test. The simple association of the hernia depth, circumference, and consistency at the beginning and end of the trial was determined using a Student’s t-test or 1-way analysis of variance (ANOVA). Results were expressed as mean ± SD. Pair-wise correlation among the sizes of hernias and weight of pigs and their significance were evaluated. The locomotor, social, vocal, and object play behaviors were summed. Spearman’s correlation coefficients of the locomotor, social, vocal, and object play markers and their significance were also determined. The simple association between UH pigs and WUH pigs with tail wagging were determined using a Chi-square test. The simple association of tail wagging with play time was determined using a Student’s t-test.

General linear models with a log link for negative binomial or Poisson models were used to model the effect of the hernia status and day of session on locomotor, vocalization, social, or object playing behaviors. Interactions between hernia status and day of session were evaluated in each model. The command “irr” was included in the models to express the results as incidence rate ratios. The use of a negative binomial model, as opposed to a Poisson model, was based on the statistical significance of the over-dispersion term, alpha. A linear mixed model was built to determine the association of hernia status and day of session with locomotor or object playing times. A mixed logistic regression model was used to determine the effect of hernia status, day of session and play-time on tail wagging. The random effect portion of the models was built to account for clustering of pig within playing groups. The variance partition coefficients (VPCs) were calculated from the random portion of the locomotor and object playing time mixed linear models to determine the percentage of variance explained by a higher level clustering.

Results

A total of 38 pigs were included in the trial: 21 UH pigs and 17 WUH pigs. One WUH pig died before the trials started.

The median depth of the hernias at the start of the trial was 12 cm (range: 2.5 to 19 cm). The median circumference of the hernias at the start of the trial was 37 cm (range: 11 to 57 cm). At the end of the trial, the median depth was 15 cm (range: 0 to 25 cm) and the median circumference of the hernias was 45 cm (range: 0 to 64 cm). The mean circumference and longitudinal diameter of the hernias within each consistency category at the start and end of the trial are summarized in Table 2. At the start of the trial, the depth and circumference of soft hernias were significantly less than for the medium/firm and hard hernias (P < 0.01) (Table 2). A total of 8 (38.1%) pigs with umbilical hernias were classified as having soft hernias, 8 (38.1%) were considered to have medium/firm hernias and 5 (23.8%) were considered to have a hard/firm hernia. At the end of the trial, there were 10 pigs (47.6%) with hard/firm and 11 pigs (52.4%) with soft and reducible hernias. The depth and circumference of the hernias were significantly different between soft and hard hernias at the end of the trial (P < 0.05) (Table 2). Only 1 pig with a hernia considered soft at the beginning of the trial had a hard/firm hernia at the end of the trial, the rest of the pigs with soft hernias (7) had a soft reducible hernia at the end of the trial. One of these pigs had a completely reduced hernia at the end of the trial (confirmed by postmortem examination). This pig had the lowest values for the circumference and depth of the hernia at the start of the trial. A total of 4 pigs (50%) with medium firm hernias had a soft reducible hernia at the end of the trial and 4 (50%) had a hard/firm hernia at the end of the trial. All 5 pigs with hard hernias at the start of the trial had firm non-reducible hernias at the end of the trial. Initial and final circumference and depth of the hernias were all positively correlated, ranging from r = 0.61 to r = 0.88 (P < 0.001; df = 20). However, the circumference and depth of the hernias were not significantly correlated with the weights of the pigs.

Agreement among observers

Less than a chance agreement among observers was noted for the pivot (K = −0.03). Poor agreement among observers was observed for scamper, head toss and lever (K ≤ 0.20). Moderate agreement was observed for pushover (K = 0.55) and only flops had a substantial agreement among observers (K = 0.70). For analysis, only the data of the observer who watched all videos were used.

Locomotor and the object play behavior markers

The means (± SD) of the locomotor, social, and vocalization behaviors and object play behaviors (bite and shake) between UH and WUH pigs are summarized in Table 4, using the number of times that a specific activity was observed in a 7-minute play session as the unit of measure. The most frequent locomotor behavior was scamper, followed by pivot and barking. Flop, lever, and pushover were less frequent. Lever and pushover were summed and considered as social behaviors. The paw playing...
behavior was not observed in any of the pigs during the 3 sessions in the play area. In the simple associations, pigs with UH showed more pivot behavior ($P = 0.001$) than pigs WUH. Head toss tended to be more frequent among UH pigs than WUH pigs ($P = 0.1$). No significant differences were observed in the frequency of scamper, social behaviors, flop, barks, and tail wagging among UH and WUH pigs. In the object trial, biting was more frequent than shaking (Table 3). Tail wagging was significantly associated with play. Pigs that wagged their tails played for a longer time (27 s, $\pm$ SD = 15.7 s) compared to pigs that did not wag their tail (18 s, SD = 13.2 s) ($P < 0.01$). No significant differences were observed for bite and shake of the toy between UH and WUH pigs (Table 3). The size of playing groups was not associated with any of the locomotor or object play behaviors or playing times ($P > 0.05$).

Scamper was positively correlated with pivot, flop, and social behaviors ($r = 0.67, P \leq 0.001$; $r = 0.52, P < 0.001$; $r = 0.30, P = 0.06$, respectively, df = 36). Pivot tended to be correlated with social behaviors ($r = 0.30, P = 0.06$, df = 36). Push-over was correlated with bite and shake ($r = 0.37, P < 0.05$ and $r = 0.35, P < 0.05$, respectively, df = 36). Bite and shake were positively correlated with each other ($r = 0.66, P < 0.001$, df = 36). Barks were correlated with scamper ($r = 0.61, P = 0.001$), pivot ($r = 0.32, P < 0.05$), social ($r = 0.31, P = 0.05$) and flops ($r = 0.43, P < 0.01$) (df = 36).

The alpha values of pivot, head toss, social, flop, and shake markers were small and not significant; therefore, Poisson models were used to analyze these data. The alpha values for scamper, barks, and bites were significant; therefore, negative binomial models were used to analyze these playing markers. No significant interactions were observed between days and the hernia status for any of the playing behaviors. The likelihood ratio test of the head toss, flop, and social models were not significant, suggesting there was not a substantial amount of variation in the observations within pigs and between pigs within playing groups. Therefore, only Poisson models were used to model the data. The rates of pivot (IRR = 1.6, 95% confidence interval (CI) = 1.1 to 2.2, $P \leq 0.01$) and head toss (IRR = 1.8, 95% CI = 1.04 to 3.2, $P < 0.05$) were higher in pigs with UH compared to pigs WUH. The rates of scamper were less frequent in session 3 (IRR = 0.83, 95% CI = 0.69 to 0.99, $P < 0.05$) than session 1. The rates of head toss were significantly less frequent in session 2 (IRR = 0.2, 95% CI = 0.08 to 0.48, $P < 0.001$) than session 1. The rate of barks increased by session IRR = 1.37, 95% CI = 0.90 to 2.1 and 2.12, 95% CI = 1.4 to 3.1 for sessions 2 and 3, respectively ($P > 0.05$ and $P < 0.001$) compared to session 1. Shake and bite of the object did not differ between pigs with UH and pigs WUH. Shake of the toy increased significantly by session 2 (IRR = 2.7, 95% CI = 1.8 to 3.9, $P < 0.001$) compared to session 1. The frequency of tail wagging was not significantly different between pigs and days but pigs that wagged their tails played 8.6 s (95% CI = 8 to 8.8 s) more than pigs that did not wag their tails ($P < 0.05$).

The mean playing time in the locomotor play trial for pigs WUH was 20.6 s ($\pm$ SD = 14.0 s) and for the pigs with UH was 26.2 s ($\pm$ SD = 16.2 s) ($P = 0.06$). The mean playing time with the toy for pigs WUH was 87.5 s ($\pm$ SD = 56.7 s) and for the pigs with UH was 102.1 s ($\pm$ SD = 66.6 s) ($P > 0.05$). The mixed linear models showed no difference in playing times between pigs with UH and pigs WUH in both the locomotor and object trial; however, playing time significantly decreased by session compared to session 1 for both the locomotor and object trial play ($P < 0.001$) (Table 4). The variance partition coefficient of the locomotor and object play-time models showed that variation of playing time was explained mostly at the pig level (40% and 32%, respectively) and between pigs within a playing group (35.3% and 52.8%, respectively). However, some amount of variation was explained between playing groups (24.4% and 16.8% for the locomotor and object play-times, respectively) (Table 4).

**Tissue samples**

Postmortem examination found that the content of the 12 hernia sacs consisted of single or multiple thin-walled cystic structures filled with variable amounts of serosanguineous fluid. The content of the hernia sacs from the remaining 8 pigs included purulent debris (abscess; $n = 1$ pig); both purulent debris and

### Table 2. Mean ($\pm$ SD) depth and circumference (cm) of soft, medium, and hard hernias and their consistency and reducibility at the beginning and end of the trial

<table>
<thead>
<tr>
<th>Consistency of hernias at the beginning of the trial</th>
<th>Consistency of hernias at the end of the trial</th>
<th>Depth</th>
<th>Circumference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft ($n = 8$)</td>
<td>Soft (reducible) ($n = 11$)</td>
<td>12.63</td>
<td>51.1</td>
</tr>
<tr>
<td>Medium firmness ($n = 8$)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hard ($n = 5$)</td>
<td>Hard/Firm ($n = 10$)</td>
<td>19</td>
<td>51.1</td>
</tr>
</tbody>
</table>

$^a$ Depth in cm, from the base to the tip of the hernia.
$^b$ Circumference: diameter in cm of middle point of the hernia.
$^c$ Significant difference.
fluid-filled cysts ($n = 2$ pigs); fat ($n = 2$ pigs); fat mixed with fibrous stroma ($n = 2$ pigs); and necrotic debris suggestive of necrotic fat ($n = 1$ pig). A distinct abdominal wall defect with smooth margins was associated with the hernia sac in 15 pigs. Bowel was not present in any of the hernia sacs at the time of examination.

**Discussion**

The effect of hernias on pig welfare has not been studied widely. Information on whether or not hernias are painful or cause discomfort is needed for the development of policies and regulations. Pain and discomfort are difficult to assess in pigs but it is reported that play may be an indicator of animal well-being. Animals that are healthy and not stressed or suffering will play more than animals in pain or discomfort (14), suggesting that play could be investigated as a potential welfare indicator and also as an instrument for improving welfare (14,22). Locomotor and object play behaviors as well as vocalizations appear to be the most promising and convenient indicators for assessing positive experiences in farm animals under commercial conditions (15). In our study, specific locomotor, social, vocal, and object playing markers were used to determine the impact of UH on the welfare and performance of growing pigs. Moreover, the changes of the circumferences of the hernias at the start and end of the trial and their association with consistency and reducibility of the hernias were analyzed. The impact of the size of hernias with growth performance of pigs was also evaluated.

The consistency and reducibility of the hernias was associated with their circumferences. Soft, small ($< 12$ cm in depth and $< 35$ cm of circumference) hernias were reducible, while firmer/hard hernias ($> 15$ cm in depth and $37$ cm of circumference) were not reducible. The size classification agrees with a study in which the depth of the hernias was classified small ($< 12$ cm) to large (13 to 20 cm) (23). In our study almost 90% of the soft hernias at the start of the trial remained small and reducible. Five soft hernias had no postmortem evidence of abdominal wall defects indicating that these might have been resolved umbilical abscesses. However, 1 soft hernia developed into a hard hernia by the end of the study. It is important for pork producers to be able to predict if hernias will increase in size or resolve and, based on this small study, it appears that there are general trends, but there are also exceptions. Producers probably need to consider culling pigs that appear to have small hernias if they are detected at the time of filling the grower-finisher barn because of the unpredictable nature of this condition.

The size of the hernias was not associated with the weight of the pigs or the growth rate of the pigs. This agrees with studies showing that differences in weight and age were not significant.

---

**Table 3.** Mean ($\pm$ SD) of the scamper, pivot, head toss, flop lever, push over, and barks behaviors evaluated during the 3-day locomotor play trial, and the bite and shake of the toy behaviors evaluated during the 2-day object play trial between pigs with umbilical hernias ($n = 21$) and pigs without hernias ($n = 16$)

<table>
<thead>
<tr>
<th>Locomotor play trial counting the number of specific behaviors in a 7-minute play session</th>
<th>Object play trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>Hernia</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Scamper</td>
<td>7.27 (4.03)</td>
</tr>
<tr>
<td>Pivot</td>
<td>3.66 (2.30)</td>
</tr>
<tr>
<td>Head toss</td>
<td>0.35 (0.66)</td>
</tr>
<tr>
<td>Flop</td>
<td>0.41 (0.61)</td>
</tr>
<tr>
<td>Social behaviors</td>
<td>0.56 (0.84)</td>
</tr>
<tr>
<td>Barks</td>
<td>3.60 (4.36)</td>
</tr>
</tbody>
</table>

**Table 4.** Mixed linear models testing locomotor and object play times by hernia status and sessions of playing groups with random effects accounting for the cluster of sessions within pigs and between pigs in playing groups

<table>
<thead>
<tr>
<th>Locomotor play time (s)</th>
<th>Object playing time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed-effects parameters</td>
<td></td>
</tr>
<tr>
<td>Hernia</td>
<td>Day 2</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Scamper</td>
<td>5.29</td>
</tr>
<tr>
<td>Pivot</td>
<td>1.36 to 11.95</td>
</tr>
<tr>
<td>Head toss</td>
<td>0.11</td>
</tr>
<tr>
<td>Flop</td>
<td>3.60 (4.36)</td>
</tr>
<tr>
<td>Social behaviors</td>
<td>0.56 (0.84)</td>
</tr>
<tr>
<td>Barks</td>
<td>3.60 (4.36)</td>
</tr>
</tbody>
</table>

**Random effects parameters**

<table>
<thead>
<tr>
<th>Play group</th>
<th>Pig</th>
<th>Residual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coefficient</td>
<td>5.81</td>
<td>8.40</td>
</tr>
<tr>
<td>95% CI</td>
<td>2.11 to 15.97</td>
<td>5.28 to 13.37</td>
</tr>
<tr>
<td>P-value</td>
<td>24.4</td>
<td>35.3</td>
</tr>
<tr>
<td>Coefficient</td>
<td>16.04</td>
<td>49.62</td>
</tr>
<tr>
<td>95% CI</td>
<td>1.23 to 209.3</td>
<td>34.6 to 71.22</td>
</tr>
<tr>
<td>P-value</td>
<td>16.83</td>
<td>52.08</td>
</tr>
</tbody>
</table>

**Note:**

- $SD$  —  standard deviation.
- $CV$  —  coefficient of variation.
- $PC$  —  percentage coefficient.
- $P$-value  —  significance levels.
- $95\%$ CI  —  lower and upper confidence interval.
factors in the development of hernias (4). It has been suggested that the presence of an umbilical hernia increases the risk of mortality, particularly if a loop of bowel becomes trapped in the hernia sac and circulation is compromised. In the present study there were no complications such as gut strangulation but this has been reported to occur and is a welfare concern. This has been reported previously in calves (24).

The assessment of play behavior in domestic pigs is lacking and our study is the first reporting specific locomotor, social, vocalization, and object play behaviors among pigs with UH and pigs WUH. In agreement with another study (25), the most frequent locomotor behaviors observed in our study were scamper, pivot, and barks. These play markers may be considered as overt bursts of energy and therefore may be more noticeable than other behaviors. Pigs that engaged in one of these activities were also likely to express other behaviors indicative of play. Correlations were noted between many of the activities, for example, scamper was associated with pivot, flop, and social behaviors. Scamper and barks were not significantly different among pigs with UH and pigs WUH. Scamper is a body activity more frequent in pigs between the ages of 2 and 6 wk (16,25) and appears to be stimulated by sudden changes and novelty. An immediate increase in scampering and running duration and rate was observed after releasing 6-week-old pigs into a corridor near their home pens (26) or in weaned sows after several weeks of low activity (25). The novelty of the hallway, and the increased space per pig, allowed for sudden bursts of this locomotor behavior and stimulated barks from all pigs.

Pivot and head tossing were more frequent in pigs with UH than in pigs WUH. Based on sequential analysis of social play markers in piglets, pivoting and head tossing are suggested to function as play signals to initiate rough-and-tumble play for this species (25) which cues the social partner that behaviors produced are not as serious as they normally would be in other contexts (27). However, agreement of these play behaviors between 2 observers in a subset of videos was low; therefore, the increased rates of these play markers in pigs with umbilical hernias need to be studied further before conclusions can be drawn.

Social (lever and pushovers) behaviors were not frequently observed. These playing markers are considered more subtle social behaviors that may be more difficult to identify (22,25). Flop and tail wagging were also behaviors that did not differ among pigs with UH and WUH or by session. In an observational study (20), tail wagging occurred only 5% of the time in a novel environment or home pen observations. Tail wagging in pigs has been described as not being a useful indicator of welfare in pigs because, although it has been associated with positive emotional states (e.g., during walking, play, or before feeding), it has also been associated with negative emotional states (e.g., injury or frustration) (20). However, in our study, tail wagging was associated with play time.

The proportion of time that pigs were engaged in locomotor or social and object play (5.6% and 31.9%, respectively) was relatively low. It is reported that the frequency of playing markers are the highest in the first 6 wk of a pig’s life (25), and although playing behaviors persist through the growing period and into adulthood, they do so at a lower frequency (14).

However, it has been reported that during periods in an animal’s life when play is naturally less frequent, spontaneous, rare adult play in captive species can still be an indicator of good welfare (15). In general, playing times in a playing area and with an object were not significantly different among pigs with UH and pigs WUH, suggesting that the presence of an umbilical hernia did not have a negative effect on playing behaviors. However, both locomotor and object playing times decreased by sessions. It has been reported that in general, pigs are thought to be neophilic and tend to lose interest quickly, particularly with playing objects (28,29).

The potential of play as a welfare indicator may encounter some difficulties because its evaluation is somewhat subjective and there is animal to animal variability (23). The poor agreement herein among observers scoring certain locomotor play behaviors supports this concern but, there was strong agreement in scoring other behaviors such as “flop.” It is possible that the variability among scorers can be overcome by implementing good training practices and establishing firm criteria before studies that use play as a welfare indicator. In the present study playing times at the pig level showed considerable variability and likewise wide variation was observed between pigs in a group. The variability in the amount of play shown in a group could be attributed to many factors in addition to fear, health, or pain; these factors include: gender, age, changes in weather, presence of “playful partners,” or random or “error” variability (14).

The overall conclusions from this study were that there was no evidence based on monitoring play behaviors that the pigs with hernias were in pain or their welfare was compromised in that there was no difference among pigs with hernias and those without hernias in their willingness to engage in locomotor and social activities.

Acknowledgments

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References


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Feline meningoencephalomyelitis of unknown origin: A retrospective analysis of 16 cases

Arianna Negrin, Sarah Spencer, Giunio Bruto Cherubini

Abstract — This study aimed to describe the signalment, clinical signs, magnetic resonance imaging (MRI) findings, cerebrospinal fluid (CSF) analysis, treatment, and outcome of feline meningoencephalomyelitis of unknown origin (FMUO). Medical records from 16 cats meeting the inclusion criteria of CSF pleocytosis, negative CSF polymerase chain reaction (PCR)-infectious disease results, and characteristic MRI findings were retrospectively reviewed. Median age was 9.4 years. Clinical signs included ataxia, proprioceptive deficits, seizures, and spinal hyperesthesia. The CSF nucleated cell count was increased (median 70.7 cells/μL), with predominantly mixed pleocytosis and CSF protein concentration was increased in 15/16 cats. Magnetic resonance imaging showed intraparenchymal infiltrative ill-defined lesions in 13 cases. All cats received a corticosteroid-based treatment protocol; additional therapies included lomustine, cytarabine, and anticonvulsant medications. Mild neurological signs were recorded in 5/12 cats but 7/12 cats were neurologically normal at re-examination. This represents the first study of feline MUO, highlighting FMUO as an important differential diagnosis in cats with variable neurological presentation. Prognosis appears to be good with immunomodulatory therapy.

Résumé — Meningo-encéphalomyélite féline d’origine inconnue : une analyse rétrospective de 16 cas. Cette étude visait à décrire le signalement, les signes cliniques, les résultats de l’imagerie par résonance magnétique (IRM), l’analyse du liquide céphalorachidien (LCR), le traitement et l’issue de la méningo-encéphalomyélite féline d’origine inconnue (MEOI). Les dossiers médicaux de 16 chats répondant aux critères d’inclusion de la pléocytose du LCR, les résultats négatifs du LCR pour des maladies infectieuses par amplification en chaîne par polymérase (ACP) et les constatations caractéristiques par IRM ont été évalués rétrospectivement. L’âge médian était de 9,4 ans. Les signes cliniques incluaient l’ataxie, les déficits proprioceptifs, les crises d’épilepsie et l’hyperséthésie spinale. La numération des cellules nucléées du LCR a augmenté (médiane de 70,7 cellules/μL), avec une pléocytose à prédominance mixte et la concentration de protéine du LCR était accrue chez 15/16 chats. L’imagerie par résonance magnétique a montré des lésions infiltrantes intraparenchymateuses mal définies dans 13 cas. Tous les chats ont reçu un protocole de traitement à base de corticostéroïde; les thérapies additionnelles incluaient la lomustine, la cytarabine et des médicaments anticonvulsifs. De légers signes neurologiques ont été observés chez 5/12 chats, mais 7/12 chats étaient neurologiquement normaux lors du réexamen. Cela représente la première étude de la MOI, ce qui souligne que la MOI est un diagnostic différentiel important chez les chats ayant une présentation neurologique variable. Le pronostic semble bon avec la thérapie immunomodulatoire.

(Traduit par Isabelle Vallières)
Introduction

Inflammatory central nervous system (CNS) disorders are one of the most common causes of neurological dysfunction in dogs and cats and can be divided into 2 broad classes: CNS inflammation due to an infectious origin and CNS inflammation without an identifiable infectious cause (1,2). The latter is commonly referred to as meningoencephalitis or meningoencephalomyelitis of unknown origin (MUO) (2,3). It is useful to consider disorders classed within MUO individually when possible, as clinical features and response to therapy tends to differ between sub-groups. However, as a histological diagnosis is often not possible, the term MUO is commonly used (2).

While MUO is extensively reported in dogs (2,4–7), few reports of non-infectious meningoencephalomyelitis have been described in cats (8–10). Bradshaw et al (10) reported that 11% of 286 cats with encephalitis or meningitis had no evidence of an infectious agent, while 5 cases of presumed feline MUO were classified in Singh et al (8) as either non-suppurative or steroid-responsive based on cerebrospinal fluid (CSF) characteristics and response to treatment. Although the underlying cause of MUO remains elusive, it appears to be associated with an aberrant immune response directed against the CNS (11) and consequently immunomodulatory therapy is the mainstay of canine MUO treatment. There are no reported treatment protocols for feline MUO (FMUO), although 2 cases were successfully treated with prednisolone (8). Response to therapy and outcome of canine MUO are highly variable while data on the prognosis of cats with the condition are currently unknown (2,9).

This report represents the largest study of presumed FMUO cases in the literature. The aim of this study was to describe the signalment, clinical signs, magnetic resonance imaging (MRI) findings, ancillary diagnostic testing, CSF analysis, treatment and outcome of FMUO, providing background information for further studies focusing on clinico-pathological features and optimal treatment protocols.

Materials and methods

Selection criteria

Medical records (2008 to 2016) of cats presented to the Neurology and Neurosurgery Service at Dick White Referrals were retrospectively reviewed. Inclusion criteria comprised CSF pleocytosis, MR characteristics indicative of inflammatory lesions, and negative CSF reverse-transcription polymerase chain reaction (RT-PCR) infectious diseases results. Where neoplasia was suspected as a differential diagnosis, further imaging and laboratory tests were performed and reviewed. Additional diagnostic investigations, including Toxoplasma gondii serology, were conducted in some cases. Cats with a history of steroid administration before presentation were excluded. Signalment, duration of clinical signs, physical and neurological examination findings, neuroanatomical localization, CSF nucleated cell count and cytological characteristics, CSF protein concentration, diagnostic imaging results including MRI, treatment, neurological examination findings at re-examination(s), and occurrence and therapy at time of relapse were recorded. Clinical signs were deemed acute if present for < 2 wk, and chronic if reported for > 2 wk.

Cerebrospinal fluid analysis

Cerebrospinal fluid was collected from the cisterna magna in all cases. Analysis was performed within 1 h of collection. Cerebrospinal fluid nucleated cell counts were classified as: normal (< 5/μL), mildly (5 to 80/μL), moderately (81 to 500/μL), or markedly (> 500/μL) increased (8). Cerebrospinal fluid protein levels were classified as: normal (< 0.3 g/L), mildly (0.31 to 1.0 g/L), moderately (1.1 to 3.0 g/L), or marked (> 3.0 g/L) increased (8). Nucleated cell population was classified as neutrophilic (> 50% neutrophils), mononuclear (> 80% mononuclear cells), eosinophilic (> 50% eosinophils), or mixed (no predominance of any 1 cell type) (6). The RT-PCR analysis on all CSF samples was carried out in all cases for the following infectious agents: feline calicivirus, feline herpesvirus, Chlamydophila felis, Toxoplasma gondii, Bornavirus, feline leukaemia virus, feline immunodeficiency virus, Leishmania infantum, feline parvovirus (panleucopenia virus), and feline coronavirus.

Magnetic resonance imaging protocol

Magnetic resonance imaging was performed using a 0.4T permanent magnet scanner (Hitachi Aperto Lucent 0.4T; Hitachi Medical Systems, Wellingborough, UK). Pulse sequences varied but in all cats transverse T1WI, T2WI, FLAIR sagittal T2WI, and post-contrast gadoteric acid (Gadovist; Bayer Schering Pharma, Reading, UK), 0.1 mmol/kg body weight (BW), IV, transverse T1WI were acquired. Images were reviewed by board-certified radiologists who were blinded to the study. Images were assessed for the presence of lesions, lesion pattern (focal, diffuse or multifocal), and location. The presence of meningeal involvement was recorded. Lesion margins were described as well-defined, irregular, or infiltrative. Mass effect was indicated by effacement of sulci, shift of midline structures, cerebellar herniation (evaluated on sagittal midline T2WI) or ventricular system deviation/compression. Pre- and post-contrast T1WI were compared to assess for contrast enhancement and the pattern of contrast uptake was described.

Treatment

Treatment depended on clinician preference and individual case requirements. All cats received clindamycin (Antirobe; Zoetis, London, UK), 12.5 mg/kg BW, PO, q12h, while waiting for 5 to 7 d for CSF infectious disease PCR results. All cats were treated with a corticosteroid-based protocol (dexamethasone only, dexamethasone followed by prednisolone, or prednisolone only). Immunosuppressive steroid doses were initially used, including prednisolone (Prednicare; Animalcare, York, UK), 1 mg/kg BW, PO, q12h and dexamethasone (Dexamethasone; Aspen, Redditch, UK), 0.2 to 0.3 mg/kg BW, PO, q24h. Corticosteroid therapy was tapered by typically halving the dose or dosage every 2 to 3 wk unless a relapse was seen. Additional immunomodulatory therapies included lomustine (Lomustine; Nova laboratories, Wigston, UK), 10 mg/cat, PO, single dose on day 1, and cytarabine (Cytarabine; Pfizer, Sandwick, UK), 50 mg/m², SC, q12h for a total of 4 doses, at the clinician’s discretion. Anticonvulsant medication was used in all cats presented with seizures and included phenobarbitone (Pheno/leptil; Animalcare), 1 mg/kg BW, PO, q12h, levetiracetam (Keppra;
UCB Pharma, Brussels, Belgium), 10 mg/kg BW, PO, q8h, or diazepam (Diazemuls; Actavis, Barnstaple, UK), 0.5 mg/kg BW, IV, in case of seizure.

Follow-up and outcome
Re-examination was scheduled in all cats 2 to 3 wk after discharge. Clinical and neurological findings and any changes in ongoing medication protocols were recorded. Subsequent follow-up was at the clinicians’ and owners’ discretion.

Results
The clinical, neurological, and diagnostic findings are summarized in Table 1.

Signalement
Sixteen cats met the inclusion criteria. Median age was 9.4 y (range: 10 mo to 12 y). The cats were domestic shorthair or longhair (14/16), Persian (n = 1), and Siamese (n = 1).

Clinical signs
Onset of clinical signs was not specified by the owners in 3 cases. Clinical signs were reported as acute in the majority of cats (14/16). Systemic signs included obtundation, mental status, anorexia (1/16), and pyrexia (1/16). The most common abnormalities on neurological examination were ataxia (8/16), paresis (8/16), and spinal hyperesthesia (8/16) (see Table 1 for further details). Generalized (4/16) or partial (2/16) seizures were the presenting sign in 6 cats. Nystagmus was observed in 3 cats and decreased or absent pupillary light reflexes (PLR) and/or menace responses were noted in 3 cats. Localization based on neurological examination was multifocal in 4 cases, forebrain in 4 cases, multifocal CNS in 3 cases, and multifocal spinal cord in 5 cases.

Cerebrospinal fluid analysis
Cerebrospinal fluid nucleated cell count was mildly increased in 12/16 and moderately increased in 4/16 cats (median: 62.2 cells μL, range: 6 to 344) (Table 1). Pleocytosis was mixed in 5/16, lymphocytic in 5/16, mononuclear in 3/16, neutrophilic in 2/16, and eosinophilic in 1/16 cases. Cerebrospinal fluid protein was increased in 15/16 as the sample was of insufficient quantity for measurement in 1 case. Protein concentration was mildly increased in 12/16 (median: 0.50 g/L, range: 0.21 to 22.25 g/L). The PCR results in CSF for T. gondii and feline coronavirus were available in 3/16 cases and were all negative.

Magnetic resonance imaging findings
The MRI findings (Table 2) correlated with neuroanatomical localization in 14/16 cases. In 10/16 cats, MRI detected multifocal CNS lesions. Single lesions were observed in 4 cats and meningeal contrast enhancement only in the remaining 2 cases. Lesions tended to be T1W isointense or hypointense, T2W hyperintense, and were variable in their contrast uptake. Lesions were ill-defined in 9 cats and infiltrative in 3 cats. Mild subventricular or cerebellar herniation was seen in 2/16 cases. Hydrocephalus was observed in 1 cat only.

Where the spinal cord was imaged, lesions were intraparenchymal in 3/5 and extraparenchymal in 2/5 cases. Meningeal contrast enhancement was seen in 2/5 cases.

Ancillary diagnostic investigations
Complete blood (cell) count (CBC) and serum biochemistry were performed in all cases; leucocytosis was documented in 5 cats. Toxoplasma gondii serology was performed in 9/16 cats; results were not supportive of recent or active infection (high IgM titer in any case, but in 3 cats (cats 4, 9, 11) results indicated previous exposure (high IgG titer but IgM titer within normal limits). Other diagnostic investigations, including abdominal ultrasound (5/16 cats), inflated chest radiographs (2/16 cases), did not reveal significant concurrent disease in any cat.

Treatment
Dexamethasone alone was given to 9/16 cats, dexamethasone followed by prednisolone was administered to 4/16 cats, and prednisolone alone to 3/16 cats. Five cats received an additional immunomodulatory therapy, including cytarabine in 3 cats, and lomustine in 2 cats. Anticonvulsant medication was used in all cats presented with seizures, including phenobarbitone (4/6) and levetiracetam (2/6). Two cats, admitted for cluster seizure/ status epilepticus, on admission received diazepam in combination with phenobarbitone (1 case) or levetiracetam (1 cat) to control seizures.

Outcome
Median duration of hospitalization was 6.8 d (range: 3 to 12 d). All cats survived to discharge (Table 1). Follow-up was unavailable in 4 cases. Median final follow-up was 5.2 mo (range: 0 to 16 mo) after presentation. At first re-examination, 7/12 cats were normal on neurological examination and remained asymptomatic at all subsequent re-examinations (2, 5, 9, 10, and 12 mo) (Table 1). The remaining cats that were presented for re-examination showed persistent mild neurological signs at first re-examination, including mild pelvic limb ataxia, mild tetraparesis, intermittent spinal hyperesthesia, and reduced frequency (> 50% reduction) of partial seizures. No further follow-up was available for 2 of these cats, while in the remaining 3 cats stable or improved clinical signs were recorded in subsequent re-examinations. One cat received an increased dose of dexamethasone, which lead to complete and long-term resolution of clinical signs (last follow-up 10 mo). This cat relapsed 1 y subsequent to remission, a few days after routine vaccination. Treatment was successfully stopped in the remaining 2 cats without deterioration (latest follow-up at 9 mo and 15 mo).

Discussion
This study represents the largest description of suspected FMUO. Findings indicate many similarities with canine MUO but also some important differences, particularly in apparent prognosis. Middle-aged and older cats appeared to be at highest risk, as the median age in this study was 9.4 y, although disease was seen in much older and younger cats. Age of dogs affected by MUO can also be highly variable (6 mo to 12 y).
### Table 1. Signalment, clinical, and diagnostic findings, treatment and outcome of 16 cases of feline meningoencephalomyelitis

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Gender</th>
<th>Breed</th>
<th>Neurological signs</th>
<th>Onset</th>
<th>Localization</th>
<th>CSF TNCC (cells/μL)</th>
<th>CSF protein (g/L)</th>
<th>CSF cytology</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9 y</td>
<td>MN</td>
<td>DSH</td>
<td>Ataxia, decreased postural reactions, horizontal nystagmus, TL hyperesthesia.</td>
<td>Acute</td>
<td>Multifocal CNS</td>
<td>6</td>
<td>NP</td>
<td>Mononuclear</td>
<td>Dex methasone then prednisolone + cytarabine.</td>
<td>Survived to discharge, LTF.</td>
</tr>
<tr>
<td>2</td>
<td>8 y</td>
<td>MN</td>
<td>DLH</td>
<td>Lethargy, generalized ataxia, cervical hyperesthesia.</td>
<td>Unknown</td>
<td>Spinal (C6-T2)</td>
<td>6</td>
<td>0.37</td>
<td>Eosinophilic</td>
<td>Dex methasone.</td>
<td>Resolved at 2 mo. FFU 5 mo.</td>
</tr>
<tr>
<td>3</td>
<td>10 mo</td>
<td>F</td>
<td>Siamese</td>
<td>Generalized tonic-clonic cluster seizures, decreased bilateral menace, bilateral vestibular system.</td>
<td>Acute</td>
<td>Multifocal brain (forebrain and central vestibular system)</td>
<td>10</td>
<td>0.21</td>
<td>Mixed</td>
<td>Dex methasone then prednisolone, levetiracetam.</td>
<td>Survived to discharge, LTF.</td>
</tr>
<tr>
<td>4</td>
<td>6 y</td>
<td>F</td>
<td>Persian</td>
<td>Partial tonic seizures, ataxia, depressed mentation, decreased bilateral menace.</td>
<td>Acute</td>
<td>Forebrain</td>
<td>14</td>
<td>2.76</td>
<td>Mononuclear</td>
<td>Dex methasone, phenobarbital.</td>
<td>Resolved at 2 mo. FFU 10 mo. Relapsed after vaccination.</td>
</tr>
<tr>
<td>5</td>
<td>11 y</td>
<td>FN</td>
<td>DLH</td>
<td>Obtunded mental status, non ambulatory right-sided hemiparesis, cervical hyperesthesia.</td>
<td>Acute</td>
<td>Multifocal CNS</td>
<td>15</td>
<td>0.52</td>
<td>Mixed mainly neutrophilic</td>
<td>Dex methasone + lomustine.</td>
<td>Mild ataxia at 3 wk.</td>
</tr>
<tr>
<td>6</td>
<td>11 mo</td>
<td>F</td>
<td>DSH</td>
<td>Partial complex seizures, TL hyperesthesia.</td>
<td>Chronic</td>
<td>Multifocal CNS</td>
<td>18</td>
<td>0.33</td>
<td>Lymphocytic</td>
<td>Dex methasone, phenobarbitone added at recheck.</td>
<td>Mild partial seizures at 6 wk. Hyperesthesia at FFU 12 mo.</td>
</tr>
<tr>
<td>7</td>
<td>6 y</td>
<td>MN</td>
<td>DSH</td>
<td>Pelvic limb ataxia, decreased pelvic limbs postural reactions.</td>
<td>Acute</td>
<td>Spinal (T3-L3)</td>
<td>24</td>
<td>0.48</td>
<td>Mixed</td>
<td>Dex methasone.</td>
<td>Survived to discharge, LTF.</td>
</tr>
<tr>
<td>8</td>
<td>4 y</td>
<td>MN</td>
<td>DSH</td>
<td>Lethargy, pyrexia, intentional tremors, ambulatory tetraparesis, vestibular ataxia, decreased bilateral menace.</td>
<td>Acute</td>
<td>Multifocal brain</td>
<td>53</td>
<td>0.33</td>
<td>Lymphocytic</td>
<td>Prednisolone + cytarabine, phenobarbitone.</td>
<td>Resolved at 2 wk. FFU 12 mo.</td>
</tr>
<tr>
<td>9</td>
<td>9 y</td>
<td>MN</td>
<td>DSH</td>
<td>Ambulatory paraparesis, decreased pelvic limbs postural reactions.</td>
<td>Acute</td>
<td>Spinal (T3-L3)</td>
<td>63</td>
<td>0.60</td>
<td>Mixed</td>
<td>Dex methasone.</td>
<td>Mild pelvic limb ataxia. FFU 15 mo.</td>
</tr>
<tr>
<td>10</td>
<td>3 y</td>
<td>FN</td>
<td>DSH</td>
<td>Pyrexia, pelvic limbs ataxia and ambulatory paraparesis, TL hyperesthesia.</td>
<td>Acute</td>
<td>Spinal (L4-S3)</td>
<td>68</td>
<td>0.51</td>
<td>Lymphocytic</td>
<td>Dex methasone.</td>
<td>Mild pelvic limb ataxia at 3 wk.</td>
</tr>
<tr>
<td>11</td>
<td>8 m</td>
<td>FN</td>
<td>DSH</td>
<td>Lethargy, pyrexia, obtunded mentation, circling to right, decreased left-sided postural reactions, decreased menace and PLR in left eye.</td>
<td>Acute</td>
<td>Forebrain</td>
<td>109</td>
<td>0.42</td>
<td>Neutrophilic</td>
<td>Prednisolone.</td>
<td>Resolved at 3 wk. FFU 9 mo.</td>
</tr>
</tbody>
</table>
Table 1. Signalment, clinical, and diagnostic findings, treatment and outcome of 16 cases of feline meningoencephalomyelitis

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (y)</th>
<th>Gender</th>
<th>Breed</th>
<th>Neurological signs</th>
<th>Clinical signs of onset</th>
<th>CSF TNCC (cells/mL)</th>
<th>CSF protein (g/L)</th>
<th>CSF cytology</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>4</td>
<td>MN</td>
<td>DSH</td>
<td>Unknown</td>
<td>Multifocal brain</td>
<td>110</td>
<td>1.67</td>
<td>Mixed</td>
<td>Dexamethasone, then prednisolone</td>
<td>Survived to discharge, LTF.</td>
</tr>
<tr>
<td>13</td>
<td>2</td>
<td>FN</td>
<td>DSH</td>
<td>Unknown</td>
<td>Multifocal brain</td>
<td>130</td>
<td>3.0</td>
<td>Lymphocytic</td>
<td>Prednisolone, then prednisolone, diazepam</td>
<td>Resolved at 3 wk, FU 2 wk.</td>
</tr>
<tr>
<td>14</td>
<td>3</td>
<td>MN</td>
<td>DSH</td>
<td>Known</td>
<td>Spinal (T3-L3)</td>
<td>344</td>
<td>2.25</td>
<td>Mononuclear</td>
<td>Dexamethasone, then prednisolone</td>
<td>No seizures, FU 5 wk.</td>
</tr>
<tr>
<td>15</td>
<td>7</td>
<td>MN</td>
<td>DSH</td>
<td>Known</td>
<td>Forebrain</td>
<td>6</td>
<td>0.52</td>
<td>Lymphocytic</td>
<td>Prednisolone, phenobarbital, diazepam</td>
<td>Good control of seizure and unremarkable neurologic examination, FU 2 wk.</td>
</tr>
<tr>
<td>16</td>
<td>4</td>
<td>MN</td>
<td>DSH</td>
<td>Known</td>
<td>Unknown</td>
<td>19</td>
<td>0.49</td>
<td>Lymphocytic</td>
<td>Dexamethasone, then prednisolone, diazepam</td>
<td>Resolved at 3 wk, FU 5 wk.</td>
</tr>
</tbody>
</table>

CSF — cerebrospinal fluid; TNCC — total nucleated cell count; DSH — domestic shorthair; CNS — central nervous system.

Clinical signs of FMUO typically corresponded to the distribution of CNS lesions. Onset of neurological signs was acute in most cases, similar to canine MUO (12,14), although the duration of signs may be underestimated in cats due to their temperament and often less time spent in close proximity to owners. Seizure activity, either partial or generalized, was the major reason for presentation in this study similar to data reported in multifocal granulomatous encephalitis (GME) in dogs (7), and NE in pugs (13) and Yorkshire terriers (2). Our findings highlight feline MUO as an important differential diagnosis for seizures, especially in young to middle-aged cats with no previous history of seizures.

Intracranial multifocal disease was the most common neuroanatomical localization, as reported in dogs (2) and previously described cases of presumed FMUO (8). Intracranial was the most common localization (50%), with equal distribution between multifocal and localized to the forebrain, while 31% of cats had a suspected lesion to the spine only, a similar percentage to the focal presentation of canine MUO (12).

Mild CSF pleocytosis was recorded in most cases in this study; previous reports of suspected FMUO show high cell count in suppurative disease but lower cell count in non-suppurative disease (8). Cerebrospinal fluid pleocytosis is highly variable in canine MUO and may even be normal (2). Severity of CSF pleocytosis did not appear to correlate with disease severity or prognosis in this study, as with dogs affected by MUO (9). Moreover, type of pleocytosis did not correlate with duration of clinical signs, being very variable leucocyte prevalence in the CSF with acute onset in most of the cases. As CSF pleocytosis is not specific for MUO, it is important to correlate it with characteristic magnetic resonance imaging (MRI) findings and negative infectious disease results, as were the inclusion criteria in this study.

Magnetic resonance imaging characteristics observed in most of the cases in this study are similar to those in canine MUO, in which the MRI findings appear to be variable, with prevalence of focal or multifocal, ill-defined hyperintense lesions on T2WI (4,6,15). T2WI hyperintensity has moderate sensitivity (68%) and a high predictive value (100%) for inflammatory CSF in dogs (4); however, gadolinium contrast has been reported to increase the sensitivity of MR for detecting inflammatory lesions (15,16). In this study, 2 cats (cases 1 and 13) with indistinct lesions on T2WI as isoointense, showed marked contrast enhancement, which helped to detect and define the nature of brain pathology. Interestingly, most intracranial lesions affected white matter only, in keeping with previous data in dogs with GME (6) and necrotizing leukoencephalitis (NLE) (2). Unfortunately, FLAIR sequence, which has been previously reported to enhance sensitivity of MRI (15) was not available in all cases. In these 2 cats, however, contrast-enhancing lesions were

(7,12,13); however, young or middle-aged dogs have been more frequently reported (2,7,13).

In these 2 cats,however, contrast-enhancing lesions were.
also heterogeneously hyperintense in FLAIR. Further studies would be needed to better elucidate the MRI characteristics of presumed MUO in cats and the possible MRI differences with infectious encephalitis.

Feline limbic encephalitis (FLE) has been recently suspected to have a primary immune-mediated etiology, as 36% of cats presenting partial seizure with orofacial involvement showed increased concentrations of antibodies against voltage-gated potassium channel complexes (VGKC-complexes) (17). Diagnosis of suspected FLE is based on clinical signs, MRI findings, characterized by the typical bilateral hippocampal T1 hypo- and iso-intensity and T2 hyperintensity, and pleocytic CSF (17). None of the cats herein showed similar clinical and MR findings; however, an underlying immune-mediated inflammatory etiology may result in shared biochemical features with FMUO. Therefore, further studies are required to elucidate possible common underlying etiology and to test sera for VGKC-complexes in FMUO patients.

All cats in this study received dexamethasone only, dexamethasone followed by prednisolone, or prednisolone only; however, the sample size was too small for statistical comparisons. Corticosteroids were tapered over a range of weeks to months, depending on response to treatment and in 2 cats long-term (>10 mo) therapy was required. Additional immunomodulatory drugs, including cytarabine and lomustine, were used in 5 cats alongside corticosteroids without adverse effects and complete remission of signs was recorded at the time of latest follow-up in all cases. Use of cytarabine and lomustine reflected clinician’s preference, mainly based on lack of response to corticosteroids while still hospitalized; however, complete information regarding this clinical decision is lacking in the records. Cytarabine and lomustine have also been used as immunomodulatory therapy in addition to steroids in canine MUO and were therefore used for their immunomodulatory effect in feline patients with suspected MUO in the present study. The dosages of these 2 drugs were based on previous descriptions of their use in feline patients (14,18–20). Moreover, cytarabine (21,22) and lomustine (23) have also been used as immunomodulatory therapy in addition to chemotherapy against several cancers including lymphoma. Corticosteroids were therefore used for their immunomodulatory drugs, including cytarabine and lomustine, were used in 5 cats alongside corticosteroids without adverse effects and complete remission of signs was recorded at the time of latest follow-up in all cases. Use of cytarabine and lomustine reflected clinician’s preference, mainly based on lack of response to corticosteroids while still hospitalized; however, complete information regarding this clinical decision is lacking in the records. Cytarabine and lomustine have also been used as immunomodulatory therapy in addition to steroids in canine MUO and were therefore used for their immunomodulatory effect in feline patients with suspected MUO in the present study. The dosages of these 2 drugs were based on previous descriptions of their use in feline patients (14,18–20). Due to the lack of definitive histopathological diagnosis, it may be reasonable to consider infiltrative neoplasia, including lymphoma, as the main differential diagnosis for.

Table 2. Magnetic resonance imaging findings in 16 cases of feline meningooencephalomyelitis

<table>
<thead>
<tr>
<th>Case</th>
<th>Region scanned</th>
<th>Lesion(s)</th>
<th>Margins</th>
<th>Hydrocephalus</th>
<th>Cerebellar herniation</th>
<th>T1WI</th>
<th>T2WI</th>
<th>Gad uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Brain</td>
<td>Diffuse intraparenchymal cerebral and cerebellar lesions.</td>
<td>Ill-defined</td>
<td>No</td>
<td>No</td>
<td>Iso</td>
<td>Iso</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>T3-L3 spine</td>
<td>Unremarkable.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Cervical</td>
<td>Intramedullary lesion C6-T2.</td>
<td>Ill-defined</td>
<td>No</td>
<td>No</td>
<td>Hypo</td>
<td>Hyper</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>Brain</td>
<td>Multiple brainstem lesions.</td>
<td>Infiltrative</td>
<td>No</td>
<td>No</td>
<td>Iso</td>
<td>Hyper</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>Brain</td>
<td>Swollen cerebrum, decreased gray/white differentiation.</td>
<td>Ill-defined</td>
<td>Yes</td>
<td>Mild</td>
<td>Hypo</td>
<td>Hyper</td>
<td>Meninges</td>
</tr>
<tr>
<td>5</td>
<td>Brain, cervical</td>
<td>Intraparenchymal multifocal cerebral lesions and intramedullary lesion at C2 and C3 level.</td>
<td>Ill-defined</td>
<td>No</td>
<td>No</td>
<td>Iso</td>
<td>Hyper</td>
<td>Yes (cerebral) N/A (cervical)</td>
</tr>
<tr>
<td>6</td>
<td>Brain and T3-S3 spine</td>
<td>Meningeal contrast enhancement.</td>
<td>N/A</td>
<td>No</td>
<td>No</td>
<td>N/A</td>
<td>N/A</td>
<td>Meninges</td>
</tr>
<tr>
<td>7</td>
<td>T3-S3 spine</td>
<td>Intraparenchymal lesion at L4-L5.</td>
<td>Ill-defined</td>
<td>No</td>
<td>No</td>
<td>Iso</td>
<td>Hyper</td>
<td>Meninges</td>
</tr>
<tr>
<td>8</td>
<td>Brain</td>
<td>Intraparenchymal lesions in cerebrum and cerebellum (gray and white matter).</td>
<td>Infiltrative</td>
<td>No</td>
<td>No</td>
<td>Mild</td>
<td>Iso</td>
<td>Hyper</td>
</tr>
<tr>
<td>9</td>
<td>T3-S3</td>
<td>Intramedullary lesion extending at T13-L2 level.</td>
<td>Ill-defined</td>
<td>No</td>
<td>No</td>
<td>Iso</td>
<td>Hyper</td>
<td>Yes</td>
</tr>
<tr>
<td>10</td>
<td>T3-S3</td>
<td>Ventral meningeal contrast enhancement extending at L4-L6 level.</td>
<td>N/A</td>
<td>No</td>
<td>No</td>
<td>N/A</td>
<td>N/A</td>
<td>Meninges</td>
</tr>
<tr>
<td>11</td>
<td>Brain, cervical</td>
<td>Multiple lesions including right temporal lobe, left thalamus, and intramedullary lesion extending at C2-C3 level.</td>
<td>Ill-defined</td>
<td>No</td>
<td>No</td>
<td>Iso</td>
<td>Hyper</td>
<td>No</td>
</tr>
<tr>
<td>12</td>
<td>Brain</td>
<td>Multiple intraparenchymal lesions in cerebrum and patchy meningeal contrast enhancement.</td>
<td>Infiltrative</td>
<td>No</td>
<td>No</td>
<td>Iso</td>
<td>Hyper</td>
<td>Yes</td>
</tr>
<tr>
<td>13</td>
<td>Brain</td>
<td>Intraparenchymal lesion in cerebrum, brainstem, and cerebellum.</td>
<td>Ill-defined</td>
<td>No</td>
<td>No</td>
<td>Hypo</td>
<td>Iso</td>
<td>Yes</td>
</tr>
<tr>
<td>14</td>
<td>T3-L3</td>
<td>Intraparenchymal lesion extending at T13-L2 level.</td>
<td>Ill-defined</td>
<td>No</td>
<td>No</td>
<td>Iso</td>
<td>Hyper</td>
<td>No</td>
</tr>
<tr>
<td>15</td>
<td>Brain</td>
<td>Multifocal intraparenchymal cerebral lesions.</td>
<td>Ill-defined</td>
<td>No</td>
<td>No</td>
<td>Iso</td>
<td>Hyper</td>
<td>No</td>
</tr>
<tr>
<td>16</td>
<td>Brain</td>
<td>Multifocal meningeal contrast enhancement.</td>
<td>N/A</td>
<td>No</td>
<td>No</td>
<td>N/A</td>
<td>N/A</td>
<td>Meninges</td>
</tr>
</tbody>
</table>

Gad — gadoteric acid; N/A — not available.
these patients and the remission of clinical signs as secondary to use of chemotherapy in potentially misdiagnosed patients. The good evolution of the clinical signs in cats reported in the present study opens one of the major key discussions on MUO, both in canine and feline patients, which is the lack of definitive histopathological diagnosis. Brain biopsies do not represent one of the routine tests for diagnosis of MUO in animals, and in feline patients, the small brain volume, may be particularly challenging. Canine MUO is usually considered to be an antemortem diagnosis and further studies are required to increase confidence in diagnostic test findings, especially MRI and CSF analysis, in the diagnosis of feline MUO.

Despite the low number of cases with long-term follow-up, for the first time in veterinary literature, this study suggests prognostic data on feline MUO. All cats survived to discharge and more than half of the cats presented for re-examination were in clinical remission by 2 to 3 wk after diagnosis and remained so until final follow-up (2 to 12 mo). Median time to final follow-up was 5.2 mo, and it is possible that relapse could have occurred in reported cats at a later date than the final follow-up in this study. Overall prognosis in cats with inflammatory CSF has been reported as poor, with 77% of cats surviving less than 1 y (8,24). However inflammatory CSF has been reported in non-inflammatory conditions, including neoplasia, and in infectious CNS diseases, including feline infectious peritonitis (FIP), which may have an important impact on the poor prognosis for cats with inflammatory lesions in the CNS (4,5,24,25). Good prognosis in feline MUO is highlighted by the present study and inflammatory CSF in cats should not always be associated with a poor outcome. Moreover, in the 12/16 cats in which follow-up was available, feline MUO was associated with better medium-term prognosis than in dogs with MUO. Prognosis in dogs affected by MUO has been assessed in several studies, some of which had number of cases similar to the present study (26) and others with larger numbers (27). However, the prognosis remains guarded to poor (9,12,28) in most affected dogs, but with 77% of cats surviving less than 1 y (8,24). However inflammatory CSF has been reported in non-inflammatory conditions, including neoplasia, and in infectious CNS diseases, including feline infectious peritonitis (FIP), which may have an important impact on the poor prognosis for cats with inflammatory lesions in the CNS (4,5,24,25). Good prognosis in feline MUO is highlighted by the present study and inflammatory CSF in cats should not always be associated with a poor outcome. Moreover, in the 12/16 cats in which follow-up was available, feline MUO was associated with better medium-term prognosis than in dogs with MUO. Prognosis in dogs affected by MUO has been assessed in several studies, some of which had number of cases similar to the present study (26) and others with larger numbers (27). However, the prognosis remains guarded to poor (9,12,28) in most affected dogs, for which death was recorded in 50% to 56% (9,28) of the treated dogs.

This study has a number of limitations. A regimented treatment protocol was not used due to the retrospective nature of the study and the need for individual management of cases of MUO. The unpredictability of relapse, differences in disease severity, and variability in treatment response mean that prospective studies investigating treatment regimes is not always practical or ethical. The lack of follow-up in 25% of cases was disappointing and it is possible that some of these cats relapsed or died due to feline MUO; future studies with more complete follow-up are required to better understand the prognosis of this disease.

No histopathological confirmation of MUO was performed due to the survival of all cats. It is therefore not possible to define the precise nature of the inflammatory conditions affecting these cats. However canine MUO is usually considered to be an antemortem diagnosis and the aim of this study was to describe the clinical features of cats with this condition rather than determine its origin. Based on histological changes, several authors have suspected non-FIP viral encephalitides as the underlying cause of most cases of feline meningoencephalitis (8,13,14). While it is possible that false negative CSF PCR results occurred or agents not tested for by CSF PCR (including West Nile virus and Aujeszky’s disease virus) were the cause of disease in this study, it is highly unlikely given the improvement/resolution of clinical signs with immunosuppressive therapy. Ideally all cats would have had T. gondii serology performed to further exclude infection.

Further studies of feline MUO are needed to determine prognosis and treatment response, as well as highlight the corresponding histological changes and possible etiologies. Long-term prognosis of feline MUO remains unknown and large-scale, prospective randomized trials are necessary to compare different treatment protocols for feline MUO as described for canine MUO.

In conclusion, MUO is an important differential diagnosis for variable neurological signs in cats. There was no age, gender, or breed predisposition, although young to middle-aged cats were more commonly affected in this study. Disease onset was usually acute and compatible with multifocal intracranial lesions in most cases, although focal lesions of the brain and spinal cord were seen. Cerebrospinal fluid pleocytosis and MRI characteristics tended to be similar to most reports of canine MUO, with mixed or lymphocytic CSF and ill-defined hyperintensities on T2W and FLAIR sequences, which show patchy contrast uptake. Definitive conclusions regarding treatment cannot be made from this study, but immunosuppressive treatment appeared to be successful in achieving rapid complete or partial remission in all cases that were available for follow-up. Prognosis therefore appears to be better than for canine MUO, but further studies of feline MUO are indicated to better understand its origin, treatment and outcome.

References


Use of topical healing agents on scrotal wounds after surgical castration in weaned beef calves

Sonia Marti, Karen S. Schwartzkopf-Genswein, Eugene D. Janzen, Daniela M. Meléndez, Désirée Gellatly, Edmond A. Pajor

Abstract — Angus bulls (n = 48) were randomly assigned to control (castrated without the application of a post-operative healing agent) or surgical castration followed by either the application of a topical germicide, aluminum powder spray, or liquid bandage. The objective of this study was to determine the efficacy of commercial topical healing agents in improving wound healing and reducing inflammation and secondary infection after surgical castration. Indicators of wound healing included scrotal area temperature (determined by infrared thermography), scrotal circumference, clinical state of the scrotum score, and the wound healing score. Pain sensitivity was measured using a Von Frey anesthesiometer. The healing agents used in this study did not improve indicators of healing such as swelling and healing rate scores or indicators of inflammation including scrotal temperature and circumference of surgical castration lesions. Pain sensation associated with surgical castration was found to last 35 d after the procedure.

Résumé — Usage d’agents cicatrisants topiques sur des blessures scrotales après la castration chirurgicale chez des veaux de boucherie sevrés. Quarante-huit taureaux Angus ont été assignés au hasard à la castration témoin (castration sans l’application d’un agent cicatrisant postopératoire) ou à la castration chirurgicale suivie soit de l’application d’un germicide topique, d’un poudre à l’aluminium en vaporisateur ou d’un pansement liquide dans le but de déterminer l’efficacité des agents cicatrisants topiques commerciaux pour l’amélioration de la guérison des plaies et la réduction de l’inflammation et de l’infection secondaire après la castration chirurgicale. Les indicateurs de cicatrisation des plaies incluaient la température de la région scrotale déterminée par thermographie infrarouge, la circonférence scrotale, le pointage de l’état clinique du scrotum et le pointage de la cicatrisation de la plaie; et la sensibilité à la douleur mesurée à l’aide d’un anesthesiomètre Von Frey. Les agents cicatrisants utilisés dans cette étude n’ont pas amélioré les indicateurs de cicatrisation comme l’enflure et les notes de la rapidité de cicatrisation ou des indicateurs de l’inflammation qui incluaient la température scrotale et la circonférence des lésions de castration chirurgicale. Il a été constaté que la sensation de douleur associée à la castration chirurgicale durait 35 jours après l’intervention.

Introduction

Surgical (knife) castration is one of the most commonly employed techniques used in North American beef cattle.
on wound healing rate, scrotal size, and inflammation; no improvements were reported. Several topical wound healing products are commercially available with recommended use in improving post-castration wound healing in cattle. However, no studies assessing the efficacy of these products for castration wounds have been published. The objective of this work was to evaluate whether selected topical wound healing agents applied directly to the wound immediately after surgical castration would improve healing rate and reduce inflammation, secondary infection, and associated pain.

Materials and methods
Angus bull calves (n = 48) 4 to 5 mo of age [body weight (BW) 187 kg ± 4.9 kg standard deviation (SD)] were managed according to the principles and guidelines of the Canadian Council on Animal Care and the procedures were approved by the local animal care committees at the Lethbridge Research Centre (ACC # 1523) and University of Calgary (AC15–0135) (9). Calves were transported approximately 30 km from a local ranch after weaning and groups of 12 calves were allocated to 1 of 4 feedlot pens at the Agriculture and Agri-Food Canada Lethbridge Research Centre, Lethbridge, Alberta, Canada. Animals were blocked by BW and allotted to 1 of the 4 treatments: control (CT, surgical castration without the application of a post-operative wound healing agent), or surgical castration followed by either the application of a topical germicide (GR, Blue-Kote; Dr. Naylor Blu-Kote, Morris, New York, USA), aluminum powder spray (AL, Aluspray; Vétoquinol, Buckingham, UK), or liquid bandage (LB, Champion seal; KeriCure, Tampa, Florida, USA). Treatments were mixed within each pen (4 treatments per pen, 3 animals per treatment). Pens had a centrally located water system and a concrete apron in front of the feed bunk. Calves were fed a total mixed ration (TMR). Two diets were used during the first 3 d after arrival, calves were fed a diet consisting of 47% chopped grass hay, 30% barley silage, 20% dry rolled barley silage was gradually increased to 67%. On day 9 after arrival, hay was removed to block treatment groups on the day of castration. Animals were also weighed on days 0, 1, 2, 5, and 7, and weekly thereafter until day 49 to calculate average daily gain (ADG).

Animals were weighed on day −1 and BW records were used to block treatment groups on the day of castration. Animals were also weighed on days 0, 1, 2, 5, and 7, and weekly until the end of the experiment, when calves were restrained in the same position in the squeeze chute to maintain a consistent focus and view of the image. The images were then processed with ThermaCam QuickView 1.3 (Flir systems) which recorded the maximum and average temperatures. Scrotal circumference was measured using a scrotal tape (Reliabull; Lane Manufacturing, Denver, Colorado, USA) on days −1, 0 (day of castration), 1, 2, 5, 7, and weekly until the end of the study (8). The clinical state of the scrotum was scored on a 5-point scale, modified from Molony et al (11): 0 — No swelling, inflammation or infection visible; 1 — Increasing degrees of swelling without obvious erythema; 2 — Increasing degree of swelling with obvious erythema but without pus; 3 — Increasing degree of swelling with presence of pus; and 4 — Inflammatory response with presence of pus with intervention needed.

Wound healing or incision state was assessed following a 5-point scale, also on days −1, 0, 1, 2, 5, 7, and weekly until the end of the study:

i) The incision ran the length of the scrotum and tissue was exposed in this area. The incision had exudate, either wet or dry. Scabbing was uncommon but may have been present in isolated locations at the edges or across the center of the wound;

ii) The incision was greater than approximately 3/4 the length of the scrotum and scabbing was present. The incision may have had exudate either wet or dry;

iii) The incision was scabbed or open and was less than 3/4 of the scrotum. The incision site may also have had exudate, either wet or dry;

iv) The wound/incision site was less than 1/4 of the scrotum. A small scab or discoloration was present at the center of the scrotum/wound site. This wound may have had exudate, wet or dry; and

v) The incision site was no longer visible, there was no tissue exposed anywhere on the scrotum. There was no scabbing and or dried exudate (8).

Castration wounds were considered completely healed when no swelling, inflammation, or infection was observed, and when there was no opening along the incision site.

Pain sensitivity was assessed using a Von Frey anesthesiometer (electronic von Frey anesthesiometer with rigid tip; 0 to 1000 g; IITC-Life Science Instruments, Woodland Hills, California, California, USA). Pain sensitivity was assessed using a Von Frey anesthesiometer (electronic von Frey anesthesiometer with rigid tip; 0 to 1000 g; IITC-Life Science Instruments, Woodland Hills, California, USA). Pain sensitivity was assessed using a Von Frey anesthesiometer (electronic von Frey anesthesiometer with rigid tip; 0 to 1000 g; IITC-Life Science Instruments, Woodland Hills, California, USA). Pain sensitivity was assessed using a Von Frey anesthesiometer (electronic von Frey anesthesiometer with rigid tip; 0 to 1000 g; IITC-Life Science Instruments, Woodland Hills, California, USA).
USA) in 2 areas, directly on the wound and on the skin surrounding the wound on the same days that wound healing rate was measured (12,13). To measure pain sensitivity, calves were standing in the chute unrestrained; the tip of the anesthesiometer was then placed on the surface of the scrotum and pressure was gradually exerted against the scrotum until the calves responded (tail flick, kick, and step forward or backwards). The tip of the anesthesiometer was immediately withdrawn and the maximum pressure elicited was recorded. Greater values indicated less pain sensitivity.

With calf as the experimental unit, all data including BW, scrotal temperature from thermographic images, scrotal circumference, and pain sensitivity were analyzed using a mixed-effect model (SAS 9.4; SAS Institute, Cary, North Carolina, USA) with repeated measures. Healing agent (HA), day, and their interactions (HA × day) were included as fixed effects, and calf within pen as a random effect. Time point was considered a repeated factor and was subjected to 3 variance-covariance structures, compound symmetry, autoregressive order one, and unstructured. The covariance structure that minimized Schwarz’s Bayesian information criterion was considered the most desirable analysis. Results are reported as least square means and a post-hoc test (PDIFF option of SAS) was used to compare the adjusted means.

Clinical state of the scrotum and wound healing score were analyzed with a Wilcoxon-Mann-Whitney test (SAS 9.4; SAS Institute) to evaluate the effect of HA on healing time (d). Medians and 95% confidence limits were calculated with univariate procedure (SAS 9.4; SAS Institute).

For all analyses, significance was declared at $P \leq 0.05$ and tendencies were discussed at $0.05 < P \leq 0.10$.

### Results

No treatment differences were observed on maximum ($P = 0.18$) or average ($P = 0.15$) temperatures of the scrotum (Table 1) and scrotal circumferences ($P = 0.60$; Table 1) were similar among treatments for 49 d after castration. The time to reach each wound or incision healing score ($Z < 2.96$; $P > 0.10$) and clinical state of the scrotum ($Z < 4.72$; $P > 0.10$) did not differ among healing agents over the 49-day study.

There were no differences in pain sensitivity among calves before castration. When the testicles were intact (measurement taken on days −1 and 0 before castration) the mean pressure on the skin required to obtain a response from the calves was $637 \pm 53.9$ g. Although no differences were observed among treatments on days 1 and 2, pressure thresholds were reduced ($P < 0.001$ to $442 \pm 52.9$ g and $331.1 \pm 53.9$ g, for days 1 and 2, respectively, compared with days −1 and 0. Values of pain sensitivity remained lower and similar ($P > 0.10$) to the pain values on days 1 and 3 until day 14, when values started to increase ($P < 0.001$). On day 42, when wounds were almost completely healed (no swelling, inflammation or infection, and almost complete closure of the incision), pressure threshold values increased ($P < 0.001$) to values similar to those observed on day −1 ($708.1 \pm 53.9$ g).

A HA × day interaction ($P < 0.09$) was observed in pain sensitivity on the surrounding skin from 48 h until day 21 post-castration (Figure 1). Calves assigned to the GR treatment exhibited the greatest pain sensitivity ($P < 0.10$) on days 2, 5, 7 and 21 compared to CT calves, and on days 2, 5, 7, 14, and 42 ($P < 0.10$) compared to AL calves. The calves in the LB group did not differ from those in the other treatments except on day 42 ($P = 0.05$) during which they exhibited more pain sensitivity than did AL calves. However, on days 2 and 5, the pressure threshold was numerically closer to that of GR calves than to those of CT and AL calves. No differences ($P = 0.48$) were observed in pain sensitivity on the wound.

No treatment differences were observed for final BW ($P = 0.87$) or ADG ($P = 0.86$; Table 2).

### Discussion

Although many studies have assessed various pain mitigation strategies during and after castration (10,14–16) few studies have assessed strategies to improve wound healing and reduce the pain associated with the wound (8). Healing is a complex event involving multiple interactions of different tissue structures, a large number of biochemical substances and infiltrating cell types (17). In addition, there are several other factors that could affect the rate of wound healing such as animal age or environmental conditions. For example, surgically castrated calves have been shown to spend more time standing after the surgery due to the pain caused by the procedure (18). As calves in the present study were housed in feedlot pens rather than on pasture, it is likely that the open castration wound came into contact with the dirt/manure floor and increased the risk of contamination and infection of the wounds. This may have

### Table 1. Least squares means of scrotal temperature, pain sensitivity, and scrotal circumference of recently weaned beef calves assessed for 49 d after surgical castration. The time to reach each wound or incision healing score ($Z$) treatments for 49 d after castration. The time to reach each wound or incision healing score ($Z < 2.96$; $P > 0.10$) and clinical state of the scrotum ($Z < 4.72$; $P > 0.10$) did not differ among healing agents over the 49-day study.

<table>
<thead>
<tr>
<th>Item</th>
<th>Treatment</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average scrotal temperature $(^\circ C)$</td>
<td>CT: 27.8</td>
<td>GR: 28.5</td>
</tr>
<tr>
<td>Maximum scrotal temperature $(^\circ C)$</td>
<td>33.4</td>
<td>33.8</td>
</tr>
<tr>
<td>Pain sensitivity skin $(g)$</td>
<td>534</td>
<td>452</td>
</tr>
<tr>
<td>Pain sensitivity wound $(g)$</td>
<td>430</td>
<td>400</td>
</tr>
<tr>
<td>Scrotal circumference (cm)</td>
<td>15.7</td>
<td>15.6</td>
</tr>
</tbody>
</table>

* Maximum pressures exerted using a Von Frey anesthesiometer.

HA — healing agent effect; day — assessed on days 1, 2, 4, 7, and weekly until day 49; CT — control; GR — topical germicide; AL — aluminum powder spray; LB — liquid bandage; SEM — standard error of the mean.
reduced the effect of the healing agents and future studies should compare pasture-housed versus feedlot housed calves. Complete healing of skin wounds normally occurs within 6 to 8 wk (19) according to 4 overlapping phases: hemostasis, inflammation, repair or proliferation, and remodeling (6,20). It is important to note that wound healing after castration not only involves the skin but also healing of the spermatic cords. In the present study, based on the clinical state of the scrotum, the inflammation phase lasted approximately 14 d after surgery, while the healing of the incision primarily occurred after 35 d. Molony et al (11) reported that swelling was completely gone 9 d after surgical castration in 5- to 7-day-old calves. However, in a study of 2- to 4-month-old beef calves by Stafford et al (21), swelling was gone 14 d after castration, and the wound was completely healed after 48 d (21). Similarly, Mintline et al (8) reported the most pronounced increase in healing occurred between 21 and 35 d after castration in calves castrated at 25 d of age. Based on the results of these studies and the present study, older calves seem to take longer to heal than younger calves; therefore, age may play a large role in the rate of healing after surgical castration.

Furthermore, castration at younger ages facilitates management, and reduces stress and risk of disease due to reduced testicular development (22,23). The CVMA recommends that castration be performed in animals as young as possible to reduce the adverse effects of the procedure. However, there is still a large percentage of cattle castrated at weaning and later in life (1). In addition, when castration is performed in recently weaned calves, cell types involved in the healing process (mainly leukocyte subsets) may be reduced due to the immunosuppressive effect associated with weaning stress, making calves more susceptible to infection and moribundity (24,25). When infection occurs during the inflammation phase of the healing process, the wound may become chronic (7) as the extended inflammation does not allow the proliferation and remodeling phase to proceed normally, thereby extending the healing time (26). In the present study, the application of healing agents did not reduce or prolong the inflammation phase most likely because we did not observe chronic wounds. In addition, the application of healing agents did not reduce healing time; thereby, not making the wound healing process in each phase faster. The wound healing agents tested in this study were selected based on their ability to facilitate wound drainage. However, as observed by the greater values of pain sensitivity from days 2 to 14, and the numerically greater clinical state values on days 2 and 5, and from days 28 to 35, the AL spray may not have facilitated

![Graph](image-url)  
**Figure 1.** Pain sensitivity as maximum pressure (g) exerted with an anesthesiometer in relation to time (d) post-castration without the application of a post-operative healing agent (CT) or with the application of a topical germicide (GR), aluminium powder spray (AL), or liquid bandage (LB) on recent weaned beef calves.

<table>
<thead>
<tr>
<th>Item</th>
<th>Treatment</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial BW, kg</td>
<td>CT</td>
<td>GR</td>
</tr>
<tr>
<td>Final BW (d 49), kg</td>
<td>185</td>
<td>187</td>
</tr>
<tr>
<td>ADG (d 49), kg/d</td>
<td>1.20</td>
<td>1.25</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Item</th>
<th>Treatment</th>
<th>P-value</th>
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<tr>
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<td>187</td>
</tr>
<tr>
<td>ADG (d 49), kg/d</td>
<td>1.20</td>
<td>1.25</td>
</tr>
</tbody>
</table>

HA — healing agent effect; ADG — average daily gain; CT — control; GR — topical germicide; AL — aluminium powder spray; LB — liquid bandage; SEM — standard error of the mean.
drainage from the scrotum resulting in the formation of scar tissue in the spermatic cords.

Despite the lack of differences in the healing process, we observed that calves had sensitive skin (measured with the Von Frey anesthesiometer) until 35 d after castration when inflammation had declined (as observed by clinical state of the scrotum score < 2) and the incision was less than 3/4 of the scrotum (as observed by wound healing score < 3). These findings indicate that calves continue to feel pain during the inflammation phase and pain is not reduced until the remodeling phase of the wound is achieved.

Our results indicate that the topical wound healing agents used in this study did not improve wound healing. However, information regarding healing time and the length of pain sensation associated with these types of wounds was documented. Further studies on castration methods (both surgical and band techniques) and wound healing according to age, breed, types of incision, and environmental factors are needed to develop strategies to reduce healing time and secondary infections in castrated beef calves.

Acknowledgments

The authors appreciate the invaluable help of Agriculture and Agri-Food Canada research feedlot staff, our technicians Randy E Wilde and Fiona Brown, and Dr. Cassandra Tucker for help in the statistical analysis. We are very thankful for the funding provided by the Beef Cattle Research Council through the Canadian Beef Industry Science Cluster. This article is Lethbridge Research Centre contribution # 16054

References

Association of unmeasured strong ions with outcome of hospitalized beef and dairy diarrheic calves

Diego E. Gomez, Jeanne Lofstedt, Luis G. Arroyo, Maureen Wichtel, Tammy Muirhead, Henri Stämpfli, J. Trenton McClure

Abstract — Increased systemic concentrations of L-lactate and unmeasured strong ions (USI) are associated with an increased risk of mortality in human neonates and adults suffering from various diseases. This exploratory study aimed to investigate if values of certain acid-base parameters, especially L-lactate and USI, on admission to hospital are associated with mortality in diarrheic calves. Fifty-five calves < 28 days old admitted to 2 teaching hospitals for diagnosis and treatment of diarrhea were included. Admission demographic, physical examination, blood gas and biochemistry analysis, and outcome data were recorded. Admission acid-base values associated with outcome were assessed using multivariable regression modeling. Calves with elevated plasma L-lactate (OR: 1.30, 95% CI: 1.08 to 1.55; \( P = 0.005 \)) and USI (OR: 1.40, 95% CI: 1.12 to 1.74; \( P = 0.003 \)) at admission were more likely to die or to be euthanized. This study revealed that elevated concentrations of L-lactate and USI at admission were positively associated with mortality.

Résumé — Association des ions forts non mesurés avec les résultats des veaux de boucherie et laitiers diarrhéiques hospitalisés. Des concentrations systémiques accrues de L-lactate et des ions forts non mesurés (IFN) sont associées à un risque accru de mortalité chez les nouveau-nés humains et les adultes souffrant de diverses affections. Cette étude exploratoire visait à vérifier si les valeurs de certains paramètres acides, particulièrement L-lactate et IFN, à l’admission à l’hôpital sont associées à la mortalité chez les veaux diarrhéiques. Cinquante-cinq veaux âgés de < 28 jours admis à deux hôpitaux d’enseignement pour le diagnostic et le traitement ont été inclus. Les données démographiques, l’examen physique, les valeurs des gaz sanguins et de l’analyse biochimique du sang ainsi que l’issue des animaux ont été consignées. Les valeurs de l’équilibre acide-base à l’admission associées à l’issue des animaux ont été évaluées en utilisant une modélisation de régression multi-variable. Il était plus probable que les veaux avec du L-lactate plasmatique élevé (RC : 1,30, IC 95 %, 1,08 à 1,55; \( P = 0,005 \)) et IFN (RC : 1,40, IC de 95 %, 1,12 à 1,74; \( P = 0,003 \)), à l’admission meurent ou soient euthanasiés. Cette étude a révélé que des concentrations élevées de L-lactate et d’IFN à l’admission étaient positivement associées à la mortalité.

Introduction

Diarrhea is the most important disease in calves < 30 d of age (1). Metabolic acidosis is the most common acid-base disorder occurring in calves with diarrhea (2–7). The quantitative physicochemical approach is a precise method for assessing metabolic acidosis and provides insight into the main underlying mechanisms that contribute to the acidemia (8,9). This approach states that plasma \([\text{H}^+]\) is determined by 3 independent factors: pCO\(_2\), strong ion difference (SID), and total weak acid concentration (\(A_{\text{tot}}^{-}\)) (10). The pCO\(_2\) levels influence pH through chemical equilibrium and depend on alveolar ventilation and metabolic CO\(_2\) production (11). Strong ion difference accounts for the contribution of the strong cations (Na\(^+\), K\(^+\), Ca\(^{2+}\), Mg\(^{2+}\)) and strong anions [principally Cl\(^-\), L-lactate\(^-\)].
(L-lac), D-lactate (D-lac), uremic anions, ketoacids, and unmeasured strong ions) to the acid-base balance (8–10). The \( \text{A}_{\text{tot}}^- \) includes important non-volatile weak buffers such as albumin, globulins, and phosphate that also exert an independent effect on plasma pH (9,10). The mechanisms contributing to acid-base disorders in sick and diarrheic calves include hyponatremia, accompanied by normochloremia or hyperchloremia, and increased unmeasured strong anions, commonly D-lac\(^-\) and L-lac\(^-\) (6,7,12–14).

Increased concentration of unmeasured strong ions (USI) other than L- and D-lac\(^-\) has been reported in critically ill human patients (15,16). The mechanisms resulting in increased concentrations of USI are not fully understood; however, concentrations are increased in patients with endotoxemia (16), tissue hypoperfusion (16), and renal and hepatic impairment (17,18). Similar to L-lac\(^-\), USI are associated with an increased risk of mortality in human neonates and adults suffering from various diseases (15–19). One study in calves assessed the prognostic value of L-lac\(^-\) and D-lac\(^-\) for hospital mortality and failed to detect an association between L-lac\(^-\) and D-lac\(^-\) values and calf mortality (13). There is little information on the association between USI and mortality in calves with neonatal diarrhea.

We hypothesized that admission values of biochemical and acid-base parameters, especially L-lac\(^-\) and USI, are associated with hospital mortality in calves with diarrhea. The objective of this exploratory study was to investigate if admission values of independent acid-base and biochemical variables in calves with diarrhea were associated with mortality during hospitalization.

**Materials and methods**

**Study population and data collection**

This prospective study was conducted with 55 calves admitted to the Atlantic Veterinary College Veterinary Teaching Hospital (AVC) \( (n = 37) \) and the Ontario Veterinary College (OVC) \( (n = 18) \) for diagnostic workup and treatment of acute diarrhea. Calves were eligible for enrolment in the study if they were < 28 d of age, had a diagnosis of neonatal diarrhea (20), and if blood gas and plasma biochemical profile values were determined within 2 h after admission, and before administration of intravenous or oral fluids in the hospital. On admission, demographic and physical examination data, volume and type of oral fluids, and antimicrobials administered before presentation were recorded. Calves suffering from umbilical infection, meningitis, or musculoskeletal diseases (e.g., septic arthritis) were excluded from the study. Survival was defined as discharge from the hospital. This study was approved by the University of Prince Edward Island’s Animal Care Committee (Protocol #13-024).

**Sample collection and measurement techniques**

Venous blood samples were collected in plastic blood collection tubes (BD Vacutainer; Becton Dickinson, Mississauga, Ontario) containing K\(_2\)EDTA (hematology) and sodium heparin (biochemical profile) from the jugular vein at the time of admission and before administration of oral or intravenous fluids. At the AVC, venous blood pH, p\(_{\text{CO}_2}\) (mmHg), and calculated HCO\(_3^-\) (mmol/L) were determined using a portable IRMA true point blood gas analyzer [International Technidyne Corporation (ITC), Edison, New Jersey, USA]. Plasma Na\(^+\), K\(^+\), Cl\(^-\), L-lac\(^-\), and creatinine were measured using a Cobas 6000 C501 automated multianalyzer (Roche Diagnostics, Indianapolis, Indiana, USA). At the OVC, venous blood pH, p\(_{\text{CO}_2}\) (mmHg), and calculated HCO\(_3^-\) (mmol/L) and strong ions (Na\(^+\), K\(^+\), Cl\(^-\), and L-lac\(^-\)) were assayed using a Radiometer 800 Flex blood gas machine (Radiometer medical Aps, Bronshoj, Denmark). The concentration of the strong electrolytes was measured on both analyzers using ion-selective electrode technology based on direct (OVC) and indirect (AVC) potentiometric measuring principles. All blood gas analyses were corrected for the calf’s rectal temperature. Total plasma protein was assessed as total solids using visual refractometry in both hospitals. Plasma D-lac\(^-\) was measured with an enzymatic method using D-lac\(^-\) dehydrogenase (21) following the manufacturer’s instructions with a range of detection between 0.0 to 30 mmol/L (BioVision; Mipitas, California, USA). For D-lac\(^-\), all assays were performed in triplicate and the mean of these measurements was taken as the plasma concentration of D-lac\(^-\). The \( \beta \)-hydroxybutyrate (\( \beta \)HB) concentration was determined using an electrode specific assay following the manufacturer’s instructions (Precision xtra; Abbot Diabetes Care, Alameda, California, USA). The range of detection of \( \beta \)HB concentration in plasma was 0.0 to 8.0 mmol/L. For both D-lac\(^-\) and \( \beta \)HB determination, blood samples were centrifuged within 30 min of collection and plasma was harvested and frozen at \(-80^\circ \text{C}\) until analysis. Plasma D-lac\(^-\) and \( \beta \)HB concentrations were also assayed in 10 calves (control) presented to the teaching hospitals for umbilical hernias \( (n = 5) \) and non-infectious orthopedic abnormalities \( (n = 5) \). The lower and higher ranges were used as reference range.

**Calculations**

Physicochemical variables were calculated as follows (6):

- Total plasma concentration of weak acids \( \text{A}_{\text{tot}}^- \) was calculated as: \( \text{A}_{\text{tot}}^- \) (mmol/L) = \( 0.343 \times (\text{TP}) \), where total protein (TP) is in g/L (6).
- Total negative charge of the plasma \( \text{A}^- \) (mmol/L) was calculated as: \( \text{A}^- \) (mmol/L) = \( \text{A}_{\text{tot}}^- \)/(1 + 10\(^{\text{pK}_a-pH}\)), where \( \text{pK}_a \) (7.08) is the effective dissociation constant of bovine plasma weak acids.
- Strong ion difference (SID\(_m\), mmol/L) has 2 components: measured strong ion difference \( \text{SID}_m \) and unmeasured strong ion difference \( \text{USI}_m \) (mmol/L) (6). The \( \text{SID}_m \) was calculated using the measured plasma concentrations of 5 strong ions as: \( \text{SID}_m = (\text{Na}^+ + \text{K}^+) + (\text{Cl}^- + \text{L-lac}^- + \text{D-lac}^-) \), whereas \( \text{USI}_m \) was calculated as: \( \text{USI}_m = \text{SID}_m - \text{HCO}_3^- \).

**Statistical analysis**

Descriptive analyses were performed on all variables. Normality of the data was tested by the Kolmogorov-Smirnov test. The mean and standard deviation (SD) were calculated for normally distributed variables and the median and interquartile ranges \( (q_{25} \) and \( q_{75} \) \) were determined for non-normally distributed variables. To determine which variables were associated with initial outcome, a Student \( t \)-test (for data normally distributed)
or Mann-Whitney U-test (for data non-normal distributed) was used to compare survivors and non-survivors. Then, Spearman's correlation coefficient was calculated to characterize associations between parameters. When 2 variables had a high correlation coefficient \((R > 0.6)\) only 1 variable was entered into the model. The variable of major clinical and biological importance was entered into the model. The following selected variables, hospital, age (days), breed (dairy and beef), gender (male and female), heart rate, temperature, respiratory rate, glucose, \(pCO_2\), \(Na^+\), \(K^+\), D-lactate, L-lactate, SID\(_m\), USI, \(A_{so}\) and creatinine were screened using a univariable logistic regression (Student \(t\)-test or Mann-Whitney U-test). Variables with a \(P\)-value < 0.1 on univariable analysis were included in the multivariable logistic model (22). The multivariable model was a backward stepwise model, whereby variables were removed sequentially starting with those having the largest \(P\)-value. Once the final model was selected, odds ratios (OR) and 95% confidence intervals (CI) were calculated. Interaction and quadratic terms were investigated for significant predictors in the multivariable models. For the model, the Pearson residuals, the standardized Pearson residuals, and the Δ\(P\) values were computed for all covariate patterns to determine if any specific covariate pattern had an undue influence on the model (22). Goodness-of-fit was evaluated using the Hosmer-Lemeshow goodness-of-fit Chi-square statistic. A \(P\)-value < 0.05 was considered significant. Statistical analyses were done using statistical software (Minitab Software, Philadelphia, Pennsylvania, USA and STATA, StataCorp LP, College Station, Texas USA).

### Results

**Study population and physical examination**

Data regarding demographic characteristics, physical examination findings, treatment, and causes of the diarrhea are presented in Table 1. Cases were presented throughout the year, with the highest number of calves being admitted between April and September. Information on administration of oral rehydration solution (ORS) and antimicrobials within 24 h before admission to the hospital was obtained in 27 (73%) of the calves presented

### Table 1. Demographic data, physical examination findings, treatment and outcome of 55 diarrheic calves presented to 2 Canadian veterinary teaching hospitals

<table>
<thead>
<tr>
<th>Demographic data</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>AVC</td>
</tr>
<tr>
<td>Female</td>
<td>Fluid therapy</td>
</tr>
<tr>
<td>43/55 (78%)</td>
<td>OES</td>
</tr>
<tr>
<td>Male</td>
<td>Intravenous</td>
</tr>
<tr>
<td>12/55 (22%)</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Breeding</td>
<td>NSAIDs</td>
</tr>
<tr>
<td>Dairy</td>
<td>Fluid therapy</td>
</tr>
<tr>
<td>43/55 (78%)</td>
<td>OES</td>
</tr>
<tr>
<td>Beef</td>
<td>Intravenous</td>
</tr>
<tr>
<td>12/55 (22%)</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Age (days)</td>
<td>NSAIDs</td>
</tr>
<tr>
<td>Median (range)</td>
<td>Fluid therapy</td>
</tr>
<tr>
<td>&lt; 7</td>
<td>OES</td>
</tr>
<tr>
<td>14 (to 28 d)</td>
<td>Intravenous</td>
</tr>
<tr>
<td>8 to 14</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>15 to 21</td>
<td>NSAIDs</td>
</tr>
<tr>
<td>22 to 28</td>
<td></td>
</tr>
<tr>
<td>Physical examination</td>
<td></td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td></td>
</tr>
<tr>
<td>116 (20 to 160)</td>
<td></td>
</tr>
<tr>
<td>Respiratory rate (rpm)</td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td></td>
</tr>
<tr>
<td>32 (12 to 66)</td>
<td></td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td></td>
</tr>
<tr>
<td>38.1 (35 to 40)</td>
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</tr>
<tr>
<td>Dehydration*</td>
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</tr>
<tr>
<td>Normal (&lt; 5%)</td>
<td>8/55 (15%)</td>
</tr>
<tr>
<td>Mild (5% to 15%)</td>
<td>9/55 (16%)</td>
</tr>
<tr>
<td>Moderate (8% to 12%)</td>
<td>20/55 (36%)</td>
</tr>
<tr>
<td>Severe (10% to 12%)</td>
<td>18/55 (33%)</td>
</tr>
<tr>
<td>Posture</td>
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</tr>
<tr>
<td>Standing</td>
<td>19/55 (33%)</td>
</tr>
<tr>
<td>Sternal</td>
<td>15/55 (27%)</td>
</tr>
<tr>
<td>Lateral</td>
<td>21/55 (38%)</td>
</tr>
<tr>
<td>Attitude</td>
<td></td>
</tr>
<tr>
<td>Bright</td>
<td>10/55 (18%)</td>
</tr>
<tr>
<td>Obtunded</td>
<td>29/55 (53%)</td>
</tr>
<tr>
<td>Stuporous</td>
<td>16/55 (29%)</td>
</tr>
<tr>
<td>Suckling reflex</td>
<td></td>
</tr>
<tr>
<td>Strong</td>
<td>15/55 (33%)</td>
</tr>
<tr>
<td>Weak</td>
<td>19/55 (35%)</td>
</tr>
<tr>
<td>Absent</td>
<td>21/55 (38%)</td>
</tr>
</tbody>
</table>

bpm — beats/min; rpm — respirations/min; AVC — Atlantic Veterinary College; OVC — Ontario Veterinary College; OES — oral electrolyte solutions; NSAIDs — non-steroidal anti-inflammatory drugs; BCoV — bovine coronavirus; BRoV — bovine rotavirus; hydration status was based on extent of enophthalmos, skin elasticity on neck and thorax, capillary refill time and moistness of the mucous membranes; \(b\) number of samples tested for a given pathogen.
to AVC and 18 (100%) of the calves admitted to OVC. Of the 27 calves admitted to AVC 23 (85%) received ORS and 11 (41%) β-lactam antimicrobials (procaine penicillin and sodium ceftiofur); 4 (15%) received long acting oxytetracycline, and 4 (15%) received trimethoprim-sulfadiazine. All 18 calves admitted to OVC received ORS and 14 (78%) received sodium ceftiofur. The attending clinician established the treatment protocol for each calf (Table 1). All calves were treated for at least 24 h and received intravenous intravenous fluids with or without glucose and oral electrolytes. Thirty-three (60%) of the calves were discharged from the hospital, while 22 (40%) either died (n = 4) or were euthanized (n = 18) due to a poor prognosis. None of the calves were euthanized due to financial constraints. Survival was significantly different between dairy and beef calves (P = 0.005). Three (25%) of the 12 beef calves and 30 (70%) of the 43 dairy calves survived. There was no difference in survival between female and male calves (P = 0.34).

**Factors associated with mortality in hospitalized calves with diarrhea**

Spearman’s correlation coefficients of all blood parameters are presented in Table 3. Factors associated with hospital mortality in the univariate analysis included rectal temperature upon admission, breed, creatinine, pCO₂, Na⁺, D-lactate, L-lactate, and USI. The final multivariate logistic regression model for predicting hospital mortality included the variables plasma L-lactate (OR: 1.30, 95% CI: 1.08 to 1.55; P = 0.005) and USI (OR: 1.40, 95% CI: 1.12 to 1.74; P = 0.003) (Table 4). The addition of interaction terms for significant predictors failed to improve the model fit. The Hosmer and Lemeshow goodness-of-fit test confirmed that the data fit the model (P = 0.23).

**Discussion**

This study documents the presence of unmeasured strong ions (USI) other than D- and L-lactate in beef and dairy calves suffering from diarrhea. The etiology and physiopathology of increased levels of USI are poorly understood. Endogenous anions may be generated in peripheral tissues during global hypoxic states (15) and through hepatic impairment (16,17). Sepsis has also been implicated as a cause of increased USI in an experimental study (16,17). Inconsistent results have been found regarding the contribution of Krebs’ cycle (TCA) intermediates in human patients with anion gap acidosis (23,24). One study found that the USI could be explained by the presence of

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**Table 2. Admission values of clinical, biochemical, and acid-base parameters of survivors and non-survivors among calves with neonatal diarrhea**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Survivors (n = 33)</th>
<th>Non-survivors (n = 22)</th>
<th>Reference range</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dairy</td>
<td>30</td>
<td>13</td>
<td>N/A</td>
<td>0.005</td>
</tr>
<tr>
<td>Beef</td>
<td>3</td>
<td>9</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>114 (68 to 160)</td>
<td>120 (44 to 154)</td>
<td>80 to 120</td>
<td>0.395</td>
</tr>
<tr>
<td>Respiratory rate (rpm)</td>
<td>29 (16 to 60)</td>
<td>36 (12 to 66)</td>
<td>30 to 60</td>
<td>0.324</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>39 (36 to 39.8)</td>
<td>37.2 (35 to 40)</td>
<td>38 to 39.5</td>
<td>0.003</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>4.6 (0.7 to 7.4)</td>
<td>4.5 (0 to 24)</td>
<td>2.5 to 4.3</td>
<td>0.971</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>6.5 (2.8 to 23)</td>
<td>12 (1.3 to 42)</td>
<td>7 to 11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>88 (51 to 430)</td>
<td>164 (21 to 611)</td>
<td>67 to 175</td>
<td>0.01</td>
</tr>
<tr>
<td>Na⁺ (mmol/L)</td>
<td>132 ± 7.3</td>
<td>137 ± 10</td>
<td>132 to 152</td>
<td>0.05</td>
</tr>
<tr>
<td>K⁺ (mmol/L)</td>
<td>4.4 (2 to 10)</td>
<td>5.1 (2.6 to 9)</td>
<td>3.9 to 5.8</td>
<td>0.03</td>
</tr>
<tr>
<td>Cl⁻ (mmol/L)</td>
<td>97 ± 8.6</td>
<td>98 ± 9.4</td>
<td>95 to 110</td>
<td>0.07</td>
</tr>
<tr>
<td>L-lactate⁻ (mmol/L)</td>
<td>2 (0.5 to 13)</td>
<td>8 (1 to 16)</td>
<td>0.6 to 2.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>D-lactate⁻ (mmol/L)</td>
<td>2 (0 to 21)</td>
<td>2.1 (0 to 16)</td>
<td>0.0 to 3.2⁺</td>
<td>0.08</td>
</tr>
<tr>
<td>βHB (µmol/L)</td>
<td>0.1 (0 to 0.4)</td>
<td>0 (0 to 0.3)</td>
<td>0.0 to 0.2⁺</td>
<td>0.14</td>
</tr>
<tr>
<td>TPP (g/L)</td>
<td>65 ± 11</td>
<td>65 ± 13</td>
<td>57 to 81</td>
<td>0.87</td>
</tr>
<tr>
<td>pH</td>
<td>7.15 ± 0.17</td>
<td>7.09 ± 0.22</td>
<td>7.35 to 7.50</td>
<td>0.2</td>
</tr>
<tr>
<td>pCO₂ (mmHg)</td>
<td>41 (25 to 71)</td>
<td>48 (26 to 136)</td>
<td>34 to 45</td>
<td>0.01</td>
</tr>
<tr>
<td>HCO₃⁻ (mmol/L)</td>
<td>16 ± 8</td>
<td>17 ± 8</td>
<td>20 to 30</td>
<td>0.36</td>
</tr>
<tr>
<td>SID⁺ (mmol/L)</td>
<td>26 (16 to 44)</td>
<td>33 (19 to 52)</td>
<td>38 to 42</td>
<td>0.45</td>
</tr>
<tr>
<td>USI (mmol/L)</td>
<td>−1.5 (−8.5 to 3.2)</td>
<td>−6 (−12 to 1)</td>
<td>−2 to 0</td>
<td>0.01</td>
</tr>
<tr>
<td>A⁻₅₅ (mmol/L)</td>
<td>22 ± 4</td>
<td>22 ± 4.5</td>
<td>13 to 25</td>
<td>0.82</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. Data with non-normal distribution are presented as median (range). P-values obtained from Student’s t-test (data with normal distribution) or Mann-Whitney U-test. Reference ranges are from references 22, 46, and 47.

*bpm — beats/min; rpm — respirations/min; βHB — β-hydroxybutyrate; TPP — total plasma protein; HCO₃⁻ — bicarbonate; pCO₂ — venous partial carbon dioxide pressure; SID⁺ — measured strong ion difference; USI — unmeasured strong ions; A⁻₅₅ — total plasma concentration of non-volatile weak acids. *Reference value determined in 10 control calves; N/A — Not available.

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Table 3. Spearman’s coefficients of correlation between selected clinicopathological variables in calves of the study population

<table>
<thead>
<tr>
<th>Term</th>
<th>pH</th>
<th>pCO₂</th>
<th>HCO₃⁻</th>
<th>SIDₙ</th>
<th>USI</th>
<th>Aₙ entire</th>
<th>D-lac</th>
<th>L-lac</th>
<th>Creat</th>
<th>TP</th>
<th>Na⁺</th>
<th>K⁺</th>
<th>Cl⁻</th>
<th>Urea</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-lac</td>
<td>1.00</td>
<td>0.22</td>
<td>1.00</td>
<td>0.87**</td>
<td>0.59**</td>
<td>1.00</td>
<td>-0.51**</td>
<td>-0.11**</td>
<td>0.30**</td>
<td>-0.42**</td>
<td>0.50**</td>
<td>0.02**</td>
<td>0.00**</td>
<td>0.33**</td>
</tr>
<tr>
<td>USI</td>
<td>-0.78**</td>
<td>0.49**</td>
<td>0.91**</td>
<td>1.00</td>
<td>0.43**</td>
<td>0.11**</td>
<td>-0.46**</td>
<td>-0.01NS</td>
<td>-0.24**</td>
<td>0.22NS</td>
<td>0.25NS</td>
<td>0.46**</td>
<td>1.00</td>
<td>0.00NS</td>
</tr>
<tr>
<td>Aₙ entire</td>
<td>-0.32**</td>
<td>-0.53*</td>
<td>0.13NS</td>
<td>-0.23NS</td>
<td>0.00NS</td>
<td>0.13NS</td>
<td>-0.23NS</td>
<td>0.00NS</td>
<td>0.14NS</td>
<td>0.14NS</td>
<td>0.01NS</td>
<td>-0.13NS</td>
<td>0.14NS</td>
<td>0.00NS</td>
</tr>
<tr>
<td>D-lac</td>
<td>-0.51**</td>
<td>-0.01NS</td>
<td>-0.42**</td>
<td>-0.47**</td>
<td>-0.12NS</td>
<td>0.22NS</td>
<td>1.00</td>
<td>0.24**</td>
<td>-0.01NS</td>
<td>1.00</td>
<td>0.24**</td>
<td>0.55**</td>
<td>1.00</td>
<td>0.00NS</td>
</tr>
<tr>
<td>L-lac</td>
<td>0.30**</td>
<td>0.22**</td>
<td>-0.14NS</td>
<td>0.06NS</td>
<td>0.46**</td>
<td>0.50**</td>
<td>0.25NS</td>
<td>0.02NS</td>
<td>0.24NS</td>
<td>0.55**</td>
<td>1.00</td>
<td>0.00NS</td>
<td>0.24NS</td>
<td>0.55**</td>
</tr>
<tr>
<td>Creat</td>
<td>-0.42**</td>
<td>0.17**</td>
<td>-0.24NS</td>
<td>0.06NS</td>
<td>0.46**</td>
<td>0.50**</td>
<td>0.25NS</td>
<td>0.02NS</td>
<td>0.24NS</td>
<td>0.55**</td>
<td>1.00</td>
<td>0.00NS</td>
<td>0.24NS</td>
<td>0.55**</td>
</tr>
<tr>
<td>TP</td>
<td>-0.46**</td>
<td>0.00NS</td>
<td>-0.33*</td>
<td>0.13NS</td>
<td>-0.23NS</td>
<td>1.00**</td>
<td>0.00NS</td>
<td>0.24NS</td>
<td>0.55**</td>
<td>1.00</td>
<td>0.00NS</td>
<td>0.24NS</td>
<td>0.55**</td>
<td>1.00</td>
</tr>
<tr>
<td>Na⁺</td>
<td>-0.11NS</td>
<td>-0.17NS</td>
<td>0.04NS</td>
<td>0.06NS</td>
<td>0.25*</td>
<td>-0.11NS</td>
<td>0.50**</td>
<td>0.08NS</td>
<td>0.14NS</td>
<td>-0.16NS</td>
<td>1.00</td>
<td>0.00NS</td>
<td>0.24NS</td>
<td>0.55**</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>0.14**</td>
<td>0.31*</td>
<td>0.31NS</td>
<td>0.13NS</td>
<td>0.53**</td>
<td>0.28*</td>
<td>0.14**</td>
<td>0.31*</td>
<td>0.39**</td>
<td>0.27**</td>
<td>0.18NS</td>
<td>1.00</td>
<td>0.00NS</td>
<td>0.24NS</td>
</tr>
<tr>
<td>Urea</td>
<td>-0.47**</td>
<td>-0.11NS</td>
<td>-0.41*</td>
<td>-0.24NS</td>
<td>-0.53**</td>
<td>-0.09NS</td>
<td>0.14NS</td>
<td>0.50**</td>
<td>0.06NS</td>
<td>-0.01NS</td>
<td>-0.13NS</td>
<td>0.61**</td>
<td>0.02NS</td>
<td>0.21NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

Table 4. Results of the multivariate logistic regression analysis of clinical, hematological, and biochemical variables associated with mortality in hospitalized diarrheic calves (n = 55)

<table>
<thead>
<tr>
<th>Term</th>
<th>OR</th>
<th>SE</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-lac</td>
<td>1.297</td>
<td>0.120</td>
<td>1.081 to 1.555</td>
<td>0.005</td>
</tr>
<tr>
<td>USI</td>
<td>1.402</td>
<td>0.157</td>
<td>1.125 to 1.748</td>
<td>0.003</td>
</tr>
<tr>
<td>Constant</td>
<td>0.470</td>
<td>0.366</td>
<td>0.106 to 0.214</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

L-lac — L-lactate; USI — unmeasured strong ions; Aₙ entire — total weak acid concentration; Creat — creatinine; TP — total protein; L-lac — L-lactate; D-lac — D-lactate.

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(NAHMS-US) dairy report stated that 57% of calf deaths before weaning resulted from diarrhea, with most cases occurring in calves < 1 mo of age (1). The 2007 NAHMS-US beef report indicated that digestive problems, which were defined to includeloat, scours, parasites, enterotoxemia, accounted for 14% of losses in calves < 3 wk old (36). These studies suggest that mortality associated with calf diarrhea in preweaned calves is higher in dairy than beef farms. The reasons for these differences are not well-established, but factors related to calving season, herd size, interventions at calving, colostrum management, and castration impacted herd-level mortality in preweaned beef calves (37,38). In dairy calves, management practices including colostrum management (failure of transfer of passive immunity), treatment, and vaccination protocols for diarrhea can influence the incidence of diarrhea and therefore the associated mortality rates in each production system. Factors associated with an increased risk of mortality in preweaned dairy calves included failure of transfer of passive immunity, herd-level incidence of pneumonia, season of birth, umbilical problems, the incidence of infectious diseases (e.g., diarrhea), higher incidence of anti-biotic treatment, and a higher proportion of purchased animals and environmental temperature (39–41).

There are several limitations to our findings, most notably the select population of diarrheic calves referred to a teaching hospital for treatment, which would tend to bias the study findings toward sicker calves with diarrhea. Treatment protocols for calves admitted to 2 different hospitals in this study were similar; however, participating hospitals were not provided with a specific treatment protocol. This may have had an impact on the survival analysis. A blinded study design would have been ideal to guarantee that no single laboratory result influenced the decision to euthanize a calf. However, all calves were treated for at least 24 h, which decreased the probability that admission clinicopathologic results did not affect a decision concerning whether or not the calf should be treated or euthanized. At both institutions, the cost of treatment for a diarrheic calf during the first 72 h is fixed, regardless of the severity of disease. Therefore, decisions of euthanasia were not influenced by economic constraints. These limitations should be considered when designing future studies to evaluate the utility of L-lac− and USI parameters to predict mortality in diarrheic calves.

The use of 2 different clinical pathology instruments by the institutions may have had an effect on the measurement of plasma strong ions, and therefore the calculation of SIDm and USI (42). The values for Na+, K+, Cl−, measured by indirect ion selective electrode technology, differ from those measured by direct technology whenever the plasma protein concentrations are above or below 70 g/L (42–44). Therefore, direct ion selective electrode technologies are recommended when accurate measurements of plasma strong ions are necessary (43,44). The data from each institution were analyzed separately, and residual standard deviations of the variables of interest were compared and found to be similar; therefore, the effect of different instrumentation on the results was likely minimal (7,35). In fact, it could be argued that having used 2 different forms of instrumentation and 2 groups of calves may actually make our findings more applicable to other institutions and regions.

Acknowledgments

The authors acknowledge Matt Saab for his technical assistance, and Henrik Stryhn and Carol McClure for their assistance in the statistical analysis.

References


Prevalence and clinical features of hypoadrenocorticism in Great Pyrenees dogs in a referred population: 11 cases

Magali Decôme, Marie-Claude Blais

Abstract — Naturally occurring hypoadrenocorticism (Addison’s disease) is uncommon, with an estimated prevalence in the canine population between 0.06% and 0.28%. This retrospective study evaluated the prevalence and clinical features of hypoadrenocorticism in Great Pyrenees (GP) dogs presented to the Centre Hospitalier Universitaire Vétérinaire of the University of Montreal between March 2005 and October 2014. During this period, 100 dogs were diagnosed with hypoadrenocorticism, representing 0.38% [95% confidence interval (CI): 0.26% to 0.5%] of the canine population studied. The highest prevalence was observed in GP (9.73%, 95% CI: 9.12% to 10.35%, P < 0.0001), followed by West Highland white terriers (4.66%, 95% CI: 4.24% to 5.09%, P < 0.0001), Great Danes (1.87%, 95% CI: 1.6% to 2.14%, P < 0.0001), standard poodles (1.76%, 95% CI: 1.5% to 2.02%, P = 0.0001), Saint Bernards (1.72%, 95% CI: 1.47% to 1.98%, P = 0.018), and Jack Russell terriers (1.48%, 95% CI: 1.24% to 1.72%, P = 0.003). Although most clinical features were nonspecific, Great Pyrenees dogs were more frequently presented with anemia, azotemia, and eosinophilia, or with hypotension and cachexia compared with dogs of other breeds.

Introduction

Canine hypoadrenocorticism, or Addison’s disease, is an endocrine disorder characterized by inadequate secretion of steroid hormones (glucocorticoid and mineralocorticoid hormones) from the adrenal glands. Adrenal insufficiency is categorized as primary or secondary based on whether the deficit is due to the destruction of the adrenal cortex (primary) or the lack of adrenocorticotropic hormone (ACTH), which normally is produced and secreted by the anterior pituitary gland (secondary) (1–3). Primary hypoadrenocorticism is the most common form in dogs. In humans, an immune-mediated process has been clearly identified...
and autoantibodies to adrenal cortex and/or 21-hydroxylase have been detected in up to 48% to 100% of patients with Addison’s disease (4–6). Although autoimmune destruction of the adrenal cortex has been reported in dogs (7), most dogs with spontaneous hypoadrenocorticism are simply classified as idiopathic (2).

Patients with hypoadrenocorticism are typically presented with nonspecific signs such as lethargy, anorexia, vomiting, diarrhea, weight loss, polyuria, and polydipsia. The severity and duration of these clinical findings vary greatly among dogs. Most dogs have chronic and often intermittent clinical signs, but signs can also be acute. Although hyperkalemia and hyponatremia are classic hallmarks of the disease, these clinicopathologic findings are not present in atypical primary and secondary hypoadrenocorticism which result in a glucocorticoid hormone deficiency alone (1,2). An adrenocorticotropic hormone (ACTH) stimulation test is required for definitive diagnosis of hypoadrenocorticism, but a basal serum or plasma cortisol concentration above 55 nmol/L has been suggested as a cut-off value to rule out hypoadrenocorticism with a sensitivity of 100% (8,9). Treatment of naturally occurring hypoadrenocorticism consists of lifelong hormone replacement, which can be expensive, especially in large breed dogs with mineralocorticoid deficiency.

Naturally occurring hypoadrenocorticism is uncommon in dogs. Its prevalence in the general canine population is estimated between 0.06% and 0.28% (10). Based on large epidemiological studies, certain breeds, including bearded collies, standard poodles, Portuguese water dogs, and Nova Scotia duck tolling retrievers, appear to have an increased risk of developing the disease with reported prevalences of 9.4%, 8.6%, 1.5%, and 1.4%, respectively (2,11–13). Data on increased risk for hypoadrenocorticism are reported in many other breeds including West Highland white terriers (WHWT), Great Danes, soft-coated wheaten terriers, rottweilers, and Saint Bernards (2,14). An autosomal recessive inheritance has been identified in standard poodles and Nova Scotia duck tolling retrievers (13,11).

To our knowledge, this is the first paper reporting an increased risk of developing naturally occurring hypoadrenocorticism in Great Pyrenees dogs. Only 1 case report of a 4-year-old female Great Pyrenees dog diagnosed with hypoadrenocorticism has been previously published. This dog was diagnosed with polyendocrinopathy due to lymphocytic adrenalitis and primary hypophysitis (15). The objective of the present study was to evaluate the prevalence and clinical features of naturally occurring hypoadrenocorticism in Great Pyrenees dogs presented to the Centre Hospitalier Universitaire Vétérinaire (CHUV) of the University of Montreal. We hypothesized that the prevalence of naturally occurring hypoadrenocorticism in Great Pyrenees dogs was significantly higher compared to the prevalence of the disease in the hospital population. We also hypothesised that clinical features in naturally occurring hypoadrenocorticism were similar between Great Pyrenees dogs and dogs of other breeds.

Materials and methods

Selection of cases

Medical records of dogs presented to the CHUV of the University of Montreal between March 2005 and October 2014 were reviewed retrospectively to include dogs with a diagnosis of naturally occurring hypoadrenocorticism. The results of an ACTH stimulation test consistent with naturally occurring hypoadrenocorticism had to be available (pre- and post-ACTH serum cortisol level ≥ 55 nmol/L) for dogs to be included in the study (8,9). Dogs diagnosed before their first presentation to the CHUV or newly diagnosed at the CHUV were included. Dogs were excluded from the study if they had received corticosteroids (oral, parenteral, or topical) in the 4 wk before the ACTH stimulation test, or they were being treated or had previously been treated with triostane or mitotane. Based on these criteria, client-owned dogs with confirmed hypoadrenocorticism were retrospectively separated into 2 groups: the Great Pyrenees dog group (GP) and the control group (CG), defined as affected dogs of other breeds.

Data collected from the medical record

The following data were collected from the records of all dogs included in the study: breed, gender, age, history, and reason for presentation, physical examination, laboratory findings, and treatment regime at diagnosis and at last evaluation at the CHUV, as well as cause of death (if available). The owners and family veterinarians were contacted by telephone to obtain any missing information.

Statistical analysis

The prevalence of hypoadrenocorticism in the studied population, as well as the prevalence per breed, were calculated and compared using a t-test. In addition, a Bonferroni correction for multiple comparisons was applied, based on the number of comparisons (number of breed, n = 34); P-values < 0.05 after Bonferroni correction were regarded as significant. Epidemiologic criteria, age at diagnosis, reason for presentation, clinical and laboratory findings were compared between the 2 groups using a t-test (for continuous variables) or a z-test (for categorical variables). The z-test was used to compare the proportions between the 2 populations. Statistical significance was set at P < 0.05. The 95% confidence interval (CI) for prevalence was calculated with exact tests based on binomial distribution.

Results

Study population

The database search of all dogs presented to the CHUV during the study period (n = 26 450) identified 105 dogs with an ACTH stimulation test consistent with hypoadrenocorticism. Five dogs were excluded from the study: 4 dogs had been treated for hyperadrenocorticism with triostane or mitotane and 1 dog had received corticosteroids a few days before the ACTH stimulation test. Therefore, a total of 100 dogs with a diagnosis of naturally occurring hypoadrenocorticism were included in our study. Fourteen dogs had already been diagnosed upon first presentation to the CHUV and ACTH stimulation test results were provided by their regular veterinarian. A total of 114 Great Pyrenees dogs were presented to the CHUV during the study period.

In addition to Great Pyrenees dogs (GP: n = 11), 34 breeds (control group: n = 89) were represented among the dogs diagnosed with hypoadrenocorticism (Table 1).
Twenty-four dogs were diagnosed with concurrent diseases: 4 with recurrent cystitis (including 1 GP); 3 with herniated disk (including 1 GP); 2 each with epilepsy, dilated cardiomyopathy, diabetes mellitus (1 of which had concurrent glomerulopathy and the other had concurrent hypothyroidism); 1 each with megaesophagus with secondary bronchopneumonia, sick sinus syndrome, degenerative valvar disease with concurrent hypothyroidism, immune-mediated hemolytic anemia, bladder stone, dirofilariasis, pancreatitis, laryngeal paralysis, chronic kidney disease, glaucoma, hip dysplasia (1 GP).

**Prevalence of hypoadrenocorticism per breed**

The overall prevalence of hypoadrenocorticism in the study population was 0.38% (95% CI: 0.26% to 0.5%). The prevalence per breed varied between 0.17% and 9.73%, with the highest prevalence observed in GP, which was significantly higher than the overall prevalence of hypoadrenocorticism in our study population (9.73%, 95% CI: 9.12% to 10.35%, P < 0.0001).

A significantly higher prevalence was also observed in WHWT (4.66%, 95% CI: 4.24% to 5.09%, P < 0.0001), Great Danes (1.87%, 95% CI: 1.6% to 2.14%, P < 0.0001), standard poodles (1.76%, 95% CI: 1.5% to 2.02%, P = 0.0001), Saint Bernards (1.72%, 95% CI: 1.47% to 1.98%, P = 0.018), collies (1.52%, 95% CI: 1.27% to 1.76%, P = 0.033), Jack Russell terriers (1.48%, 95% CI: 1.24% to 1.72%, P = 0.003), and miniature poodles (1.14%, 95% CI: 0.93% to 1.35%, P = 0.004) (Figure 1). After Bonferroni correction, the prevalence of hypoadrenocorticism per breed remained significantly higher than the overall hypoadrenocorticism prevalence in our study population in certain breeds including: GP, WHWT, Great Danes, and standard poodles.

**Clinical features of Great Pyrenees dogs with hypoadrenocorticism**

The clinical features and epidemiological factors compared between the 2 groups are detailed in Table 2. Median age at diagnosis was not statistically different between GP and the control group (Table 2). Males were over-represented in the control group (P = 0.004) and in the overall canine population seen at the CHUV during the study period (P < 0.0001), but the proportion male/female was not significantly different between these 2 groups (P = 0.61). Similarly, the proportion of males was not significantly different in GP compared with the control group.

The main reasons for presentation in the GP were lethargy and anorexia, whereas the main reasons for presentation for the dogs in the control group were gastrointestinal signs, lethargy, and anorexia. Great Pyrenees dogs were less frequently presented with gastrointestinal signs than dogs in the control group, but this difference was not significant (P = 0.05). Moreover, GP were significantly more often presented with hypotension (P < 0.0001), defined as a systolic blood pressure < 90 mmHg (measured by Doppler method or petMap blood pressure technology), and cachexia (P = 0.004), defined as a body condition score (BCS) of ≤ 3/9 than were dogs in the control group (Table 2).

There was no significant difference in frequency and severity of serum electrolyte abnormalities between the 2 groups. In both groups, most dogs were presented with typical electrolyte abnormalities, i.e., hyperkalemia (GP: n = 7/9; CG: n = 55/82) and hyponatremia (GP: n = 7/9; CG: n = 56/81). The average Na:K ratio in dogs was not significantly different between the 2 groups (GP: 21.25, CG: 23.77, P = 0.26), neither in dogs with typical hypoadrenocorticism (GP: 18.94, CG: 20.97, P = 0.117). The proportion of atypical hypoadrenocorticism was not significantly different between the 2 groups (GP: n = 2/9, CG: n = 21/82, P = 0.824).

Other major laboratory findings in both groups included azotemia, anemia, lack of a stress leukogram, eosinophilia, and hypoalbuminemia. Compared to the control group, GP were more likely to be presented with azotemia (GP: n = 8/8, CG: n = 42/81, P = 0.004), anemia (GP: n = 7/9, CG: n = 31/80, P = 0.01), and eosinophilia (GP: n = 3/8, CG: n = 11/79, P = 0.04).

The treatment initiated following diagnosis was known for 87 dogs including 9 GP. Following diagnosis, dogs were initially treated with either prednisone alone (GP: n = 2/9, CG: n = 20/78), or prednisone with fludrocortisone (GP: n = 7/9, CG: n = 47/78), or desoxycorticosterone pivalate, DOCP (GP: n = 0/9, CG: n = 11/78). Sixty-seven dogs, including 5 GP, came

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**Table 1. Dogs diagnosed with hypoadrenocorticism presented to the CHUV of the University of Montreal between March 2005 and October 2014**

<table>
<thead>
<tr>
<th>Breed</th>
<th>Number of dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Great Pyrenees</td>
<td>11</td>
</tr>
<tr>
<td>Control group (N = 89)</td>
<td></td>
</tr>
<tr>
<td>West highland white terrier</td>
<td>9</td>
</tr>
<tr>
<td>Standard poodle</td>
<td>7</td>
</tr>
<tr>
<td>Cross-bred dog</td>
<td>7</td>
</tr>
<tr>
<td>Great Dane</td>
<td>7</td>
</tr>
<tr>
<td>Miniature poodle</td>
<td>6</td>
</tr>
<tr>
<td>Labrador retriever</td>
<td>5</td>
</tr>
<tr>
<td>Golden retriever</td>
<td>5</td>
</tr>
<tr>
<td>Shih tzu</td>
<td>4</td>
</tr>
<tr>
<td>Maltese</td>
<td>4</td>
</tr>
<tr>
<td>Jack Russell terrier</td>
<td>4</td>
</tr>
<tr>
<td>Yorkshire terrier</td>
<td>2</td>
</tr>
<tr>
<td>Saint Bernard</td>
<td>2</td>
</tr>
<tr>
<td>Collie</td>
<td>2</td>
</tr>
<tr>
<td>Boxer</td>
<td>2</td>
</tr>
<tr>
<td>Boston terrier</td>
<td>2</td>
</tr>
<tr>
<td>German shepherd</td>
<td>2</td>
</tr>
<tr>
<td>Basset hound</td>
<td>2</td>
</tr>
<tr>
<td>Beagle</td>
<td>1</td>
</tr>
<tr>
<td>Australian shepherd</td>
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<tr>
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<td>1</td>
</tr>
<tr>
<td>German shorthaired pointer</td>
<td>1</td>
</tr>
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<tr>
<td>Chihuahua</td>
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<tr>
<td>Doberman pinscher</td>
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<tr>
<td>Lhasa apso</td>
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<td>Malamute</td>
<td>1</td>
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<tr>
<td>Pomeranian</td>
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<tr>
<td>Rottweiler</td>
<td>1</td>
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<td>Samoyed</td>
<td>1</td>
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<tr>
<td>Newfoundland</td>
<td>1</td>
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<tr>
<td>Wheaten terrier</td>
<td>1</td>
</tr>
<tr>
<td>Tibetan terrier</td>
<td>1</td>
</tr>
<tr>
<td>Weimaraner</td>
<td>1</td>
</tr>
</tbody>
</table>
back to the CHUV for at least 1 revaluation following diagnosis. Treatment at last recheck was known for 61/67 dogs, including 5 GP. Forty-one dogs were treated with fludrocortisone, including 4/5 GP, with an average maintenance dose of 0.025 mg/kg body weight (BW) per day, which was significantly higher than the initial dosage (average: 0.018 mg/kg BW per day, P = 0.042). The increase in dose of fludrocortisone was however not significant when considering the groups separately between the initial dosage at time of diagnosis (GP: 0.020 mg/kg BW per day, CG: 0.019 mg/kg BW per day) and at time of the last recheck (GP: 0.022 mg/kg BW per day, CG: 0.025 mg/kg BW per day). At time of the last recheck, prednisone was administered only as needed during stressful events in 25/61 dogs including 4/5 GP, and administered regularly (daily or every other day) for 36/61 dogs, (including 1/5 GP). In both groups, the maintenance prednisone dosage was significantly decreased compared to the initial dosage (average dosage at time of diagnosis 0.43 mg/kg BW per day and 0.26 mg/kg BW per day at time of the last recheck, P = 0.001). The DOCP dosage was not significantly different for both groups between time of diagnosis and time of last recheck (2.16 mg/kg BW per 25 days and 2.07 mg/kg BW per 25 days, respectively).

The Na/K ratio at time of last recheck was 29.02 in GP and 31.63 in CG, which is not significantly different.

One GP and 2 CG dogs were euthanized at diagnosis. These 3 dogs were presented in hypovolemic shock (weakness, pale mucous membrane, weak pulse and hypotension, tachycardia, and dehydration), and were euthanized for financial reasons. Another dog, presented in shock, was euthanized after 2 d of hospitalization because of lack of significant improvement. All 4 were large breed dogs [1 Labrador retriever (32.5 kg), 1 GP (48.5 kg), and 2 Great Danes (50 and 53.5 kg)].

**Discussion**

The most important finding of our study is a significantly higher prevalence of hypoadrenocorticism in Great Pyrenees dogs (9.73%) compared with the canine hospital population (0.38%). The prevalence of hypoadrenocorticism was also found to be significantly higher in WHWT (4.66%), Great Danes (1.87%), and standard poodles (1.76%).

The high prevalence of naturally occurring hypoadrenocorticism in Great Pyrenees dogs in a referral center in Quebec, Canada, strongly suggests genetic inheritance of this disease. An inherited susceptibility for Addison’s disease has been demonstrated in standard poodles (11) and suspected in the WHWT, soft-coated wheaten terrier, Great Dane, and other poodle breeds (2,10,14,16,17). Saint Bernards have previously been over-represented (18), but although they had an increased prevalence of hypoadrenocorticism in the current study, this was not statistically significant once the Bonferroni correction was applied. The previously reported prevalence in standard poodles was 8.6%, which is higher than the prevalence in our study for this breed and may be explained by the genetic variance of sires and dams in Quebec. Although the mode of inheritance (autosomal recessive) has been well-identified in standard poodles (11), it remains unknown in other breeds (19).

The overall prevalence of hypoadrenocorticism in our studied population was 0.38% (95% CI: 0.26% to 0.5%), which
is higher compared to previously reported prevalences (0.06% to 0.28%) (10). This difference could be explained by the fact that the study was performed in a secondary and tertiary referral practice.

A female predisposition has previously been described for hypoadrenocorticism, with approximately 70% of affected dogs being female (3); however, no gender predisposition has been demonstrated in the standard poodle, Portuguese water dog, Nova Scotia duck tolling retriever, or bearded collie, nor was this observed in Great Pyrenees dogs in our study. Although males with hypoadrenocorticism were over-represented in both groups (GP: 63%, CG: 60%), the higher proportion of males was significant only in the control group (P = 0.04), and likely reflects the male distribution of the overall canine population of the CHUV during the study period. The median age at time of diagnosis was not significantly different between the 2 groups in our study (GP: 3.56 y, CG: 4.85 y), and was similar to the median age of onset for all breeds (13,20,21).

Clinical signs of hypoadrenocorticism are well-described in the veterinary literature (2,3,22). Although the reasons for presentation, clinical signs, and laboratory findings were non-specific, this retrospective study was able to highlight some specific features in the clinical presentation of Great Pyrenees dogs with hypoadrenocorticism presented at the CHUV. In comparison with Addisonsians of other breeds, Great Pyrenees dogs were less frequently presented with gastrointestinal signs, but this difference was not significant, yet more frequently presented with hypotension and cachexia which may reflect misdiagnosis/late diagnosis because Great Pyrenees dogs are not known to be at higher risk of developing hypoadrenocorticism. The main clinical signs in GP were lethargy (77.7%) and anorexia (55.5%). Gastrointestinal signs (diarrhea, vomiting, or regurgitation) were noticed in 33.3% of GP and 61% of dogs in the control group. Findings for our control group are consistent with literature data (vomiting or regurgitation present in 68% to 75% of cases, and diarrhea in 35% of cases) (2,17,20).

Anemia, increased blood urea nitrogen (BUN), and creatinine and eosinophilia were also more common in the Great Pyrenees breed than in other breeds with hypoadrenocorticism. Azotemia is reported in 66% to 95% of dogs with primary hypoadrenocorticism at the time of initial diagnosis (2,3,21,23). In our study, all Addisonian GP were azotemic, which was significantly higher than the control group (51.8%). They were also more frequently anemic than the control group. In the veterinary literature, a mild normochromic nonregenerative anemia is commonly reported in Addisonsians (21% to 25% cases) (3,19,20,21). As Great Pyrenees dogs were more frequently presented with hypotension, they could be more prone to have intestinal bleeding and pre-renai azotemia than dogs of the control group.

Although not a consistent feature in Addisonian patients, lack of a stress leukogram can be a valuable finding particularly in glucocorticoid only deficient dogs (17). The lack of a stress leukogram was a common finding in our study (GP: 62.5%, CG: 63%), although less common than the 92% reported in the veterinary literature (17,20,21). Absolute eosinophilia is reported in 10% to 20% of cases (10,17,21,24). In our study, eosinophilia was observed in 37.5% of GP and in only 13.9% of the CG. This difference is surprising since eosinophilia has not been reported in Great Pyrenees dogs in the literature, nor was it observed in the entire Great Pyrenees dog population seen at the CHUV during the time of the study, except in our Addisonian population. Although this suggests that eosinophilia is a common finding in Great Pyrenees dogs with hypoadrenocorticism, no information regarding potential parasitism was recorded, which may be an alternate explanation.

In North America, DOCP is the only mineralocorticoid supplement approved for veterinary use. Because of financial concerns, all of the GP diagnosed with a primary typical hypoadrenocorticism in our study were treated with fludrocortisone, a synthetic glucocorticoid with significant mineralocorticoid activity. The starting dosage of fludrocortisone is usually 0.02 mg/kg BW, divided and given twice daily (10,21,22). The median starting dosage in our study was 0.018 mg/kg BW per day. The dosage of fludrocortisone was significantly increased concerning all of the GP diagnosed with a primary typical hypoadrenocorticism in our study were treated with fludrocortisone, a synthetic glucocorticoid with significant mineralocorticoid activity. The starting dosage of fludrocortisone is usually 0.02 mg/kg BW, divided and given twice daily (10,21,22). The median starting dosage in our study was 0.018 mg/kg BW per day. The dosage of fludrocortisone was significantly increased concerning all of the GP diagnosed with a primary typical hypoadrenocorticism in our study were treated with fludrocortisone, a synthetic glucocorticoid with significant mineralocorticoid activity. The starting dosage of fludrocortisone is usually 0.02 mg/kg BW, divided and given twice daily (10,21,22). The median starting dosage in our study was 0.018 mg/kg BW per day.
corticosteroid side effects, given the weight of the GP. There was missing information on the long-term follow-up, and time and cause of death in these cases to support any conclusion.

Although evidence supports a similar autoimmune etiology as in humans leading to the destruction of the adrenal cortex, the pathogenesis of hypoadrenocorticism in dogs is not well-established (21,25). In humans, the enzyme steroid 21-Hydrolase (21OH) has been shown to be a major adrenal autoantigen in Addison's disease, and 21OH antibodies (21OH-Ab) and/or adrenal autoantibodies are present in 48% to 100% of patients with idiopathic Addison's disease (4,6,26–30). The genetic factors involved in determining susceptibility to Addison's disease remain poorly understood, despite numerous studies. However, human leucocyte antigen (HLA) DRB1 is recognized as one of the main susceptibility loci involved, with additional risk provided by the major histocompatibility complex (MHC) class I region (29). Similarly, in dogs, several studies support an immune-mediated process with an immune mediated adrenitis being the most likely etiology for the majority of spontaneous cases of canine primary hypoadrenocorticism (21,25). Two loci have been identified in Portuguese water dogs on the Canis familiaris (CFA) chromosomes CFA 12 and 37 (12). Another study suggests an association between dog leukocyte antigen (DLA) class II haplotype and the development of hypoadrenocorticism in Nova Scotia duck tolling retrievers (30,31). As Short et al (29) have already emphasized, pedigree dogs, because of their relatively small population and existence for a relatively short time period, have a high linkage disequilibrium and long haplotypes within a breed. This provides a considerable advantage in veterinary medicine compared to human medicine in increasing the potential of identifying novel genes that contribute to canine genetic diseases. Moreover, strong similarities have been shown in the genetic background of hypoadrenocorticism between dogs and humans, thereby enabling dogs to be spontaneous, genetic models for human Addison's disease (29). The discovery of a new at-risk breed could be helpful to better understand the genetic background of this endocrine disorder.

Further studies are needed to infer a genetic basis of the disease in Great Pyrenees dogs as well as its inheritance rate and mode. The small population of Great Pyrenees dogs in Quebec with a high prevalence of the disease may provide an opportunity to identify the etiology and implicated genes in the breed. Unfortunately, it was not possible to establish the degree of relatedness of the Great Pyrenees dogs in our study.

Limits of this study include those inherent to a retrospective study (i.e., missing data, lack of standardization). Moreover, the population size of Great Pyrenees dogs was small, which can lead to type 2 statistical error. Multiple comparisons were performed between the 2 groups to identify specific clinical features of Great Pyrenees dogs suffering from hypoadrenocorticism, which can lead to type 1 statistical error. Our results, therefore, need to be confirmed by further studies. Finally, since the study was performed in a referral center, the population studied may not be representative of the general canine population and therefore our results should be considered carefully. The real prevalence of hypoadrenocorticism in the general Great Pyrenees dog population remains unknown and large epidemiological studies are required to obtain more representative values. Nevertheless, our results raise awareness about a breed predisposition.

In conclusion, Great Pyrenees dogs diagnosed with hypoadrenocorticism had a prevalence of hypoadrenocorticism of 9.73% and were over-represented in the study population. Therefore, an inherited susceptibility is suspected. Although clinical features were nonspecific, Great Pyrenees dogs were more frequently presented with signs of hypotension, anemia, azotemia, and eosinophilia. A prospective study is necessary to evaluate the prevalence of hypoadrenocorticism in a larger population of Great Pyrenees dogs and to establish its rate and mode of inheritance. (CV)

References

18. Thompson AL, Scott-Moncrieff JC, Anderson JD. Comparison of classic hypoadrenocorticism with glucocorticoid-deficient

Book Review
Compte rendu de livre


Now in its 4th edition, Crow & Walshaw’s Manual of Clinical Procedures in Dogs, Cats, Rabbits & Rodents has become somewhat of a classic. Intended for veterinary technicians, veterinary students, and new veterinarians, it tends to cover more of the basic and less advanced procedures used in clinical practice. This is in no way a bad thing. We all need to feel comfortable carrying out the “bread and butter” techniques used most often.

Each procedure is clearly outlined in step-by-step fashion, using a decent number of color and black and white illustrations. Subheadings for equipment needed, and rational for an action or complications and safety issues involved, organize the material into a very user friendly format. Since the first edition was published, you will find that some procedures are no longer included as they are now rarely used, while others have been left out because our clinical abilities have developed the procedure beyond an introductory text level.

New procedures now found in this text include placement of arterial catheters, central venous pressure measurements, and CPR. Routine clinical procedures outlined include restraint, injection techniques, dermatologic procedures, urethral catheterization, enemas, and anal sac expression.

A unique feature of this text is the inclusion of a small selection of procedures common to exotics. This includes blood collection and fluid administration in rabbits, and carrying, restraining, and examination of a variety of small exotic pocket pets.

Finally, there is an interactive webpage associated with this text that provides multiple choice questions and answers for each chapter, as well as PowerPoint slides of all figures used in the text. It is an advantage that illustrations can be copied for future reference. Overall though, I think the webpage could have been made more valuable, as its use is limited.

As the text implies, it has been used over the years in teaching settings, and I can see it being very useful in that regard. So too, would it be handy for new veterinary graduates and those vets wishing to brush up on some clinical skills.

Reviewed by Janeen Junaid, DVM, MVSc, Hamilton, Ontario.
Hypocholesterolemia and nonregenerative, suspected immune-mediated, anemia: Report of 3 canine cases

Rachel Robbins, Katrina R. Viviano

Abstract — This report describes hypocholesterolemia in 3 dogs with nonregenerative, suspected immune-mediated anemias. Common causes of hypocholesterolemia were ruled out, raising suspicion for a mechanistic link between anemia and hypocholesterolemia in dogs. As observed in humans with concurrent anemia and hypocholesterolemia, cholesterol concentrations increased to within the reference interval once the dogs’ anemia resolved.

Résumé — Hypocholestérolémie et anémie non régénérative suspectée d’origine immunitaire : rapport de 3 cas canins. Ce rapport décrit l’hypocholestérolémie chez trois chiens atteints d’une anémie non régénérative suspectée d’origine immunitaire. Les causes communes d’hypocholestérolémie ont été écartées, soulevant des doutes pour un lien mécanistique entre l’anémie et l’hypocholestérolémie chez les chiens. Tel qu’il a été observé chez les humains atteints d’anémie et d’hypocholestérolémie concomitante, les concentrations de cholestérol ont augmenté dans l’intervalle de référence une fois que l’anémie des chiens s’est résorbée.

This report describes hypocholesterolemia in 3 dogs with nonregenerative, suspected immune-mediated anemias. Common causes of hypocholesterolemia were ruled out, raising suspicion for a mechanistic link between anemia and hypocholesterolemia in dogs. As observed in humans with concurrent anemia and hypocholesterolemia, cholesterol concentrations increased to within the reference interval once the dogs’ anemia resolved.

Hypocholesterolemia has been described in humans with nonmalignant anemias resulting from various causes, including hereditary spherocytosis (1), glucose-6-phosphate dehydrogenase (G6PD) deficiency (2), thalassemias (3,4) and sickle cell disease (5,6), as well as other hematologic abnormalities, including aplastic anemia (7) and myelodysplastic syndrome (8). The level of hypocholesterolemia is variable and considered secondary to the anemia with resolution of hypocholesterolemia following normalization of the patient’s hematocrit (9). In some reports the degree of hypocholesterolemia has been described to have prognostic significance, including increased morbidity/mortality (6,10) and poor response to immunosuppression (7). Mechanisms underlying this interaction remain unexplained, but increased cholesterol utilization and altered cholesterol metabolism have been suggested (3,11–14).

Destruction of erythrocytes or erythroid precursors is associated with various etiologies, including drugs/toxin exposure, infections, and neoplasia, and may also occur as a primary disease via antibody or cell-mediated immune mechanisms (15–17). Despite immune-mediated anemias being a relatively common clinical presentation in middle-aged dogs, an association between anemia and hypocholesterolemia has not been reported (16,17). In dogs, hypocholesterolemia typically is associated with malabsorption (i.e., protein-losing enteropathies or lymphangiectasia) and malabsorption (i.e., exocrine pancreatic insufficiency), decreased production by the liver (i.e., cirrhosis, liver failure, or portosystemic shunts), or hypoadrenocorticism. This report describes 3 dogs presented to UW Veterinary Care (UWVC) with a nonregenerative anemia, suspected to result from immune-mediated mechanisms, and concurrent hypocholesterolemia, in which the more common causes of hypocholesterolemia were ruled out. For all 3 dogs, the bone marrow aspirates and histologic sections were reviewed by 2 clinical pathologists at UWVC.

Case descriptions

Case 1
An 11-year-old, spayed female, English coonhound dog was evaluated by the local veterinarian for persistent anemia [hematocrit (HCT) 28%; reference interval (RI): 35% to 55%] nonresponsive to 3 to 4 wk of treatment with doxycycline following a positive SNAP 4Dx test (IDEXX Laboratory, Westbrook, Maine, USA) for Ehrlichia canis. The dog had been diagnosed with pure red cell aplasia (PRCA) 2 y before admission based on diagnostic testing at UWVC that included complete hematologic evaluation [HCT 10%; RI: 39% to 57%, total protein (TP) 60 g/L; RI: 56 to 80 g/L; reticulocyte count 2000/μL; RI: 11 000 to 111 000/μL] and bone marrow aspirate examination, which revealed the absence of erythroid precursors and unremarkable granulocytic and megakaryocytic lineages. Underlying causes...
(i.e., toxin/drug, infection, or neoplasia) for the dog’s severe nonregenerative anemia were ruled out. The dog was responsive to treatment with immunosuppressive doses of prednisone and cyclosporine. Both drugs were tapered slowly over the course of 1 y based on resolution of the anemia. Immunosuppressive treatment was discontinued 8 mo before presentation based on a stable HCT of 47%.

When presented to the UWVC for follow-up, the dog was reported to be clinically well at home with normal appetite and energy level, and no vomiting, diarrhea, coughing, or sneezing. The dog weighed 25.5 kg with a body condition score (BCS) of 6/9, body temperature of 38.6°C, pulse rate of 116 beats/min (bpm), and respiratory rate described as panting. Mucous membranes were pink with a capillary refill time (CRT) of < 2 s, cardiac auscultation revealed a normal rhythm and no murmurs, and pulses were strong and synchronous. Abnormalities were not detected on palpation of all peripheral lymph nodes and the abdominal cavity.

Diagnostic testing included a complete blood (cell) count (CBC), reticulocyte count, direct antiglobulin (Coombs’1 test (DAT), biochemical profile, abdominal ultrasonographic examination, chest radiographs, and baseline cortisol concentration. Results indicated nonregenerative anemia with platelets and white blood cells within reference intervals, a weak positive DAT (Table 1), mildly increased alkaline phosphatase activity, and hypocholesterolemia with concentrations of other analytes, including albumin, globulin, glucose, blood urea nitrogen (BUN), and total bilirubin, within reference intervals (Table 2). Ultrasonographic findings consisted of multifocal hyperechoic foci in the liver, a subjectively enlarged spleen with a single hypoechoic nodule that did not bulge the capsule, and 2 ill-defined pinpoint hyperechoic foci that were unchanged from the previous examination performed 2 y earlier. Intra-abdominal lymphadenopathy and gastrointestinal thickening were not found, and the left adrenal gland was described as normal. Chest radiographs revealed a normal cardiac silhouette and pulmonary vasculature with no pulmonary nodules or lymphadenopathy. The resting cortisol concentration was normal (Table 2) and ruled out hypoadrenocorticism as the cause of hypocholesterolemia.

An aspirate and a core biopsy of bone marrow were collected. Cytologic evaluation revealed erythroid hyperplasia with mildly left-shifted erythroid maturation and the presence of occasional polychromatophilic erythrocytes (reticulocytes). Frequent rubribaphagocytosis (i.e., phagocytosis of erythroid precursors by macrophages) of early- and middle-stage erythroid precursors was seen. The granulocytic and megakaryocytic lineages appeared unremarkable. Histopathologic evaluation of bone marrow agreed with the cytologic abnormalities and in addition revealed mild myelofibrosis, confirmed by staining for reticulin (Gomori methenamine silver stain) and collagen (Masson’s trichrome stain). Occasional macrophages contained phagocytosed nuclear debris, supporting rubribaphagocytosis seen on the bone marrow aspirate. The bone marrow findings were interpreted as ineffective erythropoiesis with evidence of erythroid precursor destruction, which, in association with other hematologic findings, was consistent with a diagnosis of precursor-targeted immune-mediated anemia (PIMA).

Immunosuppressive therapy with prednisone (Watson Laboratories, Parsippany, New Jersey USA), 20 mg [0.8 mg/kg body weight (BW)], PO, q12h, and cyclosporine (Atopica; Novartis Animal Health, Larchwood, Iowa, USA), 100 mg (3.9 mg/kg BW), PO, q12h, was initiated. One and 2 wk after restarting the prednisone and cyclosporine, the dog’s HCT was stable (HCT 29%, TP 73 g/L, and HCT 30%, TP 74 g/L, respectively). One month later, the HCT (32%; TP 70 g/L) continued to increase, and over the course of the next 4 mo, prednisone was slowly tapered and then discontinued when the HCT reached 42% (TP 72 g/L). Six weeks after discontinuing the prednisone, anemia (nonregenerative) recurred (HCT 18%; TP 72 g/L; reticulocytes 21 000/μL). A packed red blood cell (pRBC) transfusion was administered and the prednisone was restarted at 20 mg, PO, q12h. The dog was maintained in remission (HCT 38%, 75 d after restarting prednisone) over the next 3 mo with

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**Table 1.** Results of complete blood cell count, reticulocyte count, direct antiglobulin (Coombs’) test, and 4Dx SNAP test at initial presentation for cases 1 to 3

<table>
<thead>
<tr>
<th>Case 1</th>
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<th>Case 3*</th>
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<td>23</td>
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<tr>
<td>Platelets</td>
<td>211</td>
<td>523</td>
<td>406</td>
<td>× 10⁹/μL</td>
</tr>
<tr>
<td>WBC</td>
<td>6.11</td>
<td>9.83</td>
<td>11.13</td>
<td>× 10⁹/μL</td>
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<tr>
<td>Reticulocyte count</td>
<td>0.044</td>
<td>0.025</td>
<td>0.004</td>
<td>× 10⁶/μL</td>
</tr>
<tr>
<td>Agglutination</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>—</td>
</tr>
<tr>
<td>Spherocytes</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>—</td>
</tr>
<tr>
<td>DAT</td>
<td>Weak Positive*a</td>
<td>Positive*c</td>
<td>N/A</td>
<td>Negative</td>
</tr>
<tr>
<td>4Dx SNAP test</td>
<td>Positive*a</td>
<td>Negative</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

*a Initial CBC performed following a packed red blood cell transfusion.

*b Direct antiglobulin (Coombs’) test performed at UWVC. Result details: (37°C): C3 16; IgG < 2; IgM 2; poly 4.

*c Direct, antiglobulin (Coombs’) test (37°C) performed at Marshfield laboratories (Waukesha, Wisconsin, USA) prior to referral to UWVC.

*d 4Dx SNAP test performed prior to referral and was positive for *Ehrlichia canis*/*ewsingti.*

**HCT** — hematocrit; **MCV** — mean cell volume; **MCHC** — mean corpuscular hemoglobin concentration; **WBC** — white blood cell count; **N/A** — not applicable/available; **DAT** — direct antiglobulin test; **4Dx SNAP test** — antibody enzyme-linked immunosorbent assay (ELISA) for heartworm, *Ehrlichia canis* and *Ehrlichia ewingii*, *Anaplasma phagocytophilum* and *Anaplasma platys*, and *Borrelia burgdorferi*.**
Cyclosporine 100 mg (3.9 mg/kg BW), PO, q12h, and prednisone tapered to 15 mg (0.6 mg/kg BW), PO, per day, at which time the dog was lost to follow-up. During the routine monitoring of the dog’s anemia over the 9-month observation period, the dog’s cholesterol concentration was re-checked twice and reported to be 11.2 mmol/L (HCT 35%) and 13.8 mmol/L (HCT 40%) while receiving prednisone and cyclosporine therapy.

**Case 2**

A 7-year-old, spayed female, miniature Dachshund dog was examined for assessment of pica for 5 mo and 3 collapsing (or syncopal) episodes. Eight months before presentation the dog had anemia [HCT 29%, positive DAT (Table 1)] noted on pre-dental blood analysis that responded to a short, 30-day course of prednisone. When presented to UWVC, the dog’s activity and appetite were normal. The dog weighed 6.2 kg with a BCS of 7/9. Physical abnormalities included pale pinnae, very pale and mildly tacky mucous membranes, tachycardia (HR 160 bpm), and a soft grade 2/6 cardiac murmur. Palpation of all peripheral lymph nodes and the abdominal cavity revealed no abnormalities.

Diagnostic testing included a CBC, reticulocyte count, biochemical profile, urinalysis and bacterial culture, blood pressure measurement, echocardiogram (ECG), abdominal ultrasonographic examination, and chest radiographs. Results indicated nonregenerative anemia with unremarkable platelet and white blood cell counts (Table 1). Before referral, the DAT was positive. The only abnormalities in the biochemical profile were mildly increased ALT activity, mild hyperglobulinemia, and hypocholesterolemia (Table 2). The urine culture isolated > 100 000 colony-forming units (CFU)/mL of *Escherichia coli*. The dog was normotensive, with a systolic blood pressure of 114 mmHg and the electrocardiogram (ECG) documented a sinus rhythm. Ultrasonographic abnormalities included the presence of biliary sludge, minimal bilateral renal dystrophic mineralization, and urine echogenicity. Intra-abdominal lymphadenopathy and gastrointestinal thickening were not found. Both the left and right adrenal glands were reported as normal. Chest radiographs revealed cardiovascular structures and pulmonary vasculature within normal limits and mild right-sided heart enlargement with a vertebral heart score of 10. There was no evidence of pulmonary metastasis. A resting cortisol concentration ruled out the differential diagnosis/suspicion of hypoadrenocorticism as the cause of the dog’s low cholesterol concentration.

A bone marrow aspirate and core biopsy sample were collected. The bone marrow aspirate yielded a nondiagnostic specimen with no hematopoietic particles available for examination. Histopathologic assessment of the bone marrow core biopsy revealed mild to moderate erythroid hypoplasia with distinct small islands of erythropoiesis and moderate myelofibrosis, which may explain why an evaluable aspirate could not be obtained. Myelofibrosis was confirmed by examination of histologic sections stained with Gomori silver and Masson’s trichrome stains. The granulocytic and megakaryocytic lineages appeared unremarkable, and there was equivocal mild plasmacytosis.

Bone marrow findings did not provide definitive support for immune-mediated anemia. However, immunosuppressive treatment was initiated based on clinical history and ruling out any known toxin/drug exposure, or an infectious or neoplastic cause for the dog’s anemia. The dog’s anemia was previously responsive to prednisone therapy increasing the clinical suspicion of immune-mediated erythroid destruction (response to immunosuppressive treatment alone does not support or rule out an immune-mediated mechanism).

Treatment included a blood transfusion (100 mL pRBC), prednisone (predniSONE; Qualitest Pharmaceuticals, Huntsville, Alabama, USA), 10 mg (1.6 mg/kg BW), PO, q24h, and cyclosporine (cycloSPORINE, Watson Laboratories), 25 mg (4 mg/kg BW), PO, q12h. The dog’s HCT 8 h after transfusion was 23% and TP was 78 g/L. The dog’s urinary tract infection was treated with amoxicillin/clavulanate (Clavamox; Zoetis Animal Health, Parsippany, New Jersey, USA), 125 mg (20 mg/kg BW), PO, q12h. Twenty days after initiating treatment with prednisone and

| Table 2. Summary of the results of the relevant serum biochemistry, baseline cortisol, ACTH stimulation test, bile acids test, and urine specific gravity at initial presentation for cases 1 to 3 |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| **Units** | **Reference interval** |
| ALT (U/L) | 14 to 87 |
| ALP (U/L) | 20 to 157 |
| Total bilirubin (µmol/L) | 1.7 to 13.7 |
| Cholesterol (mmol/L) | 3.9 to 8.3 |
| BUN (mmol/L) | 2.5 to 11.4 |
| Creatinine (µmol/L) | 44.2 to 132.6 |
| Glucose (mmol/L) | 3.7 to 7.3 |
| Albumin (g/L) | 23 to 39 |
| Globulin (g/L) | 22 to 35 |
| Sodium (mmol/L) | 141 to 150 |
| Potassium (mmol/L) | 3.9 to 5.3 |
| Resting cortisol (nmol/L) | ≥ 55 |
| ACTH stimulation test (pre/1 h post) | 28 to 138/276 to 552 |
| Serum bile acids (pre/2 h post-prandial) | 9.12 to 87 |
| Urine specific gravity | 10 to 12/5 to 25 |

ALT — alanine transaminase activity; ALP — alkaline phosphatase activity; BUN — blood urea nitrogen concentration; N/A — not applicable/available; ACTH — adrenocorticotropic hormone.
cyclosporine the dog’s HCT remained stable at 22%; however, the cholesterol concentration (2.9 mmol/L) continued to decrease. Six weeks following immunosuppression with prednisone and cyclosporine, the HCT had increased to 34% (TP 77 g/L) with no additional syncopal episodes or pica. At day 90, the dog was no longer anemic (HCT 42%) and the cholesterol concentration (7.6 mmol/L) was within the reference interval. Over the next 12 mo, the prednisone and cyclosporine were slowly tapered. Treatment with prednisone was discontinued 1 y after the initiation of therapy and cyclosporine was continually decreased. The dog was then managed with low-dose cyclosporine, 5 mg (0.8 mg/kg BW), PO, q12h and at last re-check, 4 y following admission, the dog’s HCT was stable at 34% and TP was 83 g/L.

**Case 3**
A 1.5-year-old, spayed female, Welsh terrier dog was evaluated for progressive anemia, lethargy, and inappetence by the local veterinarian 3 wk before referral for 2 collapsing episodes during physical activity (e.g., climbing stairs and playing with the other dogs in the household). It was determined that the dog was anemic (HCT 20%). When the dog was presented to UWVC, the dog weighed 10.4 kg with a BCS of 4 to 5/9, body temperature of 101.4, pulse rate of 128 bpm, and respiratory rate of 24 breaths/min. Mucous membranes were light pink and moist with a CRT of < 2 s. Physical abnormalities included a grade 3/6 heart murmur, hyperkinetic pulses, and a small mass on the tongue. Abdominal and thoracic radiographs and abdominal ultrasonographic studies revealed no abnormalities. Due to the dog’s persistent nonregenerative anemia (PCV 17%, TP 56 g/L) a pRBC transfusion (120 mL) and fluid therapy were initially given to address the dog’s clinical anemia. The dog’s post transfusion HCT was 23% (Table 1).

Further diagnostic testing included a biochemical profile, urinalysis, blood pressure measurement, ECG, and abdominal ultrasonographic examination. The only abnormality on the biochemical profile was hypcholesterolemia (Table 2). ACTH stimulation test results ruled out the differential diagnosis of hypoadrenocorticism (Table 2). The dog’s blood pressure was 134 mmHg and the ECG documented a sinus rhythm.

Cytologic evaluation of bone marrow revealed marked erythroid hypoplasia with the presence of rare early-stage precursors and absence of later stages. The granulocytic and megakaryocytic lineages appeared unremarkable. Rubriphagocytosis was not seen. Bone marrow findings raised suspicion for immune-mediated anemia (early-stage PIMA or marked erythroid hypoplasia progressing to PRCA), and immunosuppressive treatment was initiated with prednisone (predniSONE; Qualitest Pharmaceuticals), 20 mg (2 mg/kg BW), PO, q24h and cyclosporine (cycloSPORINE, Watson Laboratories), 30 mg (2.5 mg/kg BW), PO, q12h. One week after starting treatment, cyclosporine was stopped for 2 to 3 d due to an episode of vomiting and was then re-started at 25 mg (1.25 mg/kg BW), PO, q12h. Two days later, the HCT decreased to 18% (TP 74 g/L) and a second blood transfusion of pRBC (150 mL) was given. The dog’s HCT remained stable for 14 d then dropped to 18% (TP 62 g/L). Following a third pRBC transfusion, cyclosporine was increased to 2.5 mg/kg BW, PO, q121h. Over the following 10 mo, the dog’s HCT increased to 45% to 50% and treatment with prednisone and cyclosporine was slowly tapered. During a routine re-check (9 mo following the initiation of immunosuppression), the results of a biochemical profile indicated the cholesterol concentration had increased to within the reference interval and the HCT was stable at 47%. Treatment with prednisone and cyclosporine was discontinued 11 mo after the initial admission.

**Discussion**
Hypocholesterolemia in 3 dogs with nonregenerative, suspected to be immune-mediated, anemia is reported. In the cases presented, the diagnoses were made based on history, bone marrow findings, and diagnostic testing that ruled out other possible underlying causes (i.e., toxin/drug, infectious, or neoplasia) for anemia. In addition, common causes of hypocholesterolemia, including GI disease, liver failure, and hypoadrenocorticism were ruled out based on absence of hypoproteinemia, hyperbilirubinemia, hypoglycemia, decreased BUN, increased hepatic enzyme activities, and cortisol concentrations (either resting cortisol concentrations or ACTH stimulation testing) within reference intervals. These 3 cases suggest a possible link between non-regenerative immune-mediated anemia and hypocholesterolemia, which has not been previously reported in dogs. In all 3 cases, serum cholesterol concentrations returned to within the reference interval following resolution of the anemia.

In humans, hypocholesterolemia has been described in various non-malignant anemias (1–6). Mechanisms underlying this interaction are not well-understood. Proposed mechanisms include plasma dilution as a result of the anemia (9), increased cholesterol utilization due to altered erythropoiesis [accelerated erythropoiesis (14), stress erythropoiesis (12,13)], increased but ineffective erythropoiesis (3), increased uptake by the reticuloendothelial system (3,4), or altered cholesterol metabolism induced by macrophage system activation and cytokine release and/or oxidative stress (3,4,11,12).

The mechanism for the concurrent hypocholesterolemia in the reported 3 dogs, diagnosed with a non-regenerative, suspected immune-mediated anemia, is unknown and is likely multifactorial. Pathophysiologic mechanisms as proposed in humans are possible but remain unclear. Nonregenerative immune-mediated anemias in dogs encompass a spectrum of diseases in which the immune system is suspected to target and mediate destruction of erythrocytes at different stages of maturation. Bone marrow findings range from ineffective erythropoiesis with erythroid hyperplasia and erythroid left-shift or maturation arrest as [is commonly seen in precursor-targeted immune-mediated anemia (PIMA)], to erythroid aplasia characterized by absence of erythroid precursors [as seen in pure red cell aplasia (PRCA)] (16–19). Evidence of concurrent hemolysis (i.e., IMHA), characterized by evidence of peripheral erythrocyte destruction, such as spherocytosis, hemoglobinemia, icterus, agglutination, or DAT positivity is uncommon in dogs with PIMA (18,20). Two of the 3 dogs described were direct antiglobulin tested and were DAT positive [case 1, weak positive for C3 (complement), likely non-specific; case 2, positive], suggesting the possibility of concurrent IMHA or false positive.
result, as both dogs lacked definitive evidence of hemolysis (21). To the authors’ knowledge dogs with IMHA (15,20) or suspected nonregenerative immune-mediated-anemia (16,17) have not been reported to have concurrent hypocholesterolemia.

Mechanistic studies would be needed to further determine and define the possible relationship between hypocholesterolemia and nonregenerative immune-mediated anemias in dogs. Mechanisms to consider include the role cholesterol plays in erythropoiesis. Erythropoiesis requires the consumption of circulating cholesterol for cell membrane production; therefore, ineffective or accelerated erythropoiesis may be reasonable possible mechanisms for the reduced serum cholesterol concentration (14). The erythropoietin activity of these dogs was not evaluated, but none had reticulocytosis, characterizing the anemia as nonregenerative. Even though erythropoietin activity was not assessed in the 3 reported dogs, at least 1 dog (case 1) had evidence of erythroid hyperplasia in the bone marrow; therefore, increased erythropoiesis may have been associated with cholesterol consumption in this dog. The mechanisms of hypocholesterolemia in the 2 other dogs with erythroid hypo-plasia are unclear.

As observed in human anemic patients with hypocholesterolemia, cholesterol concentrations returned to within the reference interval with resolution of the anemia. In all 3 dogs in this report the hypocholesterolemia also resolved with resolution of anemia. In the dog (case 2), in which the cholesterol concentration was more closely monitored, anemia and hypocholesterolemia had resolved (HCT 42%, cholesterol 7.6 mmol/L) 3 mo after the initiation of immunosuppressive therapy.

In summary, this is the first report of hypocholesterolemia associated with nonregenerative immune-mediated anemia in dogs. These 3 cases suggest that hypocholesterolemia may be a previously unrecognized feature in dogs with suspected nonregenerative immune-mediated anemia. In this study hypocholesterolemia appears to have resolved with resolution of the anemia, raising the question of a possible mechanistic link between anemia and hypocholesterolemia in dogs. The underlying mechanisms and clinical significance of this observation are unknown. This case report provides awareness that dogs diagnosed with a nonregenerative, suspected to be immune-mediated, anemia may have concurrent hypocholesterolemia, which does not seem to be a result of the underlying illnesses most commonly associated with hypocholesterolemia (i.e., gastrointestinal disease, liver failure, or hypoadrenocorticism).

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References

Case Report  
Rapport de cas

Hemangiosarcoma within an intermuscular lipoma in a golden retriever dog

Claire Leriquier, Marie-Odile Benoit-Biancamano, Hugues Lacoste, Gregory D. Herndon

Abstract — A subcutaneous mass on the right pelvic limb of an 11-year-old neutered male golden retriever dog was surgically excised. A hemangiosarcoma included within an intermuscular lipoma was diagnosed upon histopathological examination. To the authors’ knowledge, this is the first case report of this nature in a dog.

Résumé — Hémangiosarcome dans un lipome intermusculaire chez un golden retriever. Une masse sous-cutanée située sur le membre pelvien droit d’un golden retriever mâle castré de 11 ans a été excisée chirurgicalement. Un hémangiosarcome inclus dans un lipome intermusculaire a été diagnostiqué à l’examen histopathologique. Selon les auteurs, il s’agirait du premier rapport de cas de ce type chez un chien.

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Lipomas are common subcutaneous tumors in small animals in any location on the body (1). Less common are infiltrative or intermuscular lipomas. Infiltrative lipomas are histologically benign but locally invasive into surrounding tissues; intermuscular lipomas are variants of subcutaneous lipomas situated between muscle planes with no local invasion (1). Both types of lipoma are typically found in the pelvic limbs of dogs (2,3) and can be difficult to differentiate without surgical evaluation (2). Hemangiosarcoma (HSA) is another neoplasm diagnosed frequently in dogs compared with those in other species (4). This neoplasm occurs primarily within the viscera of the spleen, the most common location, or less frequently the skin and subcutaneous tissues (14% of HSA) (4). It is extremely rare in both the veterinary and human literature to have a second tumor growing within another tumor (5–8). Collision tumors are defined as co-existent but independent neoplasms which can be contiguous or intermingled in the same site (9–11).

This report describes the diagnostic work-up, surgical intervention, and postoperative treatment of a hemangiosarcoma within an intermuscular lipoma on the caudal aspect of the right pelvic limb of a golden retriever dog. To the authors’ knowledge this is the first report of this nature in a dog.

An 11-year-old, neutered male golden retriever dog was initially presented to his veterinarian for muscle loss of the left pelvic limb without lameness. At this time, 7 subcutaneous masses were identified, including a mass on the right pelvic limb. The mass on the right pelvic limb was firm, non-ulcerated, and measured 22 × 22 × 4 cm. The mass adhered to the back of the right thigh (from rump to back of stifle) and had increased in size over the past year. Fine-needle aspirates (FNA) were taken from each mass. The results of cytological analyses were consistent with lipomas for 3 of the subcutaneous masses, but 3 others were too hypocellular to make a definitive diagnosis.

The mass on the right pelvic limb (the 7th mass) was described as benign adipose tissue with rare mature lymphocytes and was therefore diagnosed as a lipoma. A biopsy was recommended, but the owner declined and decided to monitor the mass for any changes in size.

Seven months later the patient was re-evaluated by his veterinarian because of some weakness and difficulty moving the right pelvic limb over the previous few days. The mass on the right pelvic limb appeared larger and pitting edema was noted on the distal limb that was painful on palpation; the other masses seemed stable in size and shape. Medical treatment had been started before referral: tramadol (Apo-Tramadol; Apotex, Toronto, Ontario), 150 mg, PO, q12h and meloxicam (M-Eloxyn; Zoetis, Kirkland, Quebec), 3.75 mg, PO, q24h.

The dog was then referred to the small animal hospital of the Faculty of Veterinary Medicine (University of Montreal) for evaluation of the large subcutaneous mass on the caudal aspect of the right pelvic limb. To the authors’ knowledge this is the first report of this nature in a dog.

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made on the caudal aspect of the right thigh. The lipoma was easily identified with a second mass localized in the caudalproximal part of the fat tissue. This second mass was approximately 7 cm in diameter and contained coagulated blood (interpreted as a hematoma). Both masses appeared to be well-encapsulated between the semitendinosus and semimembranosus muscles. The masses were removed together using both sharp and blunt dissection. Once the caudal, lateral, and medial aspects of the mass were dissected, the sciatic nerve was identified and the lipoma was carefully dissected away from the nerve. Once the dissection was complete, the mass was removed (Figure 2A). There was no evidence of infiltration into the surrounding tissues. A Jackson-Pratt drain was placed and secured in a standard fashion to eliminate dead space and reduce the risk of postoperative seroma formation. The area was lavaged and closed routinely. The dog did well in the hospital and was discharged 2 d after surgery with a short course of medication, tramadol (Tramadol; Gentes, Saint-Hyacinthe, Quebec), 2.5 mg/kg body weight (BW), PO, q8h for 7 d, cephalaxin (Apo-Cephalex; Apotex, Toronto, Ontario), 22 mg/kg BW, PO, q8h for 10 d and meloxicam (Zoetics), 0.1 mg/kg BW, PO, q24h for 5 d. The surgical wound healed without complications.

The mass was submitted for histopathological examination. At gross examination, the mass was multilobulated, soft, white, and measured 21 × 14 × 7 cm. On cut surface, its appearance was greasy and a second mass measuring 10 × 10 × 2 cm, with a consistency and color compatible with a hematoma, was enclosed within the capsule of the first mass. Both masses were fixed in 10% buffered formalin and samples were embedded in paraffin. Sections 4 µm thick were stained with hematoxylin-eosin-phloxin-saffron (HEPS). The first mass was mainly composed of adipocytes, characterized by a single, large and clear cytoplasmic vacuole and a small nucleus, often pushed to the periphery. Anisocytosis and anisokaryosis were mild and no mitoses were observed. A few areas of fat necrosis, accompanied by a variable degree of inflammation were noted. Based on the location, this mass was diagnosed as an intermuscular lipoma.

The second mass was mainly composed of a large hematoma, the periphery of which had small clusters of fusiform cells (Figure 2B). These cells also focally lined distinctly formed vascular channels (Figure 2C). They had an eosinophilic cytoplasm with poorly delineated cell borders, a round to ovoid nucleus with finely granular chromatin, and 1 or 2 small nucleoli. Anisocytosis and anisokaryosis were moderate and there were 0 to 3 mitoses per 400 × field (Figure 2D). The histologic features of this mass were consistent with a hemangiosarcoma (Figure 2C). Granulation tissue and hemosiderin-laden macrophages were also observed multifocally, within the hematoma.

Based on the diagnosis of a hemangiosarcoma, consultation with an oncologist was recommended and pursued by the owner in the DMV Center. Chemotherapy was initiated approximately 2 wk after surgery with the intent to complete a doxorubicin-based protocol (Doxorubicin; Hospira Health Care, Saint-Laurent, Quebec), 28 to 30 mg/mm² every 3 wk for 5 treatments (1). The dog received 2 doses of chemotherapy without incident except for a mild leukocytopenia, mild neutropenia, and monocytopenia at 7 d post-treatment, which had

**Figure 1.** Computed tomography image of the right pelvic limb showing 2 masses. A wide (19 × 10 × 14 cm) oval uniform mass with a mean attenuation of adipose tissue (appears black on the image) infiltrates the centrocaudal intermuscular space of the right thigh without involving the femur (appears white on the image, black asterisk). Muscles are pushed away and thinned. A capsule is variably present, poorly defined and incomplete. These characteristics are suggestive of an infiltrative lipoma (star). The fat mass contains in its centrocaudal portion an oval mass with a smooth and well-defined outline (9 × 6.7 × 8.6 cm). This mass is minimally heterogeneous and with an attenuation level compatible with some tissue or a richly cellular liquid (appears grey on the image). This mass is consistent with a hematoma (white asterisk), interpreted to have resulted from a hemorrhage (white asterisk). The fat mass contains in its centrocaudal portion an oval mass with a smooth and well-defined outline (9 × 6.7 × 8.6 cm). This mass is minimally heterogeneous and with an attenuation level compatible with some tissue or a richly cellular liquid (appears grey on the image). This mass is consistent with a hematoma (white asterisk), interpreted to have resulted from a hemorrhage (white asterisk). The fat mass contains in its centrocaudal portion an oval mass with a smooth and well-defined outline (9 × 6.7 × 8.6 cm). This mass is minimally heterogeneous and with an attenuation level compatible with some tissue or a richly cellular liquid (appears grey on the image). This mass is consistent with a hematoma (white asterisk), interpreted to have resulted from a hemorrhage (white asterisk).
resolved by the following re-check evaluation and hematology. Before every treatment, an electrocardiogram (ECG) was performed and no abnormalities were observed. At the dog’s 8th post-operative week recheck at the small animal hospital the owner reported that the dog was doing well, with the exception of 1 day following the most recent chemotherapy administration, in which the dog was mildly lethargic and confused. This episode had resolved quickly within 24 h without treatment. Approximately 4 wk after the last evaluation the owner found the dog had died in his sleep with no apparent abnormalities leading up to the time of death. No necropsy was performed.

**Discussion**

Lipomas are common subcutaneous tumors in older dogs. They were the third most common nonlymphoid cutaneous neoplasm in the dog, comprising 7.1% of 6282 cases in 1 study (1). Although lipomas are benign, infiltrative lipomas can be locally invasive into surrounding tissues including muscles, fascia, nerves, and bones (1). Infiltrative lipomas are described in dogs as well as cats and horses (1). Depending on their location, they can interfere with limb function and are often found on the extremities (12), especially in the pelvic limbs (3). Other affected areas that have been reported include the abdominal/thoracic wall, the head, and the perineal area (13, 14). Both infiltrative and intermuscular lipomas can be associated with lameness, even if there is no local invasion in the latter, because they are situated between muscle planes, causing mechanical interference. The most common site for intermuscular lipomas is the caudal thigh, typically between the semitendinosus and semimembranosus muscles (2), as was the case in this dog. However, 1 article describes intermuscular lipomas also occurring in the axillary region, typically seen between the superficial and deep pectoral muscles or the serratus and subscapular muscles (15).

Prior to surgical intervention for suspected infiltrative lipomas, a CT scan is recommended to aid with surgical planning and assess the resectability of these tumors. In the current case, the CT scan showed that this was a probable infiltrative lipoma with a secondary mass in the proximal region of the lipoma. However, during surgery the mass was well encapsulated between muscle planes and thus more consistent with an intermuscular lipoma. This is consistent with other studies which have shown that differentiation between an intermuscular lipoma and an infiltrative tumor is often only made at the time of surgery (2). This differentiation is important because it can change the prognosis for the patient as infiltrative tumors have a recurrence rate of 36% to 50% (12, 13), whereas intermuscular lipomas are unlikely to recur (2, 15, 16).

Diagnosis of lipomas can easily be performed with FNA; therefore, slides are not often sent to laboratories. That can explain the underrepresentation of lipomas (only 2 cases, without details of their location) in 1 study of more than 200 cases comparing histology with FNA (17). In this study, there was 97.9% specificity and 89.3% sensitivity with the correlation between preoperative aspiration and postoperative histology.
(17). In the current case, the FNA of the mass was consistent with a lipoma; however, there was no knowledge of the second mass most likely because it was initially too small and not found during aspiration. Once the second mass was identified on CT scan, taking an aspirate of the mass was discussed with the owner. Since no evidence of metastatic disease was found on the preoperative examination the owner elected to decline having an aspirate taken and to proceed with the surgical plan to remove the mass. In retrospect, aspirates would have likely been inconclusive, as the diagnosis of HSA via FNA can be difficult due to poor exfoliation of the tumor and the presence of excessive hemorrhage (1,18), as was observed herein.

Three stages of cutaneous HSA have been defined: stage I is confined to the dermis, stage II involves the hypodermis but does not involve invasion of the musculature, and stage III involves invasion of the musculature (4). This classification system showed that there is higher metastatic potential for stages II and III (60%) compared with stage I (30%) (4). Thus, following surgical excision, chemotherapy should be recommended for stages II and III HSA. In the current case, the HSA was considered a stage II so the treatment of choice was surgical excision with complete margins followed by a course of chemotherapy. A standard chemotherapy protocol consisting of doxorubicin dose of 30 mg/m² every 3 wk for 5 treatments used for splenic HSA is the treatment of choice for subcutaneous HSA (19,20).

Using this grading scale, survival times vary greatly when surgery alone is performed: the stage I median survival time is 780 d while the survival times for stage II is only 172 d (4). Limited data are available for cutaneous HSA after chemotherapy (19). In one study of survival rates of various forms of HSA, the median survival time of 6 cases with a subcutaneous mass was 425 d after chemotherapy but the protocol was different, consisting of a combination of vincristine, doxorubicin, and cyclophosphamide (21). The number of cases of subcutaneous HSA in this study was low; however, the median survival was significantly increased with postoperative chemotherapy when given after surgery in all types of HSA (21).

To the authors’ knowledge the presence of a HSA in a lipoma has not been described in the veterinary literature. It is difficult to know which tumor developed first, although the larger mass is generally presumed to have developed first. Also the growth rates of both tumor types would favor the hypothesis of an initial lipoma. Typically, HSA is a fast-growing and metastatic tumor, making it a less likely candidate as the initial tumor, as opposed to the lipoma, which had been diagnosed over a year prior to presentation at the small animal hospital. Only one other case of a tumor within a lipoma has been reported in the veterinary literature, which was a case of a boxer dog with a cutaneous mast cell tumor within a lipoma (5). This phenomenon is rare and it is important to differentiate between tumor growth within another tumor and tumor-to-tumor metastasis. In the human literature tumor-to-tumor metastasis is described with Campbell’s 3 criteria: i) presence of at least 2 primary tumors with the recipient being a true neoplasm; ii) exclusion of direct ingrowth or tumor emboli; and iii) exclusion of metastatic tumor of lymph nodes involved by lymphatic proliferative disease (6). In the current case there was no evidence of any other cutaneous, subcutaneous, or other tissue involvement of a HSA (although 3 of the masses initially examined had no diagnosis), making it unlikely to be a tumor-to-tumor metastasis. A different phenomenon, collision tumors, has also been reported in a few cases in the veterinary literature (9–11). However, the 2 types of tumors cells herein were not admixed while reported collision tumors are generally described as mixed cell populations. Furthermore, these reports always included a melanocytic component (9–11), which was not present in this case.

The pathophysiology of a tumor within a tumor is poorly understood; however, several theories have been proposed (7,8). Tumors that are rich in lipids such as lipomas would form microenvironments that would provide ample nutrients, making it a good growth medium for another tumor (8). Neovascularization associated with the initial tumor may make it more accessible to malignant cells in the circulation, thus allowing for the seeding of the initial tumor with another tumor (8) even if lipomas are rather poorly vascularized compared to other tumors (7). Lastly, this phenomenon could be related to the production of growth factors from the initial tumor, which could then favor the development of the second tumor (7,8,22). In the current case, a transdifferentiation phenomenon should also be considered, as mentioned in a similar case of a sinusoidal hemangiomai with lipoma in a human (22). Indeed, in prenatal adipogenesis, adipocytes come from the perivascular cells which could be a possible consideration for the origin of both tumors (22).

The reason for this patient’s death is unknown; however, there are several possibilities. One possibility is the presence of a metachronous or synchronous right atrial mass that could have resulted in complications (pericardial effusion with tamponade and/or arrhythmias) and sudden death. However, the incidence of metachronous or synchronous subcutaneous and cardiac HSA is not known. In addition, metastasis of a subcutaneous HSA to the right atrium or vice versa has not been described (4). Another possibility could have been the presence of micrometastatic lesions which could have resulted in a neoplastic embolus in brain, heart, or lungs causing sudden death. The side effects of chemotherapy should be considered, but most of these are noted in the first few days following chemotherapy, with the exception of cardiomyopathy. In the current case the dog died 5 wk after his second chemotherapy treatment, making acute septicemia due to neutropenia an unlikely cause. Cardiomyopathy can occur as a chronic cumulative effect of doxorubicin. In this case, sudden death due to fatal arrhythmias cannot be ruled out, although the dog did not show any evidence of ventricular premature contractions during any of the 2 pre-doxorubicin ECGs. He received a cumulative dose of only 58 mg/m² which is below the toxic threshold of 180 to 240 mg/m² (1). No echocardiogram was performed in this patient because he was not from a breed predisposed to dilated cardiomyopathy and had no signs of heart disease. Lastly, it is important to note that this was a geriatric patient and his death could be unrelated to his tumors. Unfortunately, a necropsy could not be performed as the patient died at home and notification of his death was not provided for several days.

To the authors’ knowledge, this is the first report describing a hemangiosarcoma within an intermuscular lipoma. This
phenomenon of a tumor growing within another tumor is extremely rare both in the veterinary and human literature. Although there are several theories attempting to explain this rare phenomenon, additional research is required to fully understand its pathogenesis.

Acknowledgment

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References

Case Report  Rapport de cas

Accidental selenium toxicosis in lambs
Christina M. McKenzie, Ahmad N. Al-Dissi

Abstract — Acute selenium toxicosis occurred in 3-week-old lambs after accidental over-supplementation by intramuscular injection and caused dyspnea, cyanosis, and sudden death. Pathological lesions included myocardial necrosis, skeletal muscle necrosis, pulmonary edema, hydrothorax, and hydropericardium.

Résumé — Toxicose accidentelle au sélénium chez des agneaux. Une toxicose aiguë au sélénium s’est produite chez des agneaux âgés de 3 semaines après une supplémentation excédentaire accidentelle par injection intramusculaire et elle a causé des signes de dyspnée, de cyanose et de mort soudaine. Les lésions pathologiques incluaient une nécrose du myocarde, une nécrose du muscle squelettique, un œdème pulmonaire, de l’hydrothorax et de l’hydropéricarde.

Can Vet J 2017;58:1110–1112

Case description

In March 2012, 40 out of 60 newborn lambs from a Saskatchewan herd died over the course of 3 d. There was a history of sudden death with possible respiratory symptoms and cyanosis. Four 3-week-old male lambs were submitted for postmortem examination to Prairie Diagnostic Services at the Western College of Veterinary Medicine in Saskatoon, Saskatchewan. All of the lambs had been treated with 4 mL of an intramuscular selenium and vitamin E product (Dystosel; Zoetis Canada, Kirkland, Quebec, 3 mg/mL sodium selenite and 136 IU/mL dl-α-tocopherol acetate) 3 d earlier, which the owner considered to be the cause of death.

Each lamb weighed between 3.42 and 4.46 kg and had mildly decreased body condition scores of 2.5/5. This was evidenced by limited subcutaneous tissues but persistent abdominal, perirenal, and pericardial adipose stores. All 4 lambs had clotted milk in the abomasum while the small intestine and colon contained variable amounts of green to yellow pasty contents. Each lamb had a moderate amount of feces caked on the perineum. All 4 lambs had moderate subcutaneous edema in the neck and along the cranial thoracic abdomen. Each animal had edematous, glistening lungs that failed to collapse, had prominent rib imprints, and oozed fluid and blood on section. The myocardium in each lamb was diffusely pale.

Lambs 1, 3, and 4 had 30 to 50 mL of pale yellow and clear fluid within the thoracic cavity and 10 to 20 mL of similar fluid within the pericardial sac, indicating hydrothorax and hydropericardium (Figure 1a). Lamb 4 had a stable froth within the trachea extending from the larynx to the tracheal bifurcation. The myocardial surface in all lambs had multifocal to coalescing pale and dull areas, suggestive of necrosis, with lamb 3 displaying biventricular dilation (Figure 1b). Two lambs had multiple 1- to 2-mm mitral valve hematocysts. In lambs 2, 3, and 4 skeletal muscles were diffusely pale. Lambs 3 and 4 had diffusely red prescapular lymph nodes, but only lamb 3 had an adjacent focal subcutaneous lesion in the left shoulder that was necrotic and hemorrhagic. Lamb 4 exhibited multifocal petechial renal cortical and pancreatic hemorrhages.

A diagnosis of acute to subacute heart failure secondary to myocardial necrosis was made in all lambs based on gross findings.

Histologically, sections from each heart showed multifocal pale areas of myocyte disarray with variable degrees of swelling, fragmentation of the sarcomplasm, hypereosinophilia, and nuclear pyknosis and karyorrhexis. Areas with contraction band necrosis were also seen. Phosphotungstic acid — hematoxylin stain emphasized the contraction bands within areas in which muscle fibers appeared pale (Figure 1c). Multifocal, alveoli of lambs 1 and 2 contained meconium and squamous epithelial cells admixed with few neutrophils indicating in utero
aspiration of amniotic fluid. Lambs 3 and 4 also had mild alveolar hemorrhage.

In lamb 1, hepatocytes contained lipid vacuoles periportally. In all 4 animals the kidney, adrenal glands, thyroid gland, mesenteric lymph node, ileum, jejunum, duodenum, colon, esophagus, thymus, and spleen all showed variable congestion.

Mineral analysis of the liver confirmed toxic selenium concentrations: selenium levels ranged from 3.8 to 10.9 ppm (wet weight). Reported toxic levels from intramuscular injections of sodium selenite range from 3.6 to 18.2 ppm on a wet weight basis (1). Selenium concentrations were measured using an atomic scan with inductively coupled plasma (ICP) spectrometer and hydride generator after an acid digestion technique (2). The liver selenium concentrations, combined with the gross and histologic evidence of myodegeneration and necrosis in the heart, edema and congestion of the lungs, support a diagnosis of acute selenium toxicity.

Discussion

This case demonstrates the typical gross and histological lesions of acute selenium toxicity in sheep resulting in myocardial necrosis, cardiac insufficiency, and death. The heart is the primary target of selenium toxicosis, and the resulting heart failure is what causes the secondary lesions including pulmonary edema, hydrothorax, and hydropericardium (3). Clinical signs of acute selenium toxicosis include ataxia, dyspnea, and depression (3–5). After an acute exposure to selenium, lambs die over 3 to 4 d, although there is variation in the severity of symptoms and lesions among lambs, even when given identical doses (4,6,7). Factors such as stress, exercise, and age can make lambs more susceptible and some lambs seem to be fundamentally more susceptible to selenosis (8).

Selenium is an essential nutrient for all mammals and is integral as an antioxidant to maintain stable cell membranes, as it is an important component of the glutathione reductase enzyme reaction (9–11). Selenium supplementation is a common practice in western Canada as the soil in some areas is selenium deficient, resulting in selenium deficient feed (12). In addition to the type of rock bed, soil pH and rainfall can affect selenium levels in feed (9,12). Ideally, there should be between 0.1 mg/kg and 0.3 mg/kg dry weight total selenium in feed crops (9,13–15). Selenium deficiency can manifest as low fertility, unthriftiness,
and white muscle disease, all of which can be prevented with oral or parenteral supplementation (4,8,9,12,14,16). Prophylactic selenium is often given to lambs at approximately 2 wk of age to prevent delayed white muscle disease (7).

Selenium has a low therapeutic index and over supplementation is a common cause of acute overdose, as occurred in this case (5,6,12,13,15,16). Ruminants are better adapted to a diet containing excessive selenium, than are monogastrics, as the ruminal microflora metabolizes selenium into a less absorbable form which is excreted in the feces (17). The product given intramuscularly in this case contained inorganic selenium in the form of sodium selenite, which is less bioavailable but more toxic than organic selenium (selenomethionine) when given orally, due to differences in solubility and bacterial metabolism (3,11). Sodium selenite also contains 41% selenium compared with sodium selenate, another formulation, which contains only 21% selenium (14). The recommended dose of Dystosel is 0.5 mL/lamb, but the lambs in this case were given 4 mL/lamb for a total of 12 mg of sodium selenite per lamb, or approximately 3 mg/kg body weight (BW). The LD50 of intramuscularly injected selenium in lambs is between 0.45 and 0.7 mg/kg BW, depending on the age of the lamb (1,5,18).

Although it is an antioxidant at low levels, selenium is metabolized to free radicals, such as superoxide and hydrogen peroxide, which can cause severe oxidative damage, especially to high-energy tissue such as the myocardium (10,15,16). The liver accumulates the highest levels of selenium, making it the ideal sample for laboratory testing, followed by the kidney and heart (4,5,12). Methylation is the primary form of metabolism, and elimination occurs in the urine and feces at normal levels and through exhalation at toxic levels (4,11). Selenium toxicity occurs when intake exceeds excretion (16).

Selenium toxicity can either be acute or chronic, depending on the dosage and the period of exposure. Most chronic forms of the disease are due to high levels of selenium in the diet (9,11,15). Some plants, such as those in the genus Astragalus (vetch), Oonopsis (goldenweed), Xylorrhiza (woody aster), and Stanleya (prince’s plume), are selenium accumulators and can build up very high levels of selenomethionine, even up to 1000 ppm in some areas (10,11,13,19). In ewes affected by chronic selenium poisoning major lesions include degeneration in cardiac muscles, pulmonary edema and congestion, and liver congestion (20).

This report of acute selenium toxicity in lambs illustrates the toxic potential of intramuscular injection of selenium and the clinical importance of its small therapeutic range. As there is no specific treatment for selenium toxicity beyond supportive therapy, preventing overexposure through vigilance is the only possible option.

References
What Can’t Be Taught
Ce qui ne s’enseigne pas

Strategies for fostering resilience as veterinary care providers

Marie K. Holowaychuk

While my time since veterinary school spans far beyond 1 year, I feel compelled to write about my experience since I graduated 13 years ago and offer some important advice to the more recently graduated veterinarians.

If you told me at graduation that I would be engaged in a "split-personality" veterinary career divided between small animal emergency and critical care and health and well-being advocacy, I would have thought you were joking. Prior to obtaining my DVM degree, I thought I was destined for a life in companion animal practice, working in the Edmonton suburb that I grew up in. But life has taken a much different turn for me, which has led me down an extraordinary path into academia, specialty private practice, the speaking circuit, and even yoga and meditation teacher training. I love the work that I do and believe that my path has been intentional as it allows me to deliver many important messages regarding veterinary wellness.

That said, my path has not been easy and has been fraught with episodes of burnout, experiences with compassion fatigue, and struggles to manage my mental health and well-being. It is because of these events that I chose to leave jobs in veterinary medicine that I otherwise loved and at times felt unable to do the work that I am so passionate about. It is due to these same difficulties that I know of veterinarian and technician colleagues and friends who have left the profession or even taken their own life; feeling inadequate to continue working in veterinary practice, but not being able to name (or tame) the underlying cause.

It is for this reason that I have become passionate about sharing my story, experiences, knowledge, and advice when it comes to maintaining (and preferably thriving) rather than just surviving a career in veterinary medicine.

I’m often asked the question...what allows a person to stay resilient within this profession, bouncing back from setbacks and not letting failure or disappointment drain her or his resolve? I have come to believe and recommend that veterinary care providers adhere to 5 "S-words" when it comes to fostering resilience within our profession because difficult clients, unanticipated outcomes, challenging cases, and co-worker conflict are not going away.

1. **Self-care** — Self-care means doing something just for yourself and not for anyone else. While this might seem selfish and unimportant, experts suggest that it is unethical for care providers not to tend to self-care (1). We’ve all had days when we didn’t get enough sleep the night before, skipped breakfast, forgot to drink water, and avoided taking breaks just to get through the day. Unfortunately, not tending to self-care ultimately harms the clients and animals we are caring for because we end up making mistakes or experiencing compassion fatigue, which is a physical, emotional, and spiritual inability to care for others. Self-care has been shown to allow physicians to continue to care for their patients compassionately and safely (2). So, how can veterinary care providers tend to self-care? By setting self-care goals that align with the 8 wellness dimensions (i.e., physical, emotional, spiritual, social, intellectual, occupational, financial, and environmental wellness). Veterinary care providers can take a holistic approach to their wellness, allowing an overall sense of mental and physical health and wellbeing (3). For example, self-care can be as simple as scheduling a massage each month (physical wellness), seeing a mental health provider once monthly (emotional wellness), writing in a gratitude journal each day (spiritual wellness), scheduling an outing with a friend each week (social wellness), signing up for a new class once a year (intellectual wellness), attending an annual workshop to learn a new veterinary technique (occupational wellness), meeting with a financial planner once a year (financial wellness), or clearing clutter from the home and workplace (environmental wellness). No matter what resonates with an individual regarding what constitutes self-care, it is important to make time for it regularly. Self-care is truly a necessity (not a luxury) in the work that we do as veterinary care providers.

2. **Saying no** — Most of us struggle with saying no to others because we want to help, appear eager, remain a team player, and avoid disappointing our colleagues, family members, and friends. However, as Steve Jobs said, “it is only by saying no to others that we can say yes to ourselves.” When people ask...
me how to make time for self-care, I urge them to consider offloading something from their calendar to free up time. So, the next time you are asked to join a committee, coach your child's sports team, or organize a work function, consider your other obligations and priorities, as well as the time commitment involved. If it is not a resounding “absolutely!” that you want to commit to the new request, then consider passing on the opportunity. Saying no is not easy, but there are some strategies that can help: be brief, be honest, be respectful, and, if possible, say no in person. That way the desire to help and thankfulness for being asked are passed along non-verbally, rather than the receiver assuming that you are disinterested or do not care. As difficult as saying no is, it is essential to fostering resilience and making time for self-care.

3. Setting boundaries — While physicians would not consider giving out their personal cell number or answering e-mails to patients on the weekend, veterinary care providers seem unable to prevent their work from creeping into their personal life. Over time, these actions can lead to resentment, frustration, and burnout. It is important to set limits in accordance with what you will and will not tolerate at work when it comes to client behavior (e.g., contacting you out of hours), co-worker conduct (e.g., treating team members with respect), and even the work that you choose to do (e.g., whether to perform declaw procedures). Feelings of discomfort or resentment are clues that a person's boundary has been crossed. Very often, a person might also feel a loss of energy, knot in the stomach, or urge to cry. If these feelings come up, notice what it is about the situation, interaction, or expectation that is bothering you. Usually it is a sense of being taken advantage of or not feeling appreciated that causes resentment. When a boundary has been crossed or a boundary needs to be expressed, it is important to be direct and assertive in your communication, so that others know explicitly what your expectations are. Then stick to the boundary so that there is no confusion as to when or to whom it applies.

4. Sleep hygiene — The benefits of sleep are numerous and not just related to the restorative effects on the physical body. Sleep is required to refresh the mind, process what has been learned during the day, manage emotional experiences, and consolidate memories. The detrimental consequences of not getting enough sleep are also becoming more well-known and can include metabolic disturbances (e.g., diabetes, weight gain) and mental health concerns (e.g., depression). Recently, a link between Alzheimer's disease and lack of sleep has also been found, suggesting that sleep is required to rid the body of waste products that have a degenerative effect on the brain (4). Insomnia affects up to 1/3 of adults at some point in their life and is typically due to worry and anxiety. However, there are many other things that can disrupt sleep including noise, interruptions, room temperature, humidity, lighting, diet, naps late in the day, lack of exercise, reduced exposure to outdoor light, negative self-talk, absent bedtime routine, or inadequate relaxation techniques. Physical stress (e.g., full bladder, poor mattress) or disruptions in circadian rhythm (e.g., shift work), can also inhibit sleep, as can alcohol or caffeine intake and use of electronics. Some pointers to help improve sleep hygiene, which is the ability to fall asleep (and stay asleep) for the recommended 7 to 9 hours per night, include the following: release daytime stress by relaxing throughout the day (e.g., stretching), make lists during the day to avoid trying to remember things in bed, avoid negative self-talk regarding sleep (e.g., “I never sleep well after a stressful shift”), allow 30 minutes to unwind before bedtime, exercise for 30 minutes each day, keep light out of the bedroom, turn off electronics (e.g., TV, cell phone) at least 1 hour before bedtime, get up and go to bed at the same time every day, use the bed only for sleep or intimacy, and avoid alcohol 2 hours before bedtime and caffeine 6 hours before bedtime.

5. Sitting still — As veterinary care providers, we spend most of our days rushing through appointments (often on autopilot), attempting to multitask (not that it's truly possible), and reacting to things that happen to us (e.g., a co-worker makes a rude remark and we shoot back with a snide comment). Making time in the day to sit in stillness during meditation is a tremendously effective way to practice mindfulness. Mindfulness is living in the present moment (e.g., not worrying about upcoming appointments or thinking about previous clients) and remaining calm when faced with difficult situations. Neuroscience research shows that practicing mindfulness regularly can enhance the brain's gray matter within the prefrontal cortex, which is responsible for holding attention, making decisions, moderating behavior, and solving problems. Mindfulness also shrinks the amygdala, which identifies physical threats and emotional triggers (5). Research in the medical field demonstrates that mindfulness training helps nurses cope more effectively with stress by improving their ability to think clearly and remain focused and calm during stressful situations. Mindfulness training also assists medical students, physicians, and nurses by promoting self-awareness and self-care, while reducing risk of professional burnout (5). Meditation is easy to do and involves sitting in a comfortable, upright position (back straight, crown of the head towards the ceiling), closing the eyes (if comfortable), and focusing attention on the senses. This can be the smells or sounds in the room, as well as sensations in the body. For many people, the sensation of breathing is a good anchor for the mind and counting each breath can allow focusing attention. It is completely normal (and expected) that the mind will wander. The key is to notice when it has and gently bring the attention back to the breath, body, or senses. Sitting in meditation for 5 minutes in the morning or even a few moments during a busy day can allow the mind and body to refresh and an emotional buffer to form between the triggers and responses that are a part of every day. If you are interested in learning more about mindfulness or trying out meditation, try downloading an application for your phone such as Headspace, Aware, or Calm.

References
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I found this 2-volume edition of Veterinary Medicine attractively put together, easy to navigate, and thoroughly useful as a comprehensive and complete reference text. In its 11th edition over 56 years it has stayed faithful to its initial ideology while encompassing the ever growing amount of new information, new diseases, and new diagnostic and therapeutic techniques. Both volumes are hefty, coming in at about 1100 pages each, but the general eye-appeal is catching, from the colorful photos on the front cover to the color-coded chapters, numerous tables, diagrams, and photographs.

The 4 main authors are from disparate parts of the world (United States, Australia, United Kingdom, and Germany), with 9 contributing authors from Canada, the United States, and Australia, giving the book an international perspective (the authors having been educated in and/or worked in 12 countries and 5 continents). The first few pages are tributes to the 3 senior authors of past editions, Radostits, Gay, and Blood, making one realize that this is an evolving and ongoing project, fueled by Blood and Henderson’s lectures and, at the time, novel approach to teaching, namely that the principles of pathophysiology explain disease syndromes (as opposed to rote learning which was popular at the time of the first edition, 1960), and that pathophysiology plus epidemiology lead to diagnosis, treatment, and control.

The current book has adhered to these principles, but also addresses the immense change we have seen in agriculture, politics, climate, trade, economics, and animal welfare since the 1960’s, and how these have impacted large animal practice. There is an excellent 7-page introduction describing the intent of the voluminous information within the text, and is definitely worth reading.

The book is divided into 21 chapters; the first 6 chapters (examinations, biosecurity, systemic states, body water, antimicrobial therapy) concern, perhaps, the more mundane aspects of the profession, but in my mind the building blocks of a solid understanding of large animal medicine. I found these chapters excellent to peruse and the old adage of Otto Radostits came to mind, “You miss more by not looking than by not knowing.” These are the chapters which new graduates might benefit from by reading — perhaps before they start their first job! The remaining 15 chapters are dedicated to diseases of specific organ systems. The detailed table of contents at the beginning of each chapter helps locate specificities within the subject. The text is broken down into headings, subheadings, and sub-sub headings, each one a different color. Important key words are in bold type, and each subject culminates in a list of further readings and references. Two useful features at the beginning and end of each heading is the “Synopsis Box” and a “Differential Diagnosis” box, and 2 small tables easily picked out and handy if just a quick reference is needed. There are many tables and pathway trees throughout; lots of these have been brought over from previous editions and some are large and a bit overwhelming, but packed with comparative information that can be studied thoroughly with time. Color photographs and diagrams are more limited, but of good quality and useful. I found the descriptive prose very thorough, perhaps too much for some tastes, but one can pick and choose the detail one wants or needs to go into because of the well-demarcated organization. In this sense the book really is what it purports to being, a comprehensive book useful for all walks of large animal medicine, whether it be the equine cardiologist (this section seems particularly detailed) or the first year student (how to conduct a clinical examination). As with most exhaustive texts, there are appendices. Strangely, the conversion tables have a convoluted method for changing metric to imperial. The Reference Lab Values (compiled from different labs, one being Prairie Diagnostic Services at the Western College of Veterinary Medicine), and the Drug Dosages are handy to have. I did notice a few typos (double/missing words), a couple of pages of blurred print, and incorrect page numbers in the index, but minor errors considering the tome.

As a practitioner, it might not be the book I grab from the shelf while the cow is standing in the chute, but it would probably be the one I sit down with at the end of the day (over a glass of wine). I would recommend it to anyone starting, or being in, a career in large animal practice as a mainstay for the bookshelf. I think it will continue to be one of the most widely used and authoritative texts in large animal veterinary medicine today.
Comments on the Ethical Question of the Month: July 2017 (CVJ 2017;58:651)

Maureen Harper

Canada is a major international supplier of horse meat in the world. In 2016, over 54,000 horses were slaughtered in this country. It is estimated that 65% to 70% of the horses slaughtered in Canada originate from the United States. This is because horse slaughter ceased in the United States in 2007. Also, according to Agriculture and Agri-Food Canada, 5839 live horses were shipped to Japan for slaughter in 2016.

Horse slaughter in Canada has become a contentious issue in recent years. There have been numerous undercover recordings showing the improper stunning of horses. This is normally accomplished through the use of a captive bolt or .22 rifle. However, the flight response of horses can make it extremely difficult to properly stun the animals. As a result, a number of horses have been documented bleeding out while still conscious. There are also issues with respect to horses being slaughtered that have been treated with drugs such as phenylbutazone and clenbuterol. Health Canada deems that such drugs is unacceptable in meat destined for human consumption. Unlike other farm animals, horses are not traditionally raised as food producing animals in North America.

The Canadian Food Inspection Agency (CFIA) is the mandated agency responsible for ensuring that animals are transported in a humane manner. The CFIA is also the agency responsible for the oversight of animal slaughter in all federal abattoirs. The Health of Animals Regulations Part XII — Transportation of Animals have been in place for about 40 years and are currently under review, awaiting updating.

With respect to transporting horses, once again through undercover footage, there has been documentation of infractions of humane transport under the Health of Animals Regulations. Many of the horses being shipped to Japan in wooden crates containing 3 or 4 horses per container and the horses are unsegregated. International Air Transport Association (IATA) Live Animal Regulations do not sanction the use of such containers for horses and IATA loading densities are not being respected with many of these shipments. The result is horses have lost their balance and fallen. And without adequate room to get up, they have been injured and killed.

Many horses, in particular ones destined for slaughter, also suffer while being transported by land. As most horses being slaughtered in Canada originate from the United States, many are transported long distances. The current federal legislation allows for horses to be transported for up to 36 hours without food, water, and rest. Studies have shown that horses become physiologically compromised and severely dehydrated at periods of more than 24 hours in transit.

The Health of Animals Regulations for transport of animals require that horses be segregated if the hind feet of the horses are shod. Animals that are incompatible by nature must also be segregated. Compromised horses (nonambulatory, injured, heavily pregnant and imminently due to give birth on the journey, distressed, sick, weak, and extremely thin animals) are not to be transported. Also, the animals must not be overcrowded. There must be adequate ventilation, the conveyance is required to be sound (no weak floors, holes in the flooring, insecure fittings or foreign objects or protrusions that could cause injuries), and there must be adequate bedding. There is no requirement, however, for horses from the United States to be off-loaded at the points of entry. Therefore, how can a proper assessment of these issues be made when these animals are arriving in Canada? Also, there are numerous documented cases of “unwanted” horses arriving at auction markets heavily pregnant, that foal shortly after arrival.

In summary, overbreeding in the equine industry is leading to a huge number of unwanted horses. If slaughter continues to be a solution to this issue, as sanctioned by the very industry that contributes to the overbreeding, then it is incumbent on the authorities to ensure that horses are transported and slaughtered humanely.

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Malassezia pachydermatis is a commensal yeast that is normally present in low numbers in the external ear canals and superficial muco-cutaneous sites in dogs. Malassezia pachydermatis is characterized by its round to oval or classical peanut shape with monopolar budding. This lipophilic, non-lipid dependent, non-mycelial saprophytic yeast organism is most often associated with Malassezia dermatitis (malasseziasis or Malassezia overgrowth) in dogs. Other Malassezia may uncommonly be noted as a cause of Malassezia dermatitis such as M. sympodialis, which is smaller than M. pachydermatis and has a more rounded bulbous shape and narrower-based monopolar budding (1).

Malassezia dermatitis in dogs is usually a secondary problem due to an underlying skin disease such as allergic disease (including canine atopic dermatitis and flea allergy dermatitis), recurrent bacterial pyoderma, and endocrine diseases (especially hypothyroidism) (2). Many predisposing factors may result in the commensal M. pachydermatis becoming a pathogen. These factors include increased humidity, presence of skin folds, altered cutaneous pH levels, previous antibiotic therapy, and prolonged corticosteroid therapy (2–4). In addition to being a secondary disease, a significant number of dogs affected with Malassezia dermatitis are affected by concurrent staphylococcal pyoderma. Malassezia pachydermatis is thought to have a symbiotic relationship with commensal staphylococci, which produce mutually beneficial growth factors and micro-environmental alterations (1,2).

Clinical findings

Malassezia dermatitis (Figure 1) is common in dogs and affected sites include lip margins, ear canals, axillae, groin, ventral neck, interdigital skin, facial folds or tail folds, perivulvar skin, and perianal skin (5). Lesions may be localized or generalized. Pruritus, a major sign, is usually severe and is accompanied by unpleasant odor. Skin lesions may present in various forms, which can be affected by chronicity of disease, primary underlying disease, previous therapy, and concurrent bacterial infection. Some common presentations of Malassezia dermatitis include:

1. Regional or generalized alopecia with erythema (exfoliative erythroderma);
2. Scaly, waxy, or greasy seborrhea (yellow or slate gray);
3. Crusts or papulocrustous lesions resembling superficial staphylococcal infection;
4. Lichenification and/or hyperpigmentation (leathery or elephant-like skin);
5. Paronychia with dark brown nail bed discoloration, with or without obsessive paw chewing;
6. Lip margin hypotrichosis and/or crusting; and
7. Intertrigo.

Several breeds are predisposed with the West Highland white terrier, basset hound, American cocker spaniel, shih tzu, poodle,
boxer, Cavalier King Charles spaniel, German shepherd dog, and dachshund showing an increased risk for *Malassezia* dermatitis.

### Diagnosis

The most useful and practical method of diagnosis of *Malassezia* dermatitis is cytologic examination (1,2,4). Samples collected using glass slide impression, acetate tape impression, superficial skin scraping, or cotton swab method are evaluated under the microscope to ascertain the numbers of *Malassezia* yeast, bacteria, and inflammatory cells present on superficial skin. If present, yeast organisms are often observed in clusters or adhered to keratinocytes (1). Each collection method has its own benefits based on patient temperament, clinician preference, and sampling site.

Cutaneous cytology is not always successful in finding *Malassezia* organisms. While some literature suggests that the clinician should rely on clinical lesion patterns to make a tentative diagnosis of *Malassezia* dermatitis in such a situation (4), in the author’s experience trial therapy is of minimal benefit in the absence of cytological evidence of *Malassezia* organisms. Although certain lesion patterns, presence of an offensive yeasty odor, and lack of response to previous appropriate therapy may be suggestive of *Malassezia* dermatitis, these should not be relied upon as diagnostic criteria without pursuing cutaneous cytology to confirm *Malassezia* organisms.

A further challenge in diagnosis of *Malassezia* dermatitis is the lack of agreement with regard to the significance of numbers of yeast present on cutaneous cytology (1,6). Varying numbers of yeast are present in different body sites, and normal numbers vary among breeds resulting in overlaps in yeast population densities in samples from clinically normal and diseased dogs (7). Ultimately the diagnosis of *Malassezia* dermatitis should rely on the combination of clinical presentation and cutaneous cytology. Even low numbers of *Malassezia* organisms noted on cytology may indicate *Malassezia* dermatitis if samples are collected from inflamed, pruritic skin. The findings of cutaneous cytology can vary between visits, and presence of a previous normal cytological analysis should not be regarded as current, if the patient exhibits new lesions or clinical symptoms.

Fungal cultures are not helpful because *M. pachydermatis* are commensal organisms, making their isolation in culture of little or no diagnostic value (1,2).

### Clinical management

Multiple treatment options for Malassezia dermatitis are available. Treatment is usually tailored according to factors such as localized versus generalized disease, overall patient health, underlying primary disease, and client preference or compliance.

It is preferable to use a combination of topical and systemic therapy in order to achieve rapid and complete remission of clinical signs. Prescribing topical or systemic therapy alone may be adequate for some patients. Extensive topical therapy can be challenging in dogs with a thick hair coat, for large or non-compliant dogs, or if the pet owners are unable to meet the physical requirements that are sometimes time-consuming, which is the nature of the treatment. Often, treatment of *Malassezia* dermatitis is accompanied by other recommendations such as a dietary elimination trial, antibiotic therapy, and antipruritic therapy. The overall workload for the pet owner should be evaluated in order to ensure compliance with sometimes numerous treatment recommendations made. Diagnostic workup and treatment for underlying primary disease should be pursued while treating *Malassezia* overgrowth, otitis, or dermatitis. Therapy should be continued for 7 to 10 d beyond clinical cure (1).

Follow-up examination is usually recommended 3 to 4 wk after initiation of treatment in order to evaluate clinical response and re-evaluate cytological *Malassezia* numbers. Clinical improvement, though welcome, is not adequate evidence to confirm treatment success. On the contrary, lack of follow-up cytology may lead to further confusion about significance of *Malassezia* yeast in the disease process, if the clinical symptoms or skin lesions were to recur.

For mild cases or for localized lesions, frequent topical therapy with antifungal products containing ingredients such as 2% ketoconazole, 1% ketoconazole–2% chlorhexidine, 2% miconazole, 2% climabazole, 2% chlorhexidine, 3% chlorhexidine, 2% miconazole–2% chlorhexidine, 2% lime sulfur, 0.2% enilconazole, or 1% selenium sulfide is usually effective (1,2,4,8–10). Shampoos containing 2 active ingredients may provide better efficacy (4). Medicated antifungal wipes or pads such as those containing 0.3% chlorhexidine, 0.5% climabazole, and Tris-EDTA solution are effective against *M. pachydermatis* (11).

For patients with generalized or multifocal lesions, oral antifungal therapy in combination with topical therapy is most effective. Oral antifungal drugs effective against *Malassezia* organisms include ketoconazole, fluconazole, terbinafine, and itraconazole (5,11–14). Griseofulvin is not effective in the treatment of *Malassezia* infection (1). Patient factors such as age, clinical history, underlying or concomitant disease, and breed predisposition should be considered before use of systemic drugs; baseline and monitoring blood testing is encouraged.

If underlying disease or predisposing factors are not controlled, or are inadequately managed, regular antifungal therapy may be indicated. Pulse therapy protocols using oral antifungal drugs such as ketoconazole, itraconazole, and terbinafine can be prescribed (12,13). Similarly, application of 2% climabazole shampoo for the control of *Malassezia* overgrowth and prevention of recurrence has been described (9).

### Malassezia hypersensitivity

One should not reach a diagnosis of *Malassezia* hypersensitivity without a complete and thorough dermatologic workup. Any dog with a classical history and cytological findings consistent with recurrent or persistent *Malassezia* dermatitis should be suspected of being affected by hypersensitivity to *Malassezia* organisms as long as underlying primary disease is well-managed or ruled out. Higher levels of *Malassezia*-specific immunoglobulin E have been found in atopic dogs compared with healthy dogs, suggesting that *Malassezia* may participate as an allergen in patients with atopic dermatitis (15). Hypersensitivity to *Malassezia* antigens is also thought to be important in atopic humans (16). If *Malassezia* hypersensitivity is suspected, intradermal allergy testing followed by observation for immediate
and delayed reactions may be used to document hypersensitivity reactions (1). In dogs diagnosed with Malassezia hypersensitivity, immunotherapy with M. pachydermatis antigens may be a useful therapeutic measure (17), but it may not be effective in some dogs suspected to be hypersensitive to M. pachydermatis, and pulse therapy may be needed to prevent recurrence.

Prognosis

Malassezia dermatitis carries a good prognosis. Thorough efforts should be made to identify causative factors such as underlying allergies, endocrine disease, neoplasia, or skin folds, to help prevent recurrent infection. Once concurrent infections and primary disease are adequately treated, management of M. pachydermatis induced dermatitis is usually straightforward.

References


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Le support des annonceurs démontre leur engagement pour l’avancement de la médecine vétérinaire au Canada. Nous vous encourageons à prendre connaissance de leurs services et produits. — NDLR
1. C) Cavalier King Charles spaniels have a higher incidence of mitral valve endocardiosis than do other breeds.  
C) L’Épagneul cavalier King Charles possède une plus grande incidence d’endocardiose de la valve mitrale que les autres races.

2. B) The measurement of abdominal fluid BUN can be helpful, but since BUN is a lower-molecular-weight substance compared with creatinine, it will be reabsorbed more quickly across the peritoneum, lowering its concentration in the abdominal fluid. Although sodium and potassium are abnormal in this fluid, their presence does not prove that the fluid is urine. Choice D is incorrect. At times, some urine is voided to the outside and some to the peritoneal cavity depending on the location of a bladder tear. Choice E is incorrect. It is possible for a urinary catheter to pass through the tear in the bladder. The fluid that is retrieved is assumed to be urine when in fact it is modified abdominal fluid (urine + fluid shifts).

B) La mesure du BUN du liquide abdominal peut être utile, mais puisque le BUN est une substance de poids moléculaire plus faible comparativement à la créatinine, il sera réabsorbé plus rapidement à travers le péritoine, abaissant sa concentration dans le liquide abdominal. Bien que le sodium et le potassium soient des substances anormales dans ce liquide, leur présence ne prouve pas que le liquide soit de l’urine. Le choix D est incorrect. À certains moments, une certaine quantité d’urine peut être éliminée à l’extérieur ou dans la cavité péritonéale, selon la localisation de la déchirure dans la vessie. Le choix E est incorrect. Il est possible pour un cathéter urinaire de passer par la déchirure dans la vessie. On assume que le liquide qui est récolté est de l’urine, alors qu’en fait il s’agit de liquide abdominal (urine + fraction de liquide).

3. D) This drug has been shown to cause fatal neutropenia in cats and is contraindicated for this species. The other listed drugs are used as immunosuppressive therapies in the cat.

D) On a démontré que ce médicament causait une neutropénie fatale chez le chat et il est contre-indiqué pour cette espèce. Les autres médicaments énumérés sont utilisés comme thérapie immunosuppressive chez le chat.

4. D) The correct answer is lethal lavender foal syndrome. Conditions A, B, and E are not fatal and can occur in any breed of horse. Answer C occurs in overo paint horses, not Egyptian Arabians, and affected foals display signs of colic rather than neurologic signs.

D) La bonne réponse est le syndrome létal du poulain lavande. Les réponses A, B, et E ne sont pas des conditions fatales et peuvent se rencontrer chez n’importe quelle race de chevaux. La réponse C se produit chez les chevaux Paint horse ovéro et non chez les chevaux Égyptiens arabes; les poulains atteints montrent des signes de coliques plutôt que des signes neurologiques.

5. C) Papillomatous digital dermatitis (hairy heel warts) can be controlled by foot bathing (e.g., copper sulfate) or topical application of antiseptic or antibiotic solutions (e.g., tetracycline). Alley scraping and hygiene are important in preventing all bacterial digital dermatitides. This disease is contagious, so it is important to determine whether the disease was recently introduced by purchased cattle, or is endemic. New, coarse concrete can be a risk factor for sole disease, not interdigital or other dermatitides.

C) La dermatite digitale papillomateuse (verrues poilues des coussinets) peut être contrôlée par des bains de pieds (p. ex., sulfate de cuivre) ou par l’application topique de solutions antiseptiques ou antibiotiques (p. ex., tétracycline). Le grattage et l’hygiène des allées sont importants pour prévenir toutes les dermatites digitales bactériennes. Cette affection est contagieuse; ainsi il est important de déterminer si la maladie a été récemment introduite par l’achat de bovins ou si elle est endémique. Du nouveau béton grossier peut être un facteur de risque pour les maladies de la sole et non pour les dermatites interdigitales ou les autres dermatites.
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Catastrophic communication

Myrna Milani

Many practices can claim clients who lean toward a more optimistic or pessimistic view of life’s events. Moreover, those views may extend to how those clients perceive what happens to their animals. Among the pessimists, one small but troublesome subgroup consists of ultra-pessimists like Ms. Rodenaur. Whereas the average pessimist views the glass half-empty, she perceives it as having a few drops at most.

“I know Spunky needs his vaccinations, but I’m terrified he’ll have a reaction, Dr. Shively. He’s such a little thing and I know you give the same big dose to every dog. All kinds of things could go wrong. The needle might break off when you stick him, or maybe...” Ms. Rodenaur’s eyes widen and the color drains from her face as she considers a new horror. “...he might have a stroke and drop dead like my father did!”

Before she continues these unproductive ruminations, Dr. Shively gently interrupts the woman and reminds her that Spunky is a healthy, young adult, mixed breed dog which weighs almost 27 kg and has never experienced any negative reactions to any vaccinations in the past. But later the veterinarian tells her associate, Dr. Trudelle, that she had no illusion that this would comfort the anxious client.

“She kept going on and on about all the asymptomatic problems Spunky might have that the stress of the trip to the clinic and his vaccination might cause to explode,” recalls Dr. Shively. “Even when I pointed out I’d vaccinated the dog while she and he were distracted and he didn’t even notice, it made no difference. She then worried that the dog would be angry with her or feel betrayed because she didn’t comfort him while I stuck needles in him. Thank goodness I had to leave for an emergency or I’d still be in that room with her!”

Had Ms. Rodenaur succumbed to chronic physical pain instead of the chronic behavioral and emotional pain associated with her extreme pessimism, the human medical community would have a word to describe her response: catastrophizing. Catastrophizing is the belief that things are far worse than they are and it has emerged as a primary biosocial factor in chronic pain perception. Because chronic physical pain serves as the primary driver of the opioid addiction crisis, treating catastrophizing has emerged as a critical element of the treatment process.

However, most practitioners know from their own experience and that of their close friends and loved ones that behavioral and emotion pain hurt every bit as much as physical pain. And, like Drs. Shively and Trudelle, they also recognize that the Ms. (and Mr.) Rodenaur’s of the world would benefit from quality mental health therapy. At the same time, though, they realize that in the great majority of their interactions with such clients, they are in no position to suggest this.

“Aside from the fact that I lack the credentials to make such a suggestion and while I do care about my clients, my first obligation is to their animals’ well-being,” notes Dr. Shively. “If I spend all our time together trying to reassure clients with no desire to be reassured instead of giving my full attention to their animals, I’m not doing my job.”

However, it is possible to lessen the effects of catastrophizing by more actively engaging these clients in the veterinary procedure. Instead of making more general comments or ignoring the clients — both of which could reinforce their already counter-productive and maddening behavior — Dr. Shively focuses on getting a detailed history of these clients’ animals instead. Admittedly the veterinarian does this already. But she also acknowledges that in the past she was apt to abbreviate the process in hopes of ending these client interactions as quickly as possible. Although it took some practice, Dr. Shively soon learned how to gracefully redirect her clients’ attention to supplying information about their animals as soon as the first sign of catastrophizing arose. Once she had the history, she found that pointing out interesting but normal anatomical features of the animal or asking these clients to assist her in some way — e.g., massage their animals’ ears, hand her something on the counter she easily could get herself — distracted them and engaged them in a meaningful way.

Difficult as that may be, however, dealing with catastrophizing clients is a great deal easier than dealing with staff members who possess that same trait. Dr. Trudelle’s predecessor, Dr. Rubio, approached anything beyond the most routine surgical
and medical cases as if he and the animal would be lucky if they survived. Because Dr. Rubio was technically competent despite his extreme pessimism, initially Dr. Shively let it go. However, two realizations caused her to change her mind.

First, the veterinarian and the rest of the staff noticed that Dr. Rubio's patients did not do as well. The more serious the animal's problem, the greater this effect appeared to be.

“It wasn't anything like wound contamination or the wrong medication or dose,” the practice owner admitted. “I think it was just that Dr. Rubio hovered over the animals and fussed over them so much they couldn't get any rest if he was around. Consequently, his patients weren't as relaxed as I thought they should be and it affected their appetites and interactions with other staff members too. While I couldn't point to anything specific, let alone its cause, I suspect some clients also noticed this because they began insisting that I treat their animals.”

However, Dr. Shively had no trouble pinpointing that Dr. Rubio’s ultra-pessimistic approach was undermining patient and client wellbeing during euthanasia because clients complained angrily about it. This did not occur because Dr. Rubio did not care about his clients and their animals at this most difficult time. If anything, it could be said that he cared too much. He became so caught up in all the things that might go wrong pre-time. If anything, it could be said that he cared too much. He

The tipping point occurred when a long-time client with extensive knowledge about and concern for her many animals presented her 15-year-old dog because he stumbled and then began limping on a front leg. Radiographs revealed a large invasive mass affecting the proximal humerus, most likely an osteosarcoma. Because of the dog’s age and other medical conditions that ruled out amputation and other options, the client raised the possibility of euthanasia. Whereas Drs. Shively and Trudelle would have recognized that the client wanted and needed some compassionate support from her veterinarian at such a difficult time, Dr. Rubio got so caught up in his catastrophic what-if scenarios that he just stood there making lame comments that only made the situation worse.

When the client realized that the veterinarian could not or would not support her in any way and requested that he euthanize her pet, he then agreed that this was the right choice under the circumstances. However, instead of comforting the client, what she perceived as his complete lack of compassion infuriated her. In addition to telling her family and friends what a dreadful experience it was, she wrote a long letter to Dr. Shively that left no doubt in the practice owner's mind how the client felt about it, either.

Unlike the vaguer effects Dr. Rubio's mindset had on animals that the practice owner and most clients could attribute to other factors and dismiss, his euthanasia-related catastrophizing caused him so much pain he became oblivious to that of these clients and their animals. At that point, Dr. Shively gave him an ultimatum: he either could seek professional help or she would terminate his employment.

“I didn't just drop letting him go on him like a ton of bricks,” she clarified. “I met with him after hours and laid out all my concerns and perceived options and asked for his input. He immediately began going on and on about how much sleep he lost worrying about his cases, making a mistake, how horrible it all was, etc. That proved my point: He needed professional help.”

Dr. Shively later confided to Dr. Trudelle that it was the most difficult thing she ever did. But keeping him on under the existing conditions benefitted no one—not the animals, the clients, and certainly not the practice. Later she learned that, although Dr. Rubio tried to convince everyone that his life was ruined by all this, etc. That proved my point: He needed professional help.

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