The Canadian Veterinary Journal
La Revue vétérinaire canadienne

March/Mars 2024 | Volume 65, No. 03

Galliprant®
(grapiprant tablets)

$#!* JACK IS BACK

Jack wasn't his usual mischievous self, but Galliprant® got him back to doing what he loves.

Galliprant offers advanced oral pain relief for canine OA[1,5,6].

- Unique MOA reduces the impact on organ health.[2,3,6]
- A treatment choice that suits every dog's OA journey.[3,4]

Great news for Jack!
Bad news for squirrels!

1. Kirkby Shaw K, et al. Vet Med Sci. 2015 Dec 21;2(1):3-9
2. Rausch-Derra L, et al. Am J Vet Res. 2015;76:853–859
3. Galliprant Canadian Product Label.
4. Rausch-Derra L, et al. J Vet Intern Med. 2016;30:756-763
5. Pye C, et al. J Small Anim Pract. 2022;63:721–738.
6. Kirkby Shaw K, et al. Vet Med Sci. 2016;2:3-9.

Scan this QR code and learn more about Galliprant

www.galliprant.ca

Help Pet Owners Hop into **Easy Financing**

Using online loan applications right from your website, pet owners can get pre-approved for LendCare financing in minutes and walk into your clinic financially ready to get their beloved pets running—or hopping—again.

Offer LendCare Financing at your Clinic Today!

LENDCARE

Scan QR code to learn more

PURINA®
PRO PLAN
VETERINARY SUPPLEMENTS®

RECOMMEND PROBIOTICS AS PART OF A HEALTHY DAILY ROUTINE FOR YOUR PATIENTS

FortiFlora® PRO Synbiotic Action™ supplement contains a powerful prebiotic and probiotic combination to support your patients GI health.

Synbiotic action of prebiotics and probiotics to manage diarrhea and support a healthy intestinal microbiome

Contains prebiotic fibre (psyllium) to stimulate the growth of specific bacteria and support a healthy GI microbiome

Contains the same probiotic strain in FortiFlora®, proven to promote normal intestinal microflora

FOR MORE INFORMATION CONTACT YOUR PURINA® PRO PLAN VETERINARY DIETS® TERRITORY MANAGER.

Visit **www.Purina.ca** or call us at **1-866-884-VETS(8387)**.

Have a case consult? We are here to help. Contact our Canadian Veterinary Resource Centre at canadavetconsult@purina.nestle.com.

PURINA® Your Pet, Our Passion®

Contents Table des matières

SCIENTIFIC RUBRIQUE SCIENTIFIQUE

Kills fleas

Kills ticks*

Credelio® CAT (lotilaner)

small size, BIG FLAVOUR

The tiny tablet they think is a treat.

As Canada's first feline oral flea and tick product, Credelio® Cat is an easy-to-administer, tiny, tasty tablet with a flavour cats love[1].

- **Tasty:** Vanilla provides an attractive aroma; yeast provides a savory flavour[1]
- **Easy to give:** 99.5% of doses successfully administered by owners to a diverse range of cats[2]
- **Effective month-long protection:** Kills 100% of fleas by 24 hours and 97-100% of black-legged ticks[3]*
- **From the makers of Milbemax®:** Use Credelio Cat with Milbemax for broad spectrum external and internal parasite coverage

Talk to your Elanco representative to learn more or visit CredelioCat.ca

1. Toutain CE et al Parasit Vect 2018 11 412 (v1.0) - vanillin and yeast flavor (p.2) The flavoring (yeast and vanillin) was specifically chosen for cats
2. Chappell K Parasites & Vectors 2021; 14:127 (v1.0) - 99.5 % success in administartion (p.2) Owners successfully administered 99 .5 % of tablets to their cats
3. Credelio Cat Product label

* Killed 97-100% of Ixodes scapularis ticks at 72 hr throughout the month.

Elanco™

Contents Table des matières

FEATURES RUBRIQUES

NOTICES ANNONCES

Contributors

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

Les « Directives à l'intention des auteurs » sont disponibles en ligne (www.veterinairesaucanada.net).

The Canadian Veterinary Journal
La Revue vétérinaire canadienne

339 rue Booth Street
Ottawa, Ontario K1R 7K1
Telephone: 613-236-1162
Fax: 613-236-9681
Email: kgray@cvma-acmv.org
Website/Site Web: www.canadianveterinarians.net
www.veterinairesaucanada.net

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

Photo by/Photo de : Shannon Wheatley, Nepean, Ontario

Typesetting/Typographie
AN Design Communications
www.an-design.ca

Printed by/Imprimé par
Dollco Print Solutions Group
Ottawa, Ontario

ISSN 0008-5286

Report undeliverable Canadian addresses to:
email: vmadaye@cvma-acmv.org

Subscriptions (2024). Online format (January to December) & Print format (January to June 2024).

Annual: Canada (personal) $275; Canada (institutional) $350, plus applicable GST or HST; foreign (personal) $290 USD; institutional $350 USD. Subscriptions must be prepaid in Canadian or USD dollars. Subscriptions to *The Canadian Veterinary Journal* are valid for 1 year beginning with the next available issue after receipt of payment at the Canadian Veterinary Medical Association (CVMA). Undelivered issues will be replaced if the Subscriptions Office is notified within 1 year of the issue date. The publisher expects to supply missing issues only when losses have been sustained in transit and when the reserve stock will permit. All subscriptions inquiries should be sent to the journals department at vmadaye@cvma-acmv.org

Abonnements (2024). Les numéros de janvier à juin seront imprimés et publiés en ligne; à partir de juillet 2024, les numéros seront publiés en ligne seulement.

Annuel : Abonnement personnel (canadienne) 275 $ CAD, abonnement d'institutional (canadienne) 350 $ + TPS ou TVH en vigueur, abonnement personnel (à l'étranger) 290 $ É-U, abonnement d'institutional (à l'étranger) 350 $ É-U. L'abonnement doit être payé à l'avance en dollars canadiens ou américains. L'abonnement à *La Revue vétérinaire canadienne* est valide pendant un an à compter du prochain numéro publié après la réception du paiement de l'abonnement à l'Association canadienne des médecins vétérinaires (ACMV). Les numéros manquants seront remplacés si le service des abonnements est avisé dans l'année qui suit la date de parution.L'éditeur ne fournira les numéros manquants que si des pertes ont été subies pendant le transport et si le nombre d'exemplaires en réserve le permet. Les demandes d'abonnement doivent être envoyées à revues, courriel vmadaye@cvma-acmv.org

Published monthly by/
Publication mensuelle de

Canadian Veterinary Medical Association

Canadian Veterinary Medical Association
Association canadienne des médecins vétérinaires

Whatever and wherever you practice, the CVMA is with you every step of your way.

We speak for you on veterinary issues of national importance and protect the integrity of our profession.

As a CVMA member, you benefit from…

- Engagement with Government and stakeholders to influence policy decisions
- International relations to provide the Canadian veterinary perspective
- Media/public relations to provide trustworthy information and promote veterinary professionals
- Position statements addressing animal welfare and national veterinary issues
- Member consultations on key veterinary issues
- Leadership initiatives on antimicrobial stewardship and surveillance, cannabinoids, telemedicine
- Administration of national veterinary exams to ensure uniform certification of professional credentials
- Accreditation of veterinary colleges and veterinary technician programs

We put money in your pocket to increase your profitability.

As a CVMA member, you benefit from preferred pricing and discounts on…

- CVMA specialized group insurance program (Western Financial)
- Scotiabank® business banking and lending solutions
- Moneris™ payment processing services
- The Personal Insurance for home/auto/travel
- CVMA Petcard™ Program – financing options for your clients
- Clinician's Brief™ (free global digital edition)
- Plumb's Veterinary Drugs™
- LifeLearn products
- CVMA Annual Convention
- Classified ads in The CVJ
- GoodLife Fitness membership
- Mont Tremblant SkiMax/GolfMax
- Hotels worldwide discount program
- National and Enterprise car rental
- Staples Advantage™ business products
- Adtel® telephone hold service and digital signage
- Bell Canada for mobile service on phones and plans
- Petro-Canada SuperPass™ wfuel/diesel discount
- WSAVA World Congress and WVA Congress

We provide resources to help you achieve a meaningful career and personal wellness.

As a CVMA member, you benefit from…

- The Canadian Veterinary Journal (CVJ)
- The Canadian Journal of Veterinary Research (CJVR)
- CVMA Source Guide
- Bi-monthly e-newsletter 'Online from 339'
- CVMA Annual Convention: sessions and CE credits
- CVMA National Issues Forum
- CVMA Summit
- CVMA Emerging Leaders Program
- CVMA Mentoring Program
- Early career DVM resource hub
- CVMA Canadian Veterinary Reserve (CVR)
- Veterinarian health and wellness resources including Togetherall and The Working Mind courses
- National Economic Report
- Practice Owners Economic Survey
- Provincial Suggested Fee Guides
- Report on Compensation and Benefits for Associate Veterinarians
- Non-DVM Wage Report
- Veterinarians in Government, Industry and Academe Report
- Practice management articles and career/business resources
- CVMA Guidelines for Veterinary Antimicrobial Use (online database & Firstline app)
- Therapeutic decision cascade poster
- Animal abuse resources for practitioners
- Preventive healthcare, nutritional assessment and client education tools and resources
- Animal Health Week, National Tick Awareness Month and Mental Health in Vet Med Awareness Week campaigns
- VetLaw Online™ legal advice column

Canadian Veterinary Medical Association

339 Booth Street
Ottawa (Ontario) K1R 7K1

t 800-567-2862
613-236-1162

admin@cvma-acmv.org
canadianveterinarians.net

06 2023

INTRODUCING

Nobivac® Intra-Trac® Oral BbPi

twist, MIST, and go!

For illustration purposes only.*

The first-ever
oral *Bordetella bronchiseptica* (Bb) and parainfluenza virus (Pi) vaccine

Offers easy administration and effective protection in just 3 simple steps

The patented Immuno-Mist-R™ applicator creates a fine mist for broad mucosal surface area contact

Creates a comfortable vaccine experience for dogs

LEARN MORE HERE

Talk to your Merck Animal Health sales representative to place your order of Nobivac® Intra-Trac® Oral BbPi.

Customer Service: 1-866-683-7838
(Monday–Friday, 8:00 AM–4:30 PM EST)

Nobivac®
Protection unites us.

*Refer to product insert for complete instructions.

MERCK Animal Health

President's Message
Le mot du président

Mentorship, growth, and the things that weren't taught in veterinary school

Le mentorat, l'épanouissement, et les choses qui ne sont pas enseignées à l'école vétérinaire

It is March 2024, less than 3 months from the time when the class of 2024 will join our ranks as veterinary professionals in a world with a faster pace and perhaps higher expectations than ever before. If you are a seasoned veterinarian like me, the approaching annual convocation likely takes you back to your first year or two in practice as you reflect on your experiences, setbacks, and growth. If you are in your first few years, you may be feeling overwhelmed or unhappy at times; and if you are approaching convocation, I suspect you are doing so with a mix of anxiety and excitement.

Over the past few years, I have travelled with students who are applying to veterinary school or some who are soon-to-be graduating veterinarians. I have found myself trying to offer a mix of career advice and clinical training to the soon-to-be minted veterinarians or those who aim to attend veterinary school — perhaps "what veterinary school didn't teach me" or "what being part of this profession is really about." I am hopeful that there is value in what I have to share: advice that many haven't received elsewhere and hopefully not too many bad habits!

Mentorship has the potential to have a major and lasting effect on both the mentor and mentee. For the mentee, it is well-known that early-career and life advice from established professionals can greatly improve career trajectory, open opportunities that may not be obvious, and build relationships of trust with clients and colleagues. Likewise, the mentor benefits from building a stronger and more resilient profession and can be truly energized when engaged with young and driven professionals by providing valuable insights and helping shape perspectives in ways only experience can do.

I was recently in touch with a colleague of a similar vintage, discussing a promising extern coming to Nova Scotia. Our conversation meandered into territory about changes we've seen in our relatively short time in our profession. We shared concerns that many new veterinarians are missing out on the truly great moments our profession has to offer, and that many seasoned veterinarians have so much to offer if only they were to be asked.

Nous sommes en mars 2024, il ne reste plus que trois mois avant que les étudiants et étudiantes de la promotion de 2024 viennent nous rejoindre en tant que professionnels vétérinaires, dans un monde où la cadence de travail et possiblement les attentes sont plus élevées que jamais. Si, comme moi, vous êtes vétérinaire depuis longtemps, cette période de l'année vous ramène probablement à vos premières années de pratique et fait remonter des souvenirs de vos expériences, de vos échecs et du chemin parcouru. Si vous êtes plutôt en début de carrière, vous ressentez peut-être du dépassement ou de l'insatisfaction parfois, et si vous vous apprêtez à obtenir votre diplôme, je soupçonne que cette étape s'accompagne d'un mélange d'anxiété et d'excitation.

Au cours des dernières années, j'ai côtoyé des jeunes qui souhaitaient s'inscrire à l'école vétérinaire et de futurs vétérinaires qui allaient bientôt terminer leurs études. J'ai essayé de leur offrir des conseils sur la carrière en plus de la formation clinique, par exemple sur ce que l'école vétérinaire ne m'a pas appris ou sur ce que signifie vraiment faire partie de notre profession. J'ose croire que ce que j'ai à partager est utile; souvent, ce sont des conseils qu'ils n'ont jamais eus, et qui, je l'espère, ne leur donneront pas trop de mauvaises habitudes!

Le mentorat peut avoir un impact majeur et durable tant sur les mentorés que sur les mentors. Pour les mentorés, les conseils sur le début de carrière et la vie en général reçus de professionnels expérimentés peuvent améliorer considérablement leur trajectoire professionnelle, leur ouvrir des perspectives qui ne sont pas forcément évidentes à première vue et les aider à établir des relations de confiance avec les clients et les collègues. Quant aux mentors, ils bénéficient du développement d'une profession plus forte et résiliente et trouvent parfois une nouvelle énergie dans leur engagement auprès de jeunes professionnels motivés, en leur prodiguant des conseils précieux et en les aidant à se forger une opinion comme seule leur expérience permet de le faire.

J'étais récemment en contact avec un collègue de mon âge pour discuter d'une étudiante prometteuse qui s'apprêtait à venir faire un stage en Nouvelle-Écosse. Notre conversation s'est

Over the past few years, we've seen evidence our relationship with the society we serve has become more transactional and less respected. Our profession has become less about relationships and more about standard operating procedures, stricter boundaries, and artificial or self-imposed restrictions on our interactions with the public we serve. This is accompanied by a suggestion that we are better off to be on this path, when in fact the evidence may be lacking to support this conclusion.

As someone who identifies as "seasoned," I think I can speak for my cohort — very few of whom would resent being asked to contribute to the growth and career paths of new veterinarians, and few who (at least in my sphere) seem to resent their choice to pursue life as a veterinarian despite the incredible amount of time and effort expended to do so successfully.

My challenge in writing this piece is for early-career veterinarians and the soon-to-be graduated veterinarians: no matter your path of companion animal, equine, food animal, public health, academia, or other, lean into the early years and accept the challenges and gifts that come with them. Align yourself with a mentor who absolutely loves our profession and is willing to share some of the most important "life lessons" they can impart from their lived experience. Remember this: so much of what will make you happy, fulfilled, and healthy in this profession didn't come from a Zoom course, a laboratory, or a lecture hall — it will come from how you decide to live and practice veterinary medicine.

For well-seasoned veterinarians who have so much to offer, accept the challenge this spring and share what you have learned and what has allowed you to thrive in our beautiful profession with the early-career veterinarians and new graduates you cross paths with!

Recently, while I was training a soon-to-be colleague from the University College Dublin and recapping some cases for the day, we spoke of safety in large animal practice and remarked that taking the time to form animal bonds is so important. She asked, "Is that why you do those little things with the horses?" I was thrilled she noticed and asked, because it is just one of the reasons I love what I do. It seems to me that this is Step 1 to a rewarding career and a healthy relationship with the clients and animals we serve, as well as loving our profession.

"For me, the magic is in all of the little details. All the things that you can never learn from a text and only from watching animals, fantastic animal handlers, and fantastic veterinarians. You never officially learn this stuff; you absorb it if you take the time to sit and just watch."

Dr. Andrea Dubé, AVC Class of 2007

Dr. Trevor Lawson

---

orientée vers les changements que nous avons observés au cours de notre relativement courte carrière, et nous trouvons tous les deux dommage que beaucoup de nouveaux vétérinaires passent à côté de moments formidables propres à notre profession alors que plusieurs vétérinaires chevronnés auraient tellement à offrir si seulement on leur demandait.

Au fil des ans, notre relation avec la société que nous servons a pris une tournure plus transactionnelle et moins respectée. Notre profession est devenue moins axée sur les relations et plus axée sur les modes opératoires normalisés, les limites mieux définies, et les restrictions artificielles ou auto-imposées à nos interactions avec le public. Cette évolution s'accompagne d'une suggestion selon laquelle il est préférable de s'engager dans cette voie, alors qu'en réalité, les preuves manquent pour étayer cette conclusion.

En tant que professionnel soi-disant « expérimenté », je pense pouvoir dire des collègues de ma promotion que très peu seraient opposés à ce qu'on leur demande de contribuer à l'accompagnement et au perfectionnement de nouveaux vétérinaires, et qu'ils sont aussi peu nombreux (du moins dans mon domaine de pratique) à regretter leur choix de devenir vétérinaire malgré le temps et les efforts considérables investis pour réussir.

J'invite les médecins vétérinaires en début de carrière et les futurs vétérinaires qui vont bientôt obtenir leur diplôme, quelle que soit la voie qu'ils empruntent (animaux de compagnie, chevaux, animaux de consommation, santé publique, milieu universitaire ou autre), à plonger dans ces premières années et à accepter les défis et les cadeaux qui les accompagnent. Trouvez un mentor qui est passionné par notre profession et qui est prêt à partager avec vous d'importantes « leçons de vie » qu'il peut vous transmettre grâce à son expérience. N'oubliez pas qu'une grande partie de ce qui vous rendra heureux, épanoui et équilibré dans cette profession ne proviendra pas d'un cours sur Zoom, d'un laboratoire ou d'une salle de classe, mais bien de la façon dont vous décidez de vivre et d'exercer la médecine vétérinaire.

Pour les vétérinaires chevronnés qui ont tant à offrir, relevez le défi ce printemps et partagez ce que vous avez appris et ce qui vous a permis de vous épanouir dans notre belle profession avec les vétérinaires en début de carrière et les nouveaux diplômés que vous rencontrez!

Récemment, alors que j'accompagnais une stagiaire de l'University College Dublin et que je récapitulais quelques cas de la journée, nous avons parlé de sécurité en pratique des grands animaux et de l'importance de prendre le temps de nouer des liens avec nos patients. Elle m'a demandé : « Est-ce pour cela que vous faites toutes ces petites choses avec les chevaux? » J'étais ravi qu'elle le remarque et qu'elle pose la question, car c'est l'une des raisons pour lesquelles j'adore mon travail. C'est, selon moi, la première étape d'une carrière gratifiante et d'une relation harmonieuse avec les clients et les animaux que nous servons, ainsi que de l'amour que nous portons à notre profession.

« Pour moi, la magie réside dans les petits détails. Toutes ces choses que l'on ne peut pas apprendre dans un livre, mais uniquement en observant les animaux, les manieurs exceptionnels et les vétérinaires extraordinaires. En fait, ces choses, on ne les apprend jamais officiellement – on les assimile si on prend le temps de s'asseoir et de regarder. »

Dre Andrea Dubé, promotion de 2007 de l'AVC

Dr Trevor Lawson

Hill's
Transforming Lives

fresh breath. sweet kisses.

Discuss the dental health benefits of t/d with your clients today

1. Clinically proven triple action fibre matrix technology helps freshen breath, clean & whiten teeth and reduce plaque & tartar buildup
2. Clinically shown to reduce the occurrence of gingivitis by up to 36%[1]
3. Vital nutrition for dogs' daily health and immune system support

SCIENCE DID THAT.

[1]Logan EI, Finney O, Hefferren JJ. Effects of a dental food on plaque accumulation and gingival health in dogs. *J Vet Dent*. 2002;19(1):15-18.

Introducing

Zenalpha®

(medetomidine and vatinoxan hydrochlorides injection)

Take the stress out of sedation with our innovative alpha-2 agonist/antagonist combination that helps minimize negative cardiovascular effects.

- Rapid onset, within 5–15 minutes in most dogs.
- Patients recover in approximately 45 minutes.
- Generally, no reversal is needed.

Scan to watch our Zenalpha playlist to **learn more.**

Speak to your Dechra Representative to learn more about how your purchase of Zenalpha can help support Not One More Vet.

Dechra Veterinary Products Inc.
Tel.: 1-855-332-9334 | **Technical Services:** technical.ca@dechra.com | **www.dechra.ca**

Dechra

Veterinary Medical Ethics
Déontologie vétérinaire

Ethical question of the month – December 2023

A veterinarian in our area has developed a reputation for significant errors that individually might be forgiven, but as they multiply, start to form a pattern. The range of concerns includes patients with mandibular fractures secondary to attempted extraction of lower canines; patients with undiagnosed masses untreated until the owners seek a second opinion, by which time the problem is aggravated; and dispensing of medications without an examination and/or without full understanding of potential deleterious effects of the medication on other factors, such as pregnancy. The veterinarian is very personable and charismatic, and the affected owners are convinced that these are onetime mistakes. To my knowledge, there has only been 1 formal complaint to a regulatory body. I am very reluctant to report a local colleague's questionable practices, but each time an animal is adversely affected, it becomes more frustrating. Attempts at direct communication have not been helpful. **At what point am I obligated to make a complaint? How do I balance my responsibility to be a reasonable professional colleague with my obligation to protect patients and the profession?**

Question de déontologie du mois – Décembre 2023

Un médecin vétérinaire de ma région a acquis la réputation de commettre des erreurs importantes qui, prises individuellement, pourraient être pardonnées, mais qui se multiplient et commencent à devenir une habitude. Parmi ces erreurs figurent des fractures de la mandibule causées par une tentative d'extraction d'une canine mandibulaire, des masses non diagnostiquées et non prises en charge jusqu'à ce que les propriétaires demandent un deuxième avis alors que le problème s'est aggravé, et la prescription de médicaments sans faire d'examen ou sans bien comprendre leurs effets nocifs potentiels sur d'autres facteurs comme la gestation. Le vétérinaire est très sympathique et charismatique, et les propriétaires des animaux affectés sont convaincus qu'il s'agit d'erreurs ponctuelles. À ma connaissance, il n'y a eu qu'une seule plainte officielle auprès d'un organisme de réglementation. J'éprouve une grande réticence à dénoncer les pratiques douteuses d'un collègue local, mais chaque fois qu'un animal en subit les conséquences, la situation devient de plus en plus frustrante. Les tentatives de communication directe ont été infructueuses. **À quel moment ai-je l'obligation de déposer une plainte? Comment puis-je concilier ma responsabilité de collègue professionnel raisonnable et mon devoir de protéger les patients et la profession?**

Ethicists' commentary on considerations when judging whether to formally report a colleague's potential misconduct

This case concerns a local veterinarian who appears to be making regular mistakes that negatively affect the welfare of animals attending their practice. We have been asked if another local veterinarian (who we will refer to as the "reporting veterinarian") should complain to a regulatory body.

Deciding on the best course of action will, in our view, come down to balancing 2 types of risk: i) the risk of causing reputational harm to a potentially innocent colleague, and ii) the risk of allowing an incompetent veterinarian to go on misdiagnosing and mistreating animals with potential negative effects for both the animals and their owners.

Our first recommendation is for the reporting veterinarian to speak with their colleague to let them know about the concerns and to hear what they have to say about these incidents. It is important to accept that everyone can make mistakes, to not judge a colleague on a single mistake, and to make a sincere attempt to understand the colleague's perspective. But if the colleague refuses to engage, as seems to be the case, or if the behavior fails to improve following an initial attempt to address it in a collegial manner, then it is appropriate to consider some sort of formal report.

Before taking this next step, the reporting veterinarian should critically consider the quality of evidence they have for a complaint. For example, do they have firsthand evidence of the problems, having either witnessed the poor practice directly or provided follow-up treatment to patients who had initially been (mis)treated by the offending veterinarian?

If the reporting veterinarian has firsthand evidence of misconduct, then we would advise reporting to the authorities. If, however, the evidence of misconduct is indirect, then the

reporting veterinarian should advise the person who shared their firsthand experience of the seriousness of the issue and urge that person to report the misconduct.

In the special case that the individual with firsthand knowledge feels unable to report this themselves, it is reasonable for the reporting veterinarian to assist them with making the complaint or, on the individual's request, to report on their behalf — especially if this person is a client (or someone with whom the reporting veterinarian has a professional relationship).

Ultimately, it is not the reporting veterinarian but the regulatory body that will have to judge whether there really is an issue here, and this can only be done if the evidence is presented for investigation.

Drs. Clare Palmer, Peter Sandøe, and Dan Weary

Ethical question of the month — March 2024

You provide veterinary services to a "no-kill" small animal shelter. A mature female bulldog crossbreed dog is presented for a spay procedure. The history supplied is that the dog was surrendered after numerous complaints about noise bylaw infractions for constant barking by the dog, which was never taken out of a fenced backyard. The dog has some fear-aggression issues and is therefore difficult to examine. Financial constraints of the shelter also limit how much preoperative workup is possible for an animal with an uncertain history. Your anesthesia team is experiencing some difficulty with both induction and maintenance of anesthesia. As you begin the surgery, it is apparent that the dog is pregnant with a large litter of puppies. The shelter manager is telephoned for direction but is unavailable. **How do you proceed? You are concerned about postponing the spay procedure, given the difficulties of both handling and anesthetizing the dog. You know the shelter is at full capacity, so you are concerned about their ability to care for a large litter of puppies. Can you override the expectations of your client in this case and spay the dog, which would effectively euthanize the litter?**

Question de déontologie du mois — Mars 2024

Vous fournissez des services vétérinaires à un refuge « sans euthanasie » pour petits animaux. Une femelle bouledogue croisée adulte vous est présentée pour sa stérilisation. Selon l'information fournie, la chienne ne sortait jamais de sa cour clôturée et elle a été abandonnée à la suite de nombreuses plaintes concernant des infractions au règlement municipal sur le bruit car elle aboyait constamment. Elle montre des signes d'agressivité liée à la peur et est donc difficile à examiner. Les contraintes financières du refuge limitent également l'étendue des examens préopératoires possibles pour un animal dont les antécédents sont incertains. Votre équipe d'anesthésie rencontre des difficultés pour l'induction et le maintien de l'anesthésie. Alors que vous commencez la chirurgie, vous constatez que la chienne est gestante de plusieurs chiots. Vous tentez de joindre le responsable du refuge par téléphone, mais il n'est pas disponible. **Que faites-vous? Vous hésitez à reporter la stérilisation, compte tenu des difficultés liées à la manipulation et à l'anesthésie de la chienne. Vous savez que le refuge est plein et vous doutez de sa capacité à prendre en charge une grosse portée de chiots. Pouvez-vous dans un tel cas ne pas tenir compte des attentes de votre client et stériliser la chienne, ce qui aurait pour effet d'euthanasier la portée?**

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 Canadian Veterinary Medical Association, Attn: Journals Department, 339 Booth Street, Ottawa, Ontario K1R 7K1; email (bettinadvm@gmail.com). A longer response may appear as a Letter to the Editor.**

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

Les réponses au cas présenté sont les bienvenues. Veuillez limiter votre réponse à environ 50 mots et nous la faire parvenir avec vos nom et adresse **par la poste (Choix déontologiques, Association canadienne des médecins vétérinaires, À l'attention de : Journals Department, 339 rue Booth, Ottawa, Ontario, K1R 7K1) ou par courriel (bettinadvm@gmail.com). Les réponses plus longues pourraient être publiées dans le courrier des lecteurs.**

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.

BRAVECTO®

Pets are individuals. The choice is yours.

The most complete offering for tailored parasite control plans. Because every pet has different needs.

BRAVECTO® ONE

BRAVECTO® SMART PROTECTION MADE EASY®

12 TWELVE-WEEK PROTECTION for dogs

12 UP TO TWELVE-WEEK* PROTECTION for cats

VITRECTO® 2 MONTH† DOSING INTERVAL

*BRAVECTO® Topical Solution for Cats provides 12-week efficacy against fleas and *H. longicornis* and 8-week efficacy against *D. variabilis* and *I. scapularis*.
†The dosing interval is 2 months; however, VITRECTO® is effective for the treatment and control of infestations with *H. longicornis* (Asian longhorned tick) for 12 weeks.
BRAVECTO® and VITRECTO® are registered trademarks of Intervet International B.V. Used under license.
SMART PROTECTION MADE EASY® is a registered trademark of Merck Canada Inc. Used under license.
MERCK® is a registered trademark of Merck Sharp & Dohme LLC. Used under license.

Round up YOUR TEAM!

2024 CVMA Convention
Calgary - June 26-30

EARLY BIRD REGISTRATION

Closes April 15, 2024

Canadian Veterinary Medical Association
Association canadienne des médecins vétérinaires

IN COLLABORATION WITH
RVTTC TTVAC

ORGANIZED IN PARTNERSHIP WITH:
ABVMA
Alberta Veterinary Medical Association

Quiz Corner
Test éclair

1. A 4-year-old Staffordshire bull terrier dog is brought to a veterinary clinic because of acute, non-weight-bearing lameness of the left pelvic limb. The location of the lameness is determined to be the left stifle. An image taken during surgical repair of the left stifle is shown below (Figure 1).

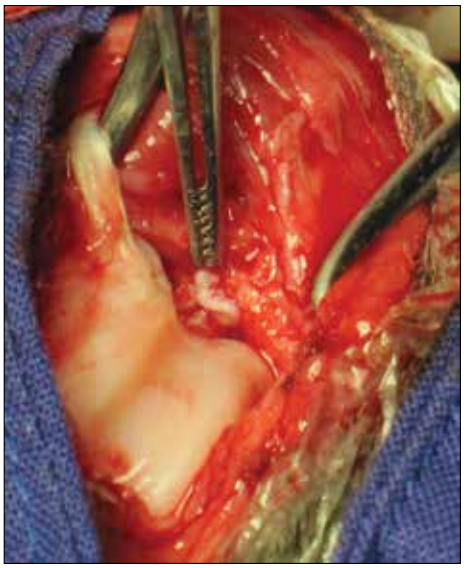


Figure 1.
Image: Wikimedia Commons (Uwe Gille), freely usable from: https://commons.wikimedia.org/wiki/File:Kreuzband-op-situs.jpg
Image de Wikimedia Commons (Uwe Gille) pouvant être utilisée gratuitement (https://commons.wikimedia.org/wiki/File:Kreuzband-op-situs.jpg)

What concurrent condition is likely to occur with the lesion seen in the image?

A. Hypothyroidism
B. Ununited anconeal process
C. Contralateral hip dysplasia
D. Medial meniscal injury
E. Left pelvic angular limb deformity

1. Un bull-terrier du Staffordshire de 4 ans est amené dans une clinique vétérinaire pour une boiterie sans appui aiguë du membre postérieur gauche. La partie du membre affectée est le grasset (genou). Une image prise pendant la réparation chirurgicale du grasset gauche est présentée ci-dessous (figure 1).

Quelle affection concomitante est probable avec la lésion observée sur l'image?

A. Hypothyroïdie
B. Non-union du processus anconé
C. Dysplasie de la hanche controlatérale
D. Lésion du ménisque médial
E. Déformation angulaire du membre postérieur gauche

2. An artificial insemination technician breeds 5 heifers that are demonstrating strong natural standing heat.

When is it appropriate to start watching to see if the heifers settled (*i.e.*, were successfully bred) on this service?

A. 5 d from service
B. 18 d from observed heat
C. 21 d from service
D. 10 d from observed heat
E. 22 d from observed heat

2. Un technicien en insémination artificielle procède à la saillie de 5 génisses qui présentent de fortes chaleurs naturelles et un comportement de réceptivité à la monte.

Quand convient-il de commencer à observer les génisses pour déterminer si la saillie a réussi?

A. 5 jours après la saillie
B. 18 jours après l'observation des chaleurs
C. 21 jours après la saillie
D. 10 jours après l'observation des chaleurs
E. 22 jours après l'observation des chaleurs

(See p. 291 for answers./Voir les réponses à la page 291.)

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

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

Letter to the Editor Courrier des lecteurs

Michelle Lem's convocation address to Ontario Veterinary College graduates — A comment

To the Editors,

I am grateful to my friend and former classmate, Dr. Michelle Lem, for her honest and thought-provoking convocation address to recent graduates of the Ontario Veterinary College, published in *The CVJ* (1). It is another testament to her thoughtful and caring approach to advancing veterinary medicine and society for the better.

Submitted by Jason Coe, DVM, PhD, Professor, Ontario Veterinary College, Guelph, Ontario.

Reference

1. Michelle Lem. Convocation address to the Ontario Veterinary College '23 graduating students, June 16, 2023. Can Vet J 2024;65:177–181.

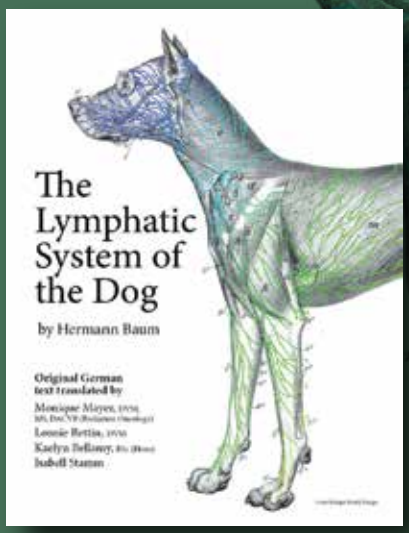
FREE RESOURCE TOOLS FOR YOUR CLINIC

Two vital veterinary resources that will benefit your entire clinical team— *at no cost!*

The Lymphatic System of the Dog

by Dr. Hermann Baum

English translation of the 1918 German text with additional digital resources



Ideal for staging of canine cancer patients, this open-access textbook balances the legacy of Dr. Baum's research with new assessments and design to engage today's veterinary professionals.

KEY SECTIONS

- Anatomical location and drainage pathways of lymph nodes
- Lymphatic drainage pathways of major organs

MORE FEATURES

- Notes on key clinical points
- Flashcards, labelling exercises and other interactive learning tools

LINK TO OPEN TEXT RESOURCE

Radiation safety training video for veterinary workers

Layperson-level video available in English, French, Spanish and Portuguese

This seven-minute video provides step-by-step training on the correct use of aprons, thyroid shields, gloves, glasses and other radiation shielding tools during manual restraint of animals for diagnostic radiography. Veterinary teams worldwide rely on this educational video for employee training.

UNIVERSITY OF SASKATCHEWAN

Questions? Contact:
Dr. Monique Mayer
Western College of Veterinary Medicine
University of Saskatchewan
monique.mayer@usask.ca | 306-966-7088

INTERCEPTOR® PLUS
(milbemycin oxime/praziquantel)

A NEW THREAT MAY BE IN THEIR OWN BACKYARD.

Don't leave a gap in their worm coverage.

As the presence of coyotes and foxes continues to increase throughout urban and residential areas in Canada, so does the prevalence of the parasites they carry, including the zoonotic tapeworm *Echinococcus multilocularis*[1-8*]. This means more domestic dogs are now at risk – along with their owners.

Interceptor® Plus is the only monthly chew that provides broad-spectrum coverage against all five major worms, including tapeworm. Avoid gaps in coverage by protecting your canine patients – and the humans around them – with Interceptor® Plus.

Order today or contact your Elanco representative to learn more.

NoMoreGap.ca

References:
1. Peregrine *et al.* 2016. 2. Jenkins Clin. Brief 207. 3. Catalano *et al.* 2012. 4. Gesy *et al.* 2014. 5. Luong *et al.* 2018. 6. Kolapo *et al.* 2019. 7. Tse *et al.* 2019 * (scat study). 8. Kotwa *et al.* 2019. *Elanco-sponsored research with Dr. Prada (FMV)

Elanco™

Case Report Rapport de cas

Median lingual hair heterotopia associated with pyogranulomatous glossitis in a Labrador retriever: Surgical treatment using carbon-dioxide laser

Eliot Gougeon, Chloé Touzet, Cyrill Poncet

Abstract — A 9-year-old male Labrador retriever dog was presented with dysphagia and presence of hairs on the tongue. Buccal examination revealed ulcerative glossitis and lingual hairs along the midline. Ultrasound and magnetic resonance imaging of the tongue showed multiple hair shafts contained in a proliferative tissue along the midline and extending in a fistulous tract towards the right ventral aspect of the tongue at mid-length. Surgical excision was completed using a carbon-dioxide laser. Histopathological examination revealed a pyogranulomatous inflammation centered on growing hairs, confirming the diagnosis of glossitis and lingual hair heterotopia. At 10 mo after surgery, all clinical signs and glossitis had disappeared despite partial recurrence of hair on the dorsal sulcus and in the sublingual fistula.

Key clinical message:

i) Although lingual hair heterotopia usually has no clinical repercussions, associated ulcerative lesions should support imaging and biopsy.
ii) Resection of the lesion using a carbon-dioxide laser resulted in a good outcome in this case, but recurrent hair growth is possible.

Résumé — Hétérotopie pilaire linguale associée à une glossite pyogranulomateuse chez un chien labrador : traitement chirurgical à l'aide d'un laser au dioxyde de carbone. Un chien Labrador mâle entier de 9 ans est présenté pour une dysphagie et la présence de poils sur la langue. L'examen de la cavité buccale met en évidence une glossite sévère associée à des implantations pilaires. L'échographie et l'imagerie par résonance magnétique de la langue mettent en évidence de multiples poils contenus dans du matériel tissulaire s'étendant le long de la ligne médiane et présentant un trajet fistuleux vers la partie ventrale droite de la langue à mi-longueur de cette dernière. Une exérèse est réalisée à l'aide d'un laser au dioxyde de carbone. L'examen histopathologique de la pièce d'exérèse révèle une inflammation pyogranulomateuse centrée sur des poils en croissance, confirmant le diagnostic de glossite et d'hétérotopie pilaire linguale. Dix mois après la chirurgie, aucun signe clinique n'est réapparu et la glossite a disparu, malgré la récidive partielle de poils sur la partie dorsale de la langue et en région sublinguale droite.

Message clinique clé :

i) Bien que l'hétérotopie pilaire linguale n'ait généralement pas de répercussion clinique, les lésions ulcéreuses associées devraient justifier une imagerie et une biopsie.
ii) La résection de la lésion à l'aide d'un laser au dioxyde de carbone a donné de bons résultats dans ce cas, mais une pousse récurrente des poils est possible.

(Traduit par les auteurs)

Can Vet J 2024;65:213–219

CHV Frégis, rue Jacques Destrée, 75013 Paris, France.

Address all correspondence to Eliot Gougeon; email: eliot.gougeon@gmail.com

This study was funded by the IVC Evidensia Publication support grant.

Unpublished supplementary material (Video 1) is available online from: www.canadianveterinarians.net

Congenital conditions of the tongue are uncommon in dogs; the most frequent are microglossia, macroglossia, and ankyloglossia. Acquired conditions are more common and can be neoplastic, traumatic, or inflammatory (1). Penetrating foreign bodies are among the most common cause of tongue inflammation and result in a pyogranulomatous glossitis (1).

Heterotopia, also called choristoma, is a subtype of ectopia; it refers to the ectopia of a particular tissue type that usually coexists with the original tissue. Heterotopia is not uncommon in the oral cavity in humans (2–9). For example, Fordyce syndrome, referring to the presence of heterotopic sebaceous glands in the lips or tongue, can affect up to 1 in 3 humans (10). In dogs, buccal heterotopia is uncommon, with few reports of cartilage and hairs in this location (11,12). Median lingual hair heterotopia (MLHH), or *pili heterotopici mediani linguae,* is a rare condition in which hair follicles and associated hair shafts are observed in the median plane of the tongue (13–15). No diagnostic protocol or preferred treatment have been proposed for this condition in dogs or humans.

This article reports a case of MLHH associated with severe pyogranulomatous glossitis in a 9-year-old Labrador retriever dog. The MLHH was not responsive to antibiotic treatment and was surgically excised using a carbon-dioxide laser.

Case description

A 9-year-old male Labrador retriever dog was presented with dysphagia, halitosis, buccal swelling, dysphagia, and ptyalism associated with ulcerative lesions and hairs on the tongue. Five months before presentation, tongue swelling and ulcerations associated with the proliferation of hairs extending along the dorsal surface of the tongue were observed by the owners, with no previous clinical signs. Before referral, the dog had been presented to 3 first-opinion practices. Each reported 2 ulcerative lesions associated with hairs: 1 lesion on the median sulcus and 1 right sublingual lesion. Before referral, the dog underwent 4 surgical removals of hairs present on the tongue and received multiple medical treatments: 1 treatment of amoxicillin/clavulanate (12.5 mg/kg, PO, q12h) and prednisolone (1 mg/kg per day, PO) for 5 d; 2 treatments of amoxicillin/clavulanic acid (12.5 mg/kg, PO, q12h) and meloxicam (0.1 mg/kg per day, PO) for 5 d; and 3 treatments of clindamycin (11 mg/kg per day, PO) and meloxicam (0.1 mg/kg per day) for 5 to 10 d. Temporary clinical improvement was observed, with recurrence of clinical signs and hair regrowth after treatment. The dog had lost 3 kg of body weight, and the owners reported the dog had a dull coat all over its body since the condition started.

The dog was referred for examination 5 mo after detection of the lesion. On admission, there were no abnormalities detected on a general physical examination. The dog was anesthetized (propofol, 4 mg/kg, IV and midazolam 0.2 mg/kg, IV, with isoflurane in oxygen) and buccal cavity examination revealed an invaginated linear ulcerative lesion on the median sulcus of the tongue with hair implantation into the lesion. All hairs had the same orientation (shafts' apices pointing dorsally). The superficial part of the main lesion started 1 cm caudal to the lingual apex and extended caudally 8 cm along the midline (Figure 1 A). The lesion was 1 cm wide, and invagination and ulceration of the median sulcus ranged from 5 to 10 mm deep after hair removal (Figure 1 B). A similar, but focal, lesion was observed at the base of the lingual frenulum on the right side (Figure 1 C). Submandibular soft tissue swelling was attributed to tongue swelling and mandibular lymphadenomegaly.

Ultrasonographic examination of the tongue (Aplio a-series; Canon Medical Systems, Tochigi, Japan) was completed under anesthesia using a 12 to 18 MHz broadband linear transducer. Thin hyperechoic linear elements continuous with the hairs protruding on the external surface of the tongue were contained in a 15-millimeter wide and 22-millimeter deep groove of hypoechoic soft tissues extending along the tongue's midline from 1 cm caudal to the apex to the base of the tongue. The right sublingual lesion had a similar ultrasonographic aspect and extended caudodorsally toward the main lesion (Figure 2).

Morphine was administered and 4 punch biopsies ranging from $3 \times 2 \times 5$ mm^3 to $3 \times 4 \times 10$ mm^3 were obtained. Histopathological examination revealed a pyogranulomatous glossitis developing mainly around the hair shafts and hair bulbs, and more rarely around small, vegetal foreign bodies. All hair shafts and bulbs had a normal appearance with no suggestion of neoplastic proliferation. An antibiogram was not conducted on the lingual biopsy due to the presence of commensal oral bacteria posing a risk of contamination and misinterpretation. A combination of spiramycin (75 000 IU/kg per day, PO) and metronidazole (12.5 mg/kg per day, PO) was prescribed for 15 d to attempt to alleviate bacterial contamination. An Elizabethan collar was recommended to ensure the hairs were not originating from self-licking with a wounded tongue. After 15 d of treatment, surgery was delayed 6 wk for owner-related reasons, and antibiotic treatment continued during this period.

After 8 wk, halitosis and dysphagia had disappeared and the dog had gained 4 kg. Visual inspection of the tongue revealed persistent lingual ulcers and a slightly reduced presence of hairs compared to 2 mo earlier. On ultrasound, the lesions were similar to those previously noted. Magnetic resonance imaging (MRI) of the tongue was obtained for surgical planning purposes, using a 0.2 T low-field machine (Vet-MRgrande; Esaote, Genova, Italy). Transverse T2-weighted (T2W) and T1-weighted (T1W) pre- and post-contrast sequences were acquired (thickness: 0.5 mm; T2W: TE 100 ms, TR 5540 ms; T1W: 26 ms, 660 ms), along with a 3D T1W post-contrast sequence (thickness: 0.08 mm, TE 16 ms, TR 38 ms) to allow multiplanar reconstruction. On MRI images, the lesion appeared as a markedly T2W-hyperintense, mildly T1W-hyperintense and intensely enhancing tract, consistent with the inflammatory tissue previously identified histologically, and contained central T2W- and T1W-hypointense elements consistent with the hairs (Figure 3). The MRI allowed good visualization of the communication of the right ventral fistulous tract at the base of the tongue with the midline lesion, as well as determination of the precise extension of the lesion at the base of the tongue and anatomical localization of the lesion relative to lingual arteries and veins.

Despite clinical improvement with antibiotic treatment, surgical excision of the lesion was recommended due to the

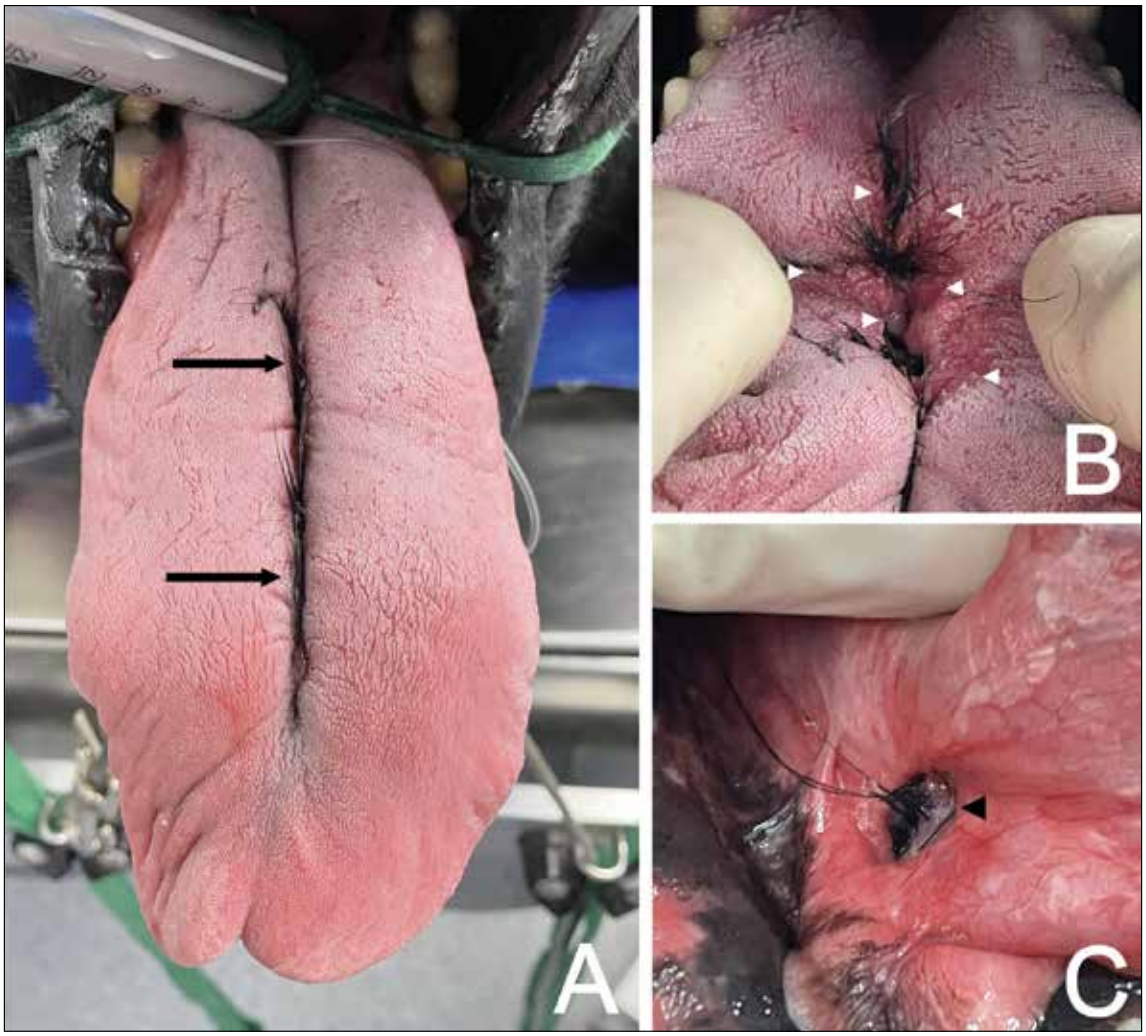


Figure 1. Macroscopic appearance of canine lingual median lingual hair heterotopia. A – Dorsal aspect of the tongue before surgery. Presence of hairs on the median sulcus of the tongue is evident (black arrows). B – Dorsal aspect of the tongue before surgery. Note the focal glossitis at the point of contact of the hairs (white arrowheads). C – Right sublingual aspect of the tongue before surgery. A fistula containing hairs and inflammatory exudate is present (black arrowhead).

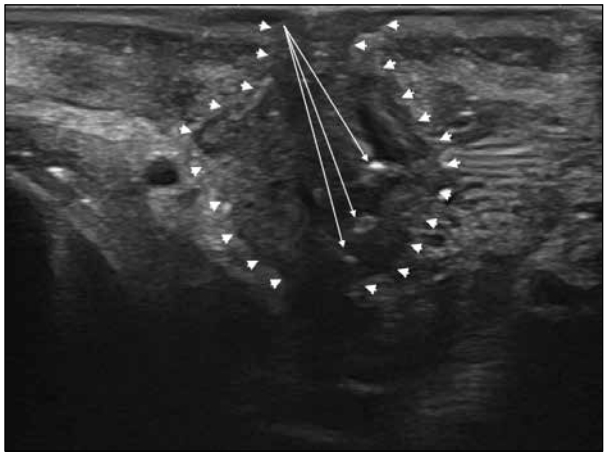


Figure 2. Ultrasound image of the tongue in cross section, showing on midline the groove of hypoechoic soft tissues (arrowheads) containing central hyperechoic linear discrete elements (arrows).

high risk of recurrence after antibiotic discontinuation and the benefits of performing the surgery on healthier tissue. Resection of the lesion and associated hair shafts was done from rostral to caudal into lingual mucosa and musculosa using a 6- to 12-W noncontact super-pulsed, scanned-mode small-size carbon-dioxide laser (Space Vet; Deka, Manchester, New Hampshire, USA) with 2 to 5-millimeter lateral and 2 to 5-millimeter-deep margins using the MRI landmark and preserving the lingual arteries and hypoglossal nerves (Figure 4 A, B; see Video 1, available online from: www.canadianveterinarians.net). The fistula was also debrided along its fistulized tract, all the way to its junction with the median lesion. Abundant saline lavages were performed. The final incision was closed in 3 continuous layers using resorbable poliglecaprone 25 sutures (Advantime; Peters Surgical, Boulogne-Billancourt, France): 2-0 USP for the deep part of the musculosa, 3-0 USP for the superficial part of the musculosa, and 4-0 USP for the mucosa (Figure 4 C, D). An esophagostomy tube (Nutrifit, 14 Fr, 125 cm; Vygon, Ecouen,

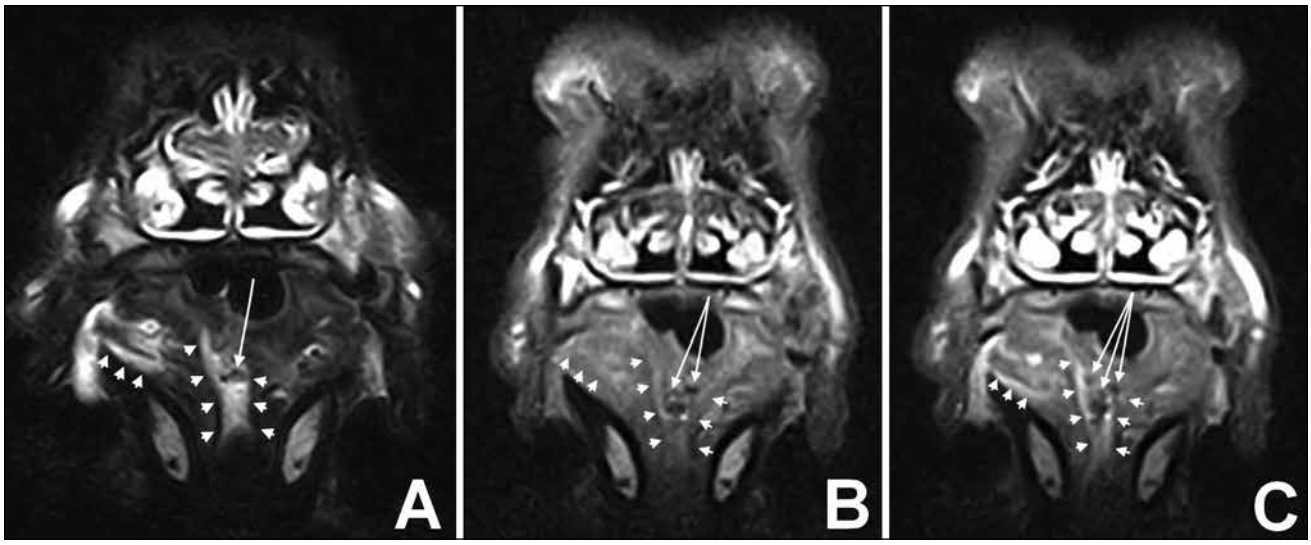


Figure 3. Magnetic resonance images showing the midline tongue lesion in transverse section. A – T2-weighted image. B – T1-weighted image. C – T1-weighted image after intravenous injection of contrast medium (gadolinium). The midline groove is lined by T2W- and T1W-hyperintense tissues that display intense enhancement (arrowheads), and contains central T1W- and T2W-hypointense discrete elements (arrows).

France) was placed. Mild sublingual edema occurred on the day after surgery but did not require treatment. There were no other complications and the dog was discharged from the hospital 48 h after surgery.

Postoperative recommendations were as follows: feed the dog only *via* the tube for 15 d, limit activity for 2 wk, avoid hard objects in the mouth for 3 wk, and have the dog wear an Elizabethan collar for 3 wk. The dog was allowed to drink water. Postoperative treatment consisted of cefalexin, 15 mg/kg, PO, q12h for 5 d; prednisolone, 0.5 mg/kg, q12h for 7 d; and tramadol, 2 mg/kg, q8h for 3 d.

Histopathological evaluation of the excised tissue revealed a multifocal-to-coalescent pyogranulomatous and ulcerative glossitis centered on multiple hair shafts and, more rarely, on vegetal foreign bodies (Figure 5 A, B).

At follow-up 21 d after surgery, the owners reported the dog had no complications, a good appetite, and a less dull coat. Visually, the tongue exhibited complete healing and an absence of hair shafts. At 5 mo after surgery, there were no recurrent clinical signs and no discomfort reported when the dog was chewing or swallowing. Antibiotic treatment had not been given. Examination of the tongue was completed under sedation and revealed a small number of hairs on the dorsal sulcus and in the sublingual fistula, without associated ulceration (Figure 6). At 10 mo after surgery, no clinical signs were reported, and owner satisfaction was excellent.

Discussion

This is apparently the first case report of MLHH associated with a pyogranulomatous glossitis with clinical repercussions. Antibiotic treatment resulted in temporary improvement of the clinical signs and lingual lesions. However, due to a lack of complete healing and recurrence of clinical signs after discontinuation of antibiotic treatment, surgery was performed. The lesion was excised, resulting in complete resolution of clinical signs despite partial recurrence of heterotopic hairs after surgery.

In humans, hair heterotopia has been reported to occur in various locations, including the conjunctiva, buccal cavity, and bone (2,4–6,16,17). In dogs, hair heterotopia is an uncommon condition reported in the uterus and buccal cavity (13,14,18). Living follicular tissue experimentally implanted into the peritoneal cavity in dogs resulted in liver and bone marrow proliferation of hairs (19). Similarly, transplantation of isolated whisker follicles in an injured spinal cord resulted in heterotopic pigmented hair shafts in the spinal cord 90 d after implantation (20), indicating that hair follicles can develop in heterotopic locations. Lingual hair heterotopia is reported in both humans and dogs (3,8,12–15,21). In some cases, this condition is congenital, probably after abnormal embryonic development (13). However, acquired cases are sometimes associated with concomitant diseases such as dermoid cyst, teratoma, anterior trauma, or dysendocrinia (hirsutism) (3,15,21). In a case report, heterotopic hairs were observed in the tongue of a dog after suture of a lingual wound (15). In another case, no circumstantial event was reported (8). In the current case, the dog was 9 y old and the owners had not noticed the presence of hairs before manifestation of clinical signs. Although differential diagnoses for such lesions include congenital conditions such as dermoid cyst or teratoma, these were unlikely in a dog of this age and in the absence of a preexisting condition, evocative clinical signs, or histopathological findings. An acquired process was therefore expected, and despite no history of trauma, a traumatic etiology cannot be excluded as an inciting cause.

Imaging the canine tongue is challenging due to the paucity of literature for this organ. Magnetic resonance imaging is used in both humans and dogs (22–24). Despite excellent sensitivity to detect soft tissue changes, it has low specificity for discriminating between neoplastic and inflammatory processes (24).

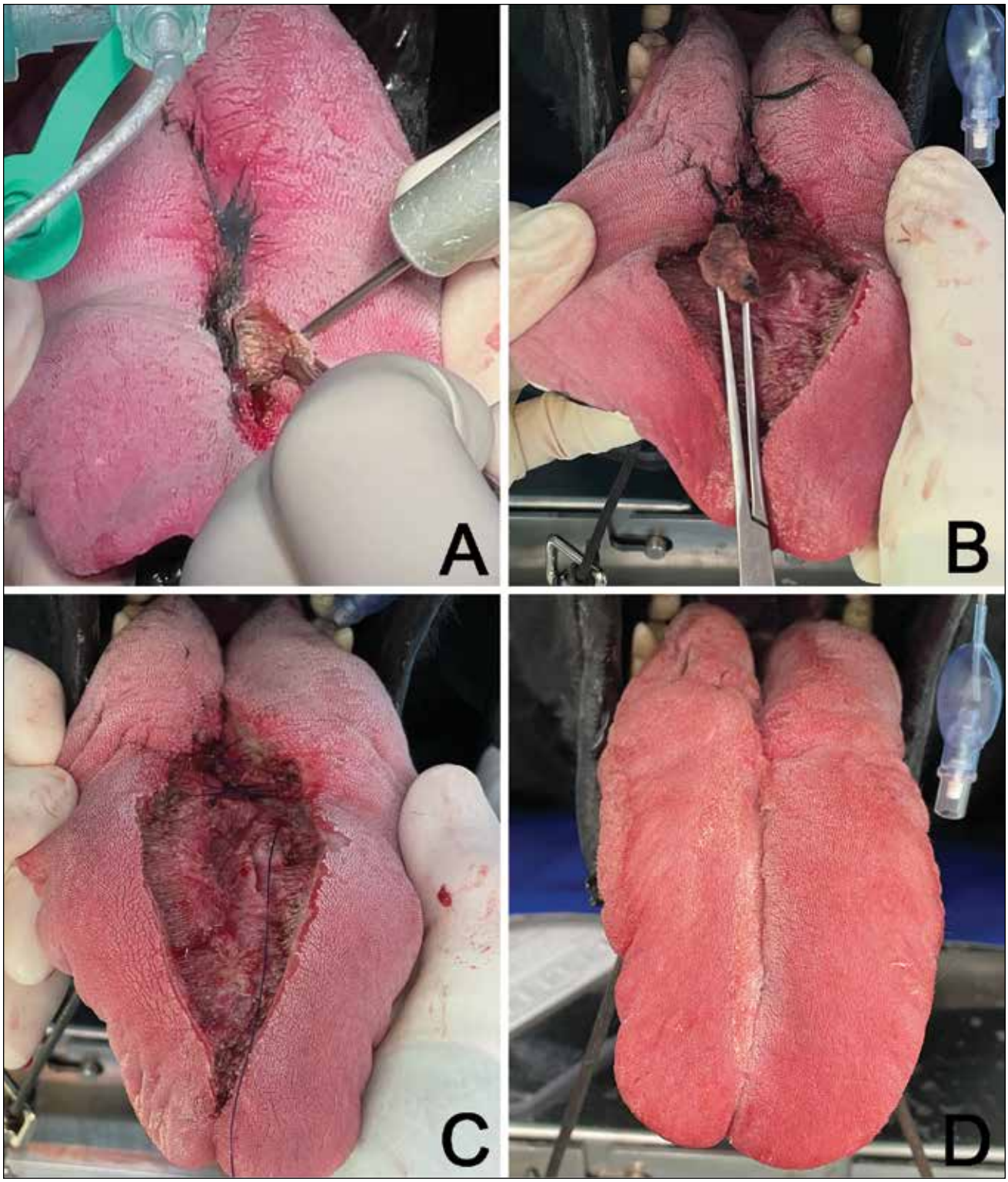


Figure 4. Illustration of the surgical technique. A – Beginning the excision of the heterotopic lesion at the rostral part of the tongue. The tongue is manually stretched bilaterally to improve laser section using 3- to 5-millimeter margins. B – The excision is extended caudally. The tongue is maintained in a stretched position and excised tissue is clamped with an Allis forceps. C – Dorsal aspect of the tongue after complete removal of macroscopically visible lesion. The deep muscular part of the tongue is sutured with poliglecaprone 2-0 USP. D – Final aspect of the dorsal aspect of the tongue after surgery. Muscular and mucosal layers have been closed. No hairs or inflammatory lesions are visible macroscopically and the tongue has a normal shape.

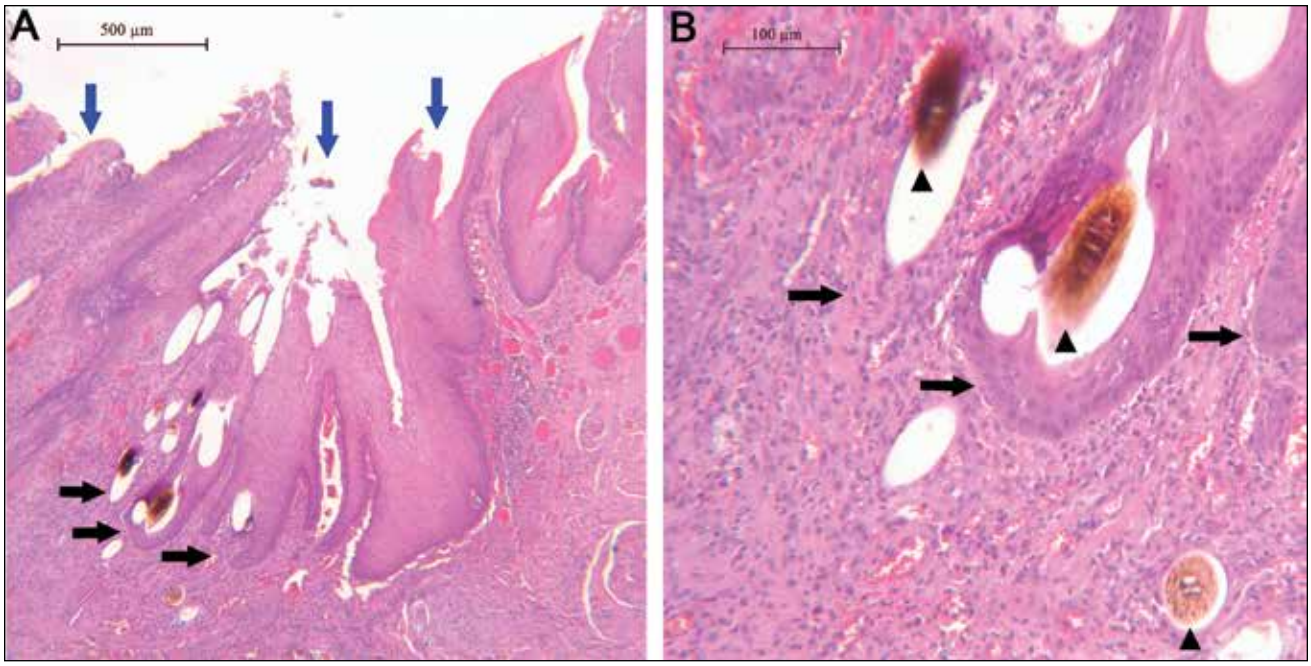


Figure 5. Histopathologic images of the excised lingual tissue, revealing canine lingual median lingual hair heterotopia. Hematoxylin, eosin, and saffron staining; scale bars: 500 µm (A), 100 µm (B). A – Gross aspect. Hair bulbs and their associated hair shafts are observed (black arrows) with ulceration of the lingual mucosa (blue arrows). B – High-power view. Hair bulbs and their associated hair shafts are observed (arrows). Diffuse inflammatory infiltrate and neovascularization can be observed around the hair bulbs (arrowheads).

Although both MRI and ultrasound can detect hair follicles and foreign bodies, ultrasound allows a better assessment and has been successfully used to identify foreign hair material in pathologic conditions (17,25–27). In this case, MRI identified the exact extension and anatomy of the lesion for surgical planning, but hair detection was better with ultrasound than with low-field MRI. Regardless, the accuracy of ultrasound *versus* high-field MRI remains to be determined.

In dogs, most instances of pyogranulomatous glossitis are caused by penetrating foreign bodies (1). It is well-known that keratin outside the hair tract can act as a foreign body and provoke an intense sterile inflammatory reaction (27,28). Pyogranulomatous inflammation has been reported around hairs of MLHH, similar to that produced by foreign bodies (14). In this case, most of the pyogranulomatous reaction was centered on hair shafts, with only a small proportion centered on scarce vegetal foreign bodies. In this case, a penetrating vegetal foreign body may have initiated an inflammatory process that was subsequently enhanced by a keratin inflammatory reaction on heterotopic hair shafts.

In this dog, several antibiotic treatments failed due to the persistence of foreign bodies (hairs) into the tongue. Preoperative antibiotic treatment was prescribed to ensure a cleaner surgical site. No antibiogram was obtained due to potential commensal bacterial contamination, with antibiotics chosen based on pharmacokinetics and antimicrobial activity. Spiramycin and metronidazole were selected for their excellent buccal diffusion and aerobic and anaerobic activity (29). Although the lesion improved with this treatment, the hairs had to be surgically removed, along with their bulbs, to prevent recurrence.

A carbon-dioxide laser was chosen over electrocautery for excision of the lingual lesion due to its superiority with respect to hemostasis, operating time, and outcomes in various oral surgeries (30,31). The precise section given by the laser was helpful in not extending the section too far laterally, enabling preservation of the lingual arteries and hypoglossal nerves. The tongue was sutured in 3 layers using poliglecaprone 25 due to its rapid absorption that promoted fast healing of lingual tissue and avoided the presence of a persistent foreign body suture that could support bacteria (32). Corticosteroids were selected over NSAIDs with the aim of a greater reduction in postoperative inflammation.

Although all macroscopically visible hairs were removed during surgery, there was partial hair regrowth several months after surgery, suggesting that a portion of the active hair follicles were not surgically removed. A more aggressive approach could have created a full median section of the tongue, but this approach was not chosen because it would have been associated with more complications and a reduction in tongue width. Moreover, marginal resection of the lesion led to the complete disappearance of clinical signs with no additional antibiotic treatment and excellent owner satisfaction at 10 mo after surgery.

The authors have observed in their clinical practice several incidental cases of MLHH without inflammation or clinical consequences. For most dogs, lingual hair heterotopia is asymptomatic and surgery is generally unnecessary. However, in rare instances, glossitis, bacterial superinfection, or lingual ulcers can occur, causing clinical signs (*e.g.,* halitosis, pain, dysphagia, dysorexia, and weight loss). Antibiotic treatment may be initially attempted to control bacterial superinfection, but some cases

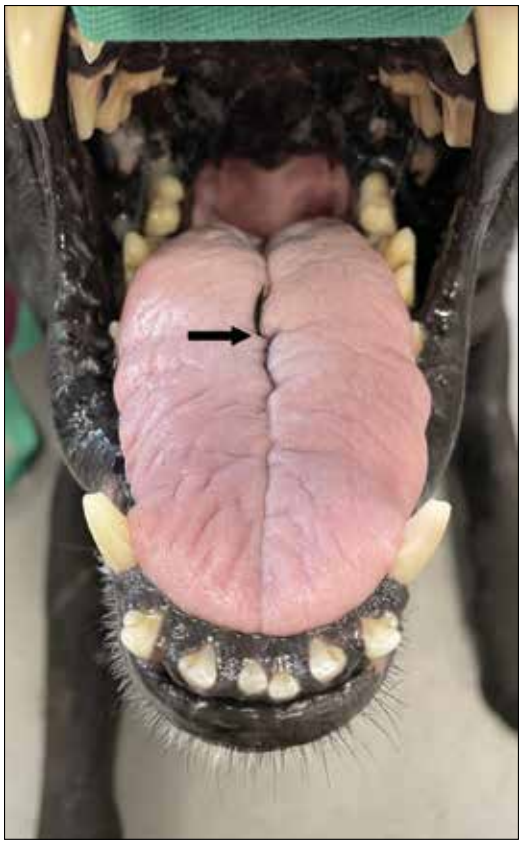


Figure 6. Dorsal aspect of the tongue 5 mo after surgery. Partial recurrence of hair is visible, but without invagination and not along the entire median sulcus (arrow).

may require surgical excision of heterotopic and inflamed lingual tissue. Owners should be informed of the potential for relapse of the heterotopic tissue after surgery, which may require additional surgical intervention if clinical signs recur.

This is apparently the first reported case of pyogranulomatous glossitis caused by heterotopic hairs. Surgical excision completed with a carbon-dioxide laser resulted in total resolution of clinical signs.

Acknowledgment

The authors acknowledge IVC Evidensia for financial support.

CVJ

References

1. Hernandez SZ, Negro V. Surgery of the tongue in the dogs: Diseases and surgical techniques. Canine Pract 1999;24:11–16.
2. Agha-Hosseini F, Etesam F, Rohani B. A boy with oral hair: Case report. Med Oral Patol Oral Cir Bucal 2007;12:E357–E359.
3. Arya A, Babanagare S, Naik C, *et al.* Hair discharging from the frenulum: Unusual presentation of a lingual dermoid cyst. Natl J Maxillofac Surg 2014;5:251.
4. Baughman RA, Heidrich PD. The oral hair: An extremely rare phenomenon. Oral Surg Oral Med Oral Pathol 1980;49:530–531.
5. Femiano F, Rullo R, Serpico R, *et al.* An unusual case of oral hirsutism in a patient with polycystic ovarian syndrome. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;108:e13–e16.
6. Fetkowska-Mielnik K, Piatkowska A, Mielnik-Bjaszczak M. Rare case of numerous oral hairs in a 13-year-old boy with alopecia areata. Oral Surg Oral Med Oral Pathol 1986;62:267–269.
7. Miles AEW. A hair follicle in human cheek mucosa. Proc Royal Soc Med 1960;53:527–528.
8. Rochefort J, Guedj A, Lescaille G, *et al.* A hair on the tongue. J Stomatol Oral Maxillofac Surg 2016;117:357–358.
9. Zhurakivska K, Toni G, Laino G, *et al.* An unusual case of recurrent gingival hirsutism. Oral Surg Oral Med Oral Pathol Oral Radiol 2020;129:e200–e203.
10. Seifert G, Doerr W, Uehlinger E. Mundhöhle, mundspeicheldrüse, tonsillen und rachen. Spezielle Pathologische Anatomie. Berlin, Germany: Springer, 1966:23–25.
11. Lee SH, Go DM, Woo SH, *et al.* Cartilaginous choristoma of the lip in a dog. J Vet Med Sci 2017;79:68–70.
12. McGavin MD, Zachary JF. Chapter 7: Alimentary system. Pathologic Basis of Veterinary Disease. Vol 4. Maryland Heights, Missouri: Mosby, 2006:317.
13. Swanson EA. Hair follicles in the canine tongue. Oral Surg Oral Med Oral Pathol 1981;51:277–280.
14. Teifke JP, Löhr CV. Heterotopic hairs in the tongue of two dogs. J Comp Path 1997;117:267–270.
15. Reifinger M. Implantation von haareh in die zunge von hunden nach schnittverletzung. Berliner und Miinchener 77erarztliche Wochenschrift 1994;107:35.
16. Vetter VK, Correa-Perez ME, Chaloupka K, Mihic-Probst D. Rare choristoma of the tarsal conjunctiva: Critical inspection prevents unnecessary mutilation. Case Rep Ophthalmol 2022;13:599–603.
17. Katsura C, Chuo CB. Unusual ultrasound diagnosis of hair implantation osteomyelitis of the thumb. BMJ Case Rep 2022;15:e250596.
18. Malm C, Serakides R, Silva JF. Diffuse heterotopic hair in a canine uterus: Case report. Arquivo Brasileiro de Medicina Veterinária e Zootecnia 2013;65:1281–1285.
19. Doyon M. Migration of hair into the bone canals and into the liver parenchyma. Archives d'Anatomie Microscopique 1929;25:395–404.
20. Cao W, Li L, Mii S, *et al.* Long-term extensive ectopic hair growth on the spinal cord of mice from transplanted whisker follicles. PLoS One 2015;10:e0133475.
21. Burger MF, Holland P, Napier B. Submental midline dermoid cyst in a 25-year-old man. Ear Nose Throat J 2006;85:752–753.
22. Costanzo G, Minei S, Zini E, *et al.* Radiographic, MRI, and CT findings in a young dog with Becker-like muscular dystrophy. Vet Radiol Ultrasound 2023;64:E19–E22.
23. Sigmund AB, Hecht S, Ward DA, *et al.* Retrobulbar and tongue base pyogranulomatous myositis resulting in strabismus in a dog: Case report. Front Vet Sci 2020;7:360.
24. Jiang ZH, Xv R, Xia L. Foreign body granuloma in the tongue differentiated from tongue cancer: A case report. World J Clin Cases 2022;10:6247–6253.
25. Wortsman X, Carreño L, Ferreira-Wortsman C, *et al.* Ultrasound characteristics of the hair follicles and tracts, sebaceous glands, Montgomery glands, apocrine glands, and arrector pili muscles. J Ultrasound Med 2019;38:1995–2004.
26. Soga S, Koyama T, Mikoshi A, *et al.* Quantitative analysis of the anatomical changes in the scalp and hair follicles in androgenetic alopecia using magnetic resonance imaging. Skin Res Technol 2021;27:56–61.
27. de Campos Fonseca Pinto ACB, Murakami M, Steinbach SML, *et al.* Ultrasonographic diagnosis of a hair foreign body in the urinary bladder of a dog. Vet Radiol Ultrasound 2021;62:e25–e28.
28. Kim HJ, Cho KO, Baek YB. Foreign body reaction to ruptured follicular cysts in dogs. Vet Med Sci 2021;7:1509–1513.
29. Poulet PP, Duffaut D, Barthet P, *et al.* Concentrations and *in vivo* antibacterial activity of spiramycin and metronidazole in patients with periodontitis treated with high-dose metronidazole and the spiramycin/metronidazole combination. J Antimicrob Chemother 2005;55:347–351.
30. Dunié-Mérigot A, Bouvy B, Poncet C. Comparative use of CO_2 laser, diode laser and monopolar electrocautery for resection of the soft palate in dogs with brachycephalic airway obstructive syndrome. Vet Rec 2010;167:700–704.
31. Karaman M, Gün T, Temelkuran B, *et al.* Comparison of fiber delivered CO_2 laser and electrocautery in transoral robot assisted tongue base surgery. Eur Arch Otorhinolaryngol 2017;274:2273–2279.
32. Tsugawa AJ, Verstraete FJM. Chapter 7: Suture materials and biomaterials. In: Verstraete FJM, Lommer MJ, eds. Oral and Maxillofacial Surgery in Dogs and Cats. Philadelphia, Pennsylvania: Saunders Elsevier, 2012:69–78.

Step up to exclusive home and auto insurance

Get **preferred rates** and **stand-out service** when you switch to **The Personal.**

Profitez d'assurances auto et habitation exclusives

Choisissez **La Personnelle** pour obtenir **des tarifs préférentiels** et **un service hors pair.**

thePersonal
Home and Auto Group Insurer
Group rates. Preferred service.

2024 Affinity Partner
CVMA ACMV

laPersonnelle
Assureur de groupe auto et habitation
Tarifs de groupe. Service unique.

Get your quote today.
thepersonal.com/cvma
1-866-860-2862

Obtenez votre soumission
lapersonnelle.com/acmv
1 866 860-2862

Case Report Rapport de cas

Successful interventional occlusion of muscular ventricular septal defect in a dog

Jiyoung Park, Sunyoung Kim, Ji-Heui Sohn, Jong-in Kim, Changbaig Hyun

Abstract — Ventricular septal defect (VSD) is a rare congenital heart disease in dogs. Hemodynamically important interventricular defects must be closed to improve the prognosis. This case report describes successful interventional transcatheter closure of a muscular VSD in a young Maltese and poodle mixed-breed dog with a large muscular interventricular defect (~5 mm in diameter) with a high rate of left-to-right shunt flow. The VSD was closed with a customized Amplatzer-type VSD occluder *via* a percutaneous transvenous (jugular) approach. We concluded that interventional occlusion of a muscular VSD with an Amplatzer-type occluder is a viable treatment option for dogs. A regular follow-up study for this dog is ongoing and has not detected complications.

Key clinical message:
Interventional occlusion of a muscular VSD with an Amplatzer-type occluder is a viable treatment option for dogs.

Résumé — Occlusion interventionnelle réussie d'une communication interventriculaire musculaire chez un chien. La communication interventriculaire (VSD) est une maladie cardiaque congénitale rare chez le chien. Les anomalies interventriculaires hémodynamiquement importantes doivent être fermées pour améliorer le pronostic. Ce rapport de cas décrit la fermeture interventionnelle réussie par cathéter d'un VSD musculaire chez un jeune chien de race mixte (maltais et caniche) présentant un défaut interventriculaire musculaire important (~5 mm de diamètre) avec un débit de shunt élevé de gauche à droite. Le VSD a été fermé avec un obturateur VSD personnalisé de type Amplatzer via une approche trans-veineuse percutanée (jugulaire). Nous avons conclu que l'occlusion interventionnelle d'un VSD musculaire avec un obturateur de type Amplatzer est une option de traitement viable pour les chiens. Une étude de suivi régulière de ce chien est en cours et aucune complication n'a été détectée.

Message clinique clé :
L'occlusion interventionnelle d'un VSD musculaire avec un obturateur de type Amplatzer est une option de traitement viable pour les chiens.

(Traduit par Dr Serge Messier)

Can Vet J 2024;65:221–226

Ventricular septal defect (VSD), which is a hole(s) in the interventricular septum of the heart separating the right and left ventricles, is a congenital heart disease often progressing to congestive heart failure and pulmonary hypertension. Depending on the location and anatomic features of the defect, it is broadly classified as a membranous, muscular, or perimembranous type (1). Although several studies reported VSD as the 4th- to 6th-most common canine congenital heart disease (1–4), the prevalence rate of VSD in dogs is not well-documented, especially for muscular-type VSD, as these are rarer than other types (5–7). Most VSD are predominantly incidental findings and, as isolated, small VSD may not cause obvious clinical signs, even in adulthood (5,7), the actual prevalence rate is likely higher than reported in the literature.

Small defects may not cause a hemodynamically significant shunt or any clinical signs, even if untreated. However, large defects causing a hemodynamically significant shunt should be treated medically and/or surgically before the shunt causes severe pulmonary hypertension (*i.e.,* right-to-left shunt). Ventricular septal defect can be closed surgically or by an intervention. The first successful interventional closure of VSD in humans was reported in 1988 (8,9). Since then, technology for interventional closure of VSD has continued to evolve, with improvements in devices used for closure and techniques used to access the heart (10–18). The first successful interventional closures of VSD in dogs were reported in the 2000s (19–21). Although interventional closure of VSD is now a well-established treatment option for dogs with VSD, a large defect, especially of a muscular type, is still challenging to successfully close. This case report describes a successful closure of a large VSD with a customized Amplatzer-type VSD occluder in a dog.

VIP Animal Medical Center (Chungdam), Seoul, Korea 06068.
Address all correspondence to Changbaig Hyun; email: changbaig@gmail.com

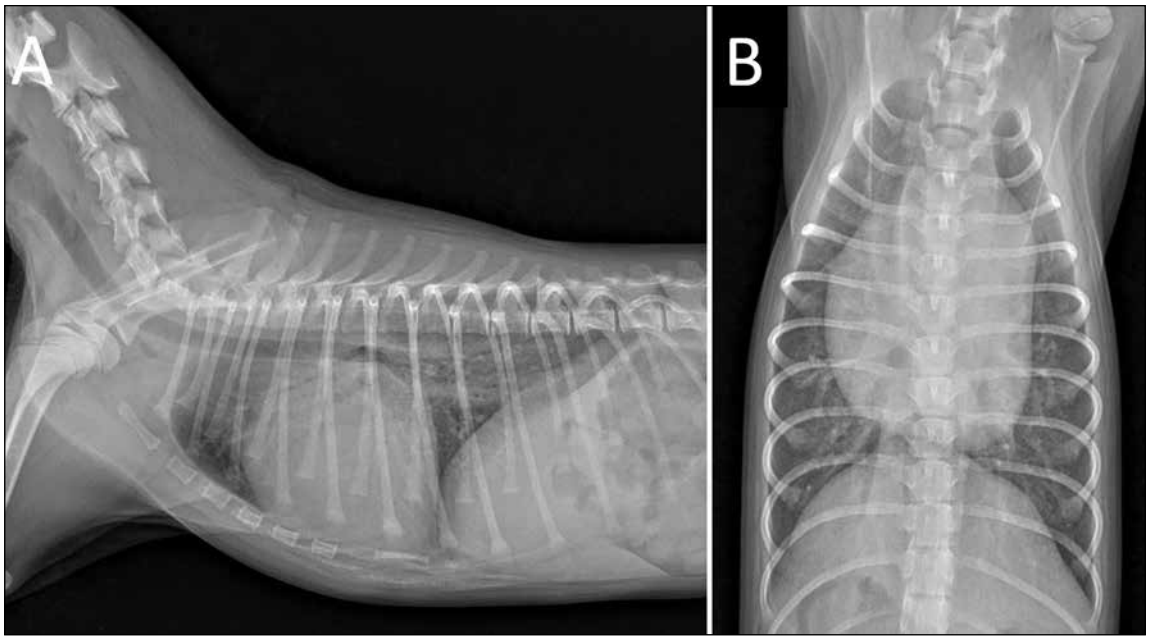


Figure 1. Thoracic radiography at presentation. A – Right lateral projection revealed marked generalized cardiomegaly (vertebral heart scale: 11.6 V, intercostal space: 3.5) and distended caudal vena cava. B – Ventrodorsal projection showed "reverse D"-shaped cardiac silhouette along with prominent dilation of main pulmonary artery, indicating enlargement of right cardiac chamber.

Case description

A 5-month-old male Maltese and poodle mixed-breed dog weighing 2.7 kg was presented for VSD closure. The chief complaint was a nonproductive cough. The dog was being given cardiac medications including sildenafil (Viagra; Pfizer, Seoul, Korea), 2 mg/kg, PO, q8h and pimobendan (Vetmedin; Boehringer Ingelheim, Ingelheim, Germany), 0.3 mg/kg, PO, q12h, in addition to drugs for a lower respiratory tract infection. On physical examination, a mild precordial thrill and a grade V/VI systolic murmur on the right heart base were present. Jugular vein distension was noted during blood collection but the hepatojugular reflex was negative. The remainder of the physical examination was unremarkable, including a normal systolic blood pressure of 126 mmHg. Red blood cell concentration was within the normal range (5.79 M/μL, reference range: 5.65 to 8.87 M/μL) and a remarkable increase in nucleated RBCs was not detected on the blood smear, indicating that the dog was not suffering from severe hypoxemia. There were no remarkable findings from the laboratory examinations.

The electrocardiogram indicated sinus tachycardia (180 to 200 beats per min) with deep S-wave, suggesting right ventricular enlargement. There was no heart block during the ECG. Thoracic radiographs revealed generalized cardiomegaly (vertebral heart scale: 11.6 V, intercostal space: 3.5; Figure 1 A). The caudal vena cava (CVC) was distended [CVC to T7 vertebral length (VL) ratio: 1.8]. In addition to enlargement of the right cardiac silhouette, the main pulmonary artery (MPA) and pulmonary vessels were dilated and over-circulated (Figure 1 B). However, there was no pulmonary edema. On abdominal radiographs, there was no evidence of ascites despite mild hepatomegaly.

On echocardiography, right ventricular enlargement with interventricular septal flattening was observed (Figure 2 A), but there were no detectable anatomical abnormalities on cardiac valves, including the tricuspid valve. The left ventricular internal dimension at diastole (LVIDd) to right ventricular internal dimension at diastole (RVIDd) ratio was < 1, whereas the MPA to aorta (AO) ratio and the right pulmonary artery (RPA) to AO ratio were 1.41 and 0.72, respectively, indicating significant pulmonary hypertension (LVIDd/RVIDd < 1, MPA/AO > 1.1, and RPA/AO > 0.6 are suggestive of pulmonary hypertension; Figure 2 B). The pulmonary regurgitation peak velocity was measured as 4.3 m/s, suggesting that the systolic pressure of the pulmonary artery was > 74 mmHg (Figure 2 C). A large muscular interventricular defect (~5 mm in diameter) with a large volume of left-to-right shunt flow was visualized. The calculated pulmonary blood flow (Qp) to systemic blood flow (Qs) ratio was 2.75, suggesting that the interventricular defect was hemodynamically important (Figure 2 D). No additional congenital heart diseases (*i.e.,* patent ductus arteriosus, atrial septal defects) were observed.

The presence of cardiac remodeling and shunt flow ratio (Qp/Qs) indicated that the muscular VSD was hemodynamically significant and required repair to improve the prognosis. Therefore, transcatheter VSD occlusion was chosen and was performed in this dog 5 wk after the first visit. The diameter of the defect, the thickness of the interventricular septal wall, and the distance to the valves or *chordae tendineae* were taken into consideration when choosing the size and type of occlusion device. To cover this defect well, the occlusion device was customized by a commercial company (S&G Biotech, Seoul, Korea) based on the echocardiographic measurement (waist length: 5 mm, waist diameter: 6 mm, and disc diameter: 10 mm; Figure 3).

The body weight of the dog had increased to 3.7 kg. For the transcatheter VSD occlusion, the dog was premedicated with

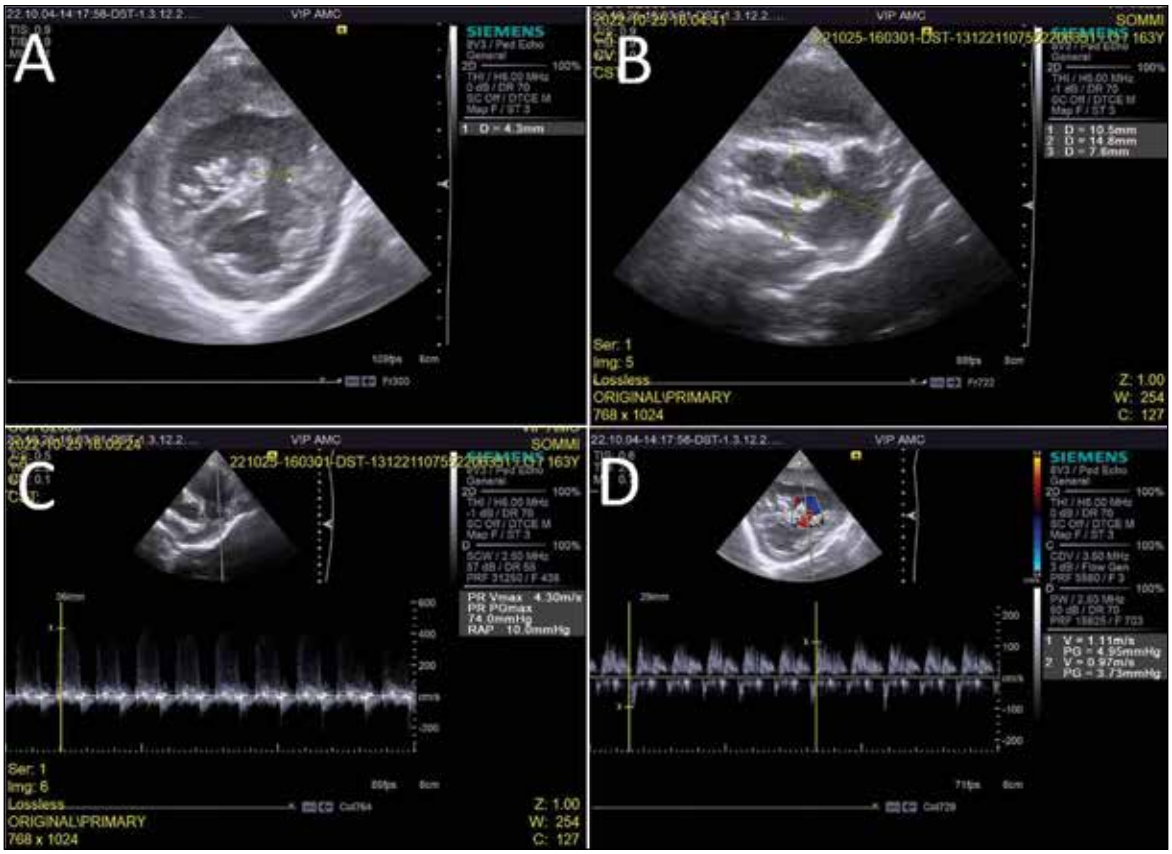


Figure 2. Echocardiography at presentation. A – Two-dimensional image of right parasternal short axis view at papillary muscle level. A large muscular interventricular defect (measuring ~5 mm in diameter) was clearly visualized. B – Two-dimensional image of right parasternal short axis view at pulmonary artery level. Note the marked dilation of main and right pulmonary arteries, indicating pulmonary hypertension. The main pulmonary artery to aorta ratio was 1.41, whereas the aorta to right pulmonary artery ratio was 0.72. C – Pulse Doppler interrogation of the pulmonary artery. The peak velocity of pulmonary regurgitation was 4.3 m/s (pressure gradient: 74 mmHg), indicating severe pulmonary hypertension. D – Continuous Doppler interrogation at the interventricular defect detected a marked left-to-right shunt at systole but minimal right-to-left shunt at diastole. The calculated pulmonary blood flow (Qp) to systemic blood flow (Qs) ratio was 2.75, indicating left-to-right shunt direction.

butorphanol (0.2 mg/kg, IV) and midazolam (0.2 mg/kg, IV). Anesthesia was induced with alfaxalone (2 mg/kg, IV) and maintained with 1 to 5% sevoflurane in oxygen. In addition, a preventive antibiotic (cefazolin; 30 mg/kg, IV) was administered before the intervention. The dog was positioned in left lateral recumbency to expose a right jugular vein.

A 5 Fr introducer-dilator set (Flexor Check-Flo Introducer Set; Cook Medical, Bloomington, Indiana, USA) was placed in the right jugular vein. Then, a guide wire (Roadrunner UniGlide Hydrophilic Wire Guide, 0.035″ × 150 cm; Cook Medical) was advanced through it. The angiocatheter (Renal Access Cobra Catheter, 5 Fr × 90 cm; Cook Medical) was then located at the VSD through the guide wire. After confirming the location of the angiocatheter across the VSD hole, the delivery catheter (Flexor Tuohy-Borst Side-Arm Introducer, 5 Fr × 0.038″ × 90 cm; Cook Medical) replaced the angiocatheter. A self-expandable VSD occluder (customized Amplatzer-type VSD occluder; S&G Biotech, Seoul, Korea) was then inserted into the delivery catheter until the first disc was exposed fully. Then, the occluder was

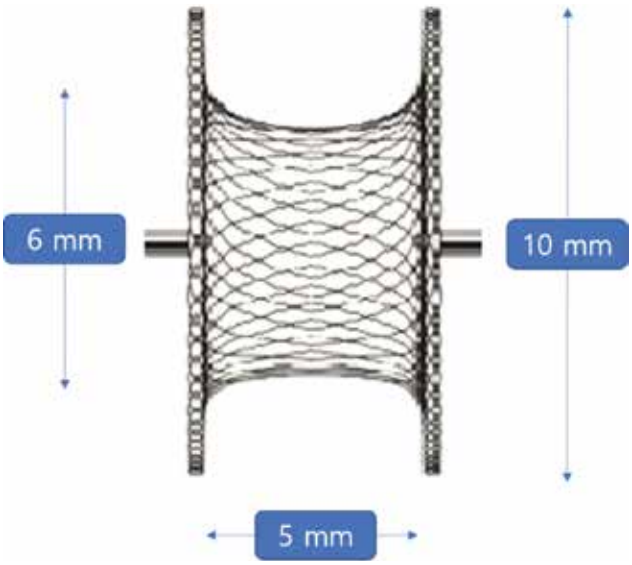


Figure 3. Schematic diagram of the occluder used in this dog.

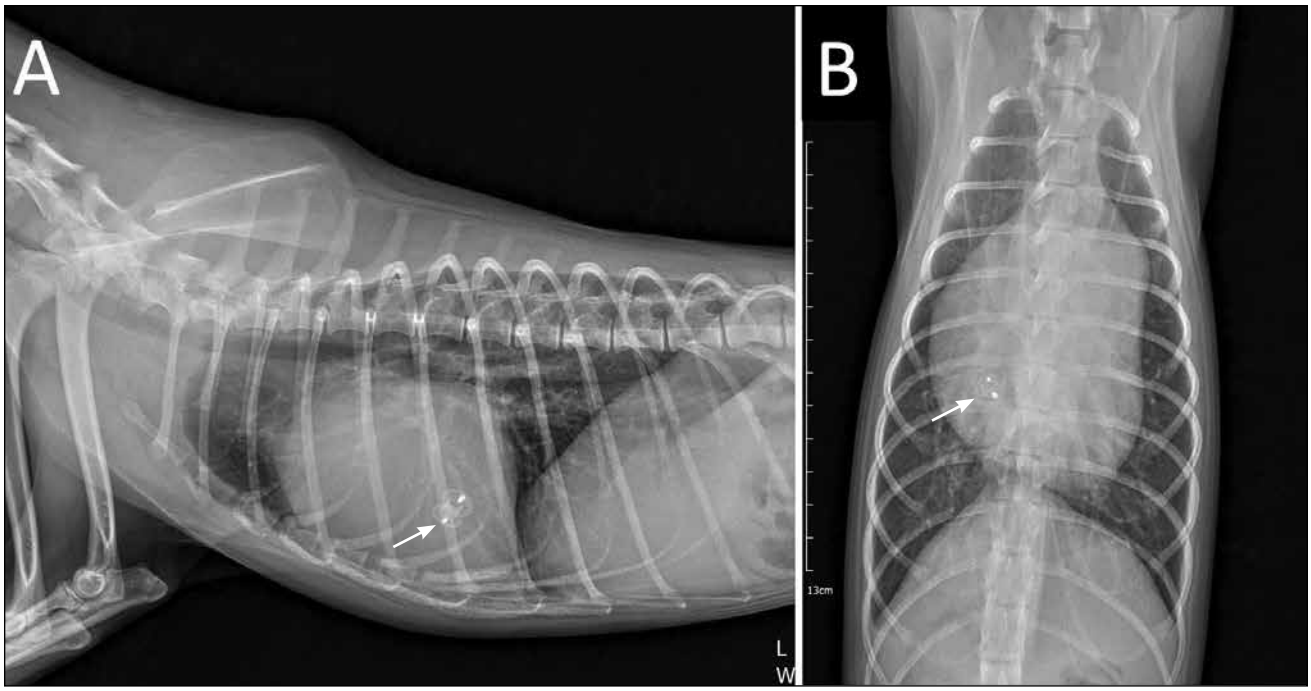


Figure 4. Thoracic radiography at 1 mo after intervention. Right lateral (A) and ventrodorsal (B) projections indicated the occluder (arrow) remained in place and in shape.

pulled back to stick to the left-sided interventricular septal wall. After confirming the first disc was not moving, the second disc was exposed by gently pulling back the delivery catheter. After confirming that the occluder was positioned appropriately, it was detached from the delivery wire by rotating it counterclockwise.

The dog recovered uneventfully. Post-procedural thoracic radiography confirmed that the device was positioned properly (Figure 4). After the procedure, heart size was not dramatically reduced, although the CVC/VL ratio was reduced from 1.8 to 1.4 (Figure 4). The dog was discharged with oral antimicrobial medication (cephalexin; 30 mg/kg, PO, q12h) and a pulmonary vasodilator (sildenafil; 1 mg/kg, PO, q12h). The dog was in good condition 1 mo after the procedure, with considerably improved activity, and the device remained in place despite mild residual shunt flow.

The LVIDd to RVIDd ratio was 2.1, whereas the AO/MPA ratio and AO/RPA ratios were 0.81 and 0.6, respectively, indicating a dramatic reduction of pulmonary hypertension. The pulmonary regurgitation peak velocity was measured as 1.84 m/s (pulmonary arterial pressure gradient was reduced from 74 to 13.5 mmHg; Figure 5 A), whereas tricuspid regurgitation peak velocity was measured as trivial. The calculated Qp/Qs ratio was 1.35 (right ventricular outflow tract diameter and velocity time integral were 13.0 mm and 6.7 cm, respectively; left ventricular outflow tract diameter and velocity time integral were 12.0 mm and 5.8 cm, respectively), indicating successful reduction of left-to-right shunt flow. The occluder was placed at the defect and successfully closed the shunt flow, although there was minimal residual flow at the occlusion site (Figure 5 B, C).

There were no detectable short-term complications associated with transcatheter occlusion (*e.g.,* aortic thromboembolism). Follow-up studies (at 1, 2, 4, and 6 mo after the procedure) confirmed that the device was well-maintained and the clinical condition had gradually normalized after a successful VSD closure. The dog was medicated with a pulmonary vasodilator (sildenafil; 0.5 mg/kg, PO, q12h) for 3 mo after surgery.

Approximately 9 mo after the procedure, the dog was returned to this clinic due to foreign body ingestion. At that time, there was no detectible murmur and were no clinical signs related to heart disease. The owner also confirmed the absence of clinical signs. Thoracic radiographs revealed the device was in the same position without changes in its morphology. However, the owner declined additional echocardiographic evaluation.

Discussion

Since left ventricular pressure is typically higher than right ventricular pressure, the shunt direction in most VSD is left to right. However, as right ventricular diastolic pressure increases over left ventricular diastolic pressure with time, the shunt may be reversed and cause severe pulmonary hypertension and secondary polycythemia (5). However, 1 human study reported that 40% of the VSD closed spontaneously and an additional 25 to 30% of defects became small enough to not cause a hemodynamically significant shunt (17). Therefore, not all VSD need to be closed.

Most isolated VSD in dogs and cats are associated with a good long-term prognosis and may not affect either quality or duration of life (5). An important criterion for surgical or interventional closure of VSD is Qp/Qs (pulmonary to systemic flow ratio) > 2.5. The Qp/Qs ratio is an index reflecting the direction and magnitude of shunt flow (22–24). A Qp/Qs < 1.0 indicates a right-to-left shunt, whereas Qp/Qs > 1.0 indicates a left-to-right shunt. In this case, the Qp/Qs at the first presentation was 2.75, along with evidence of severe

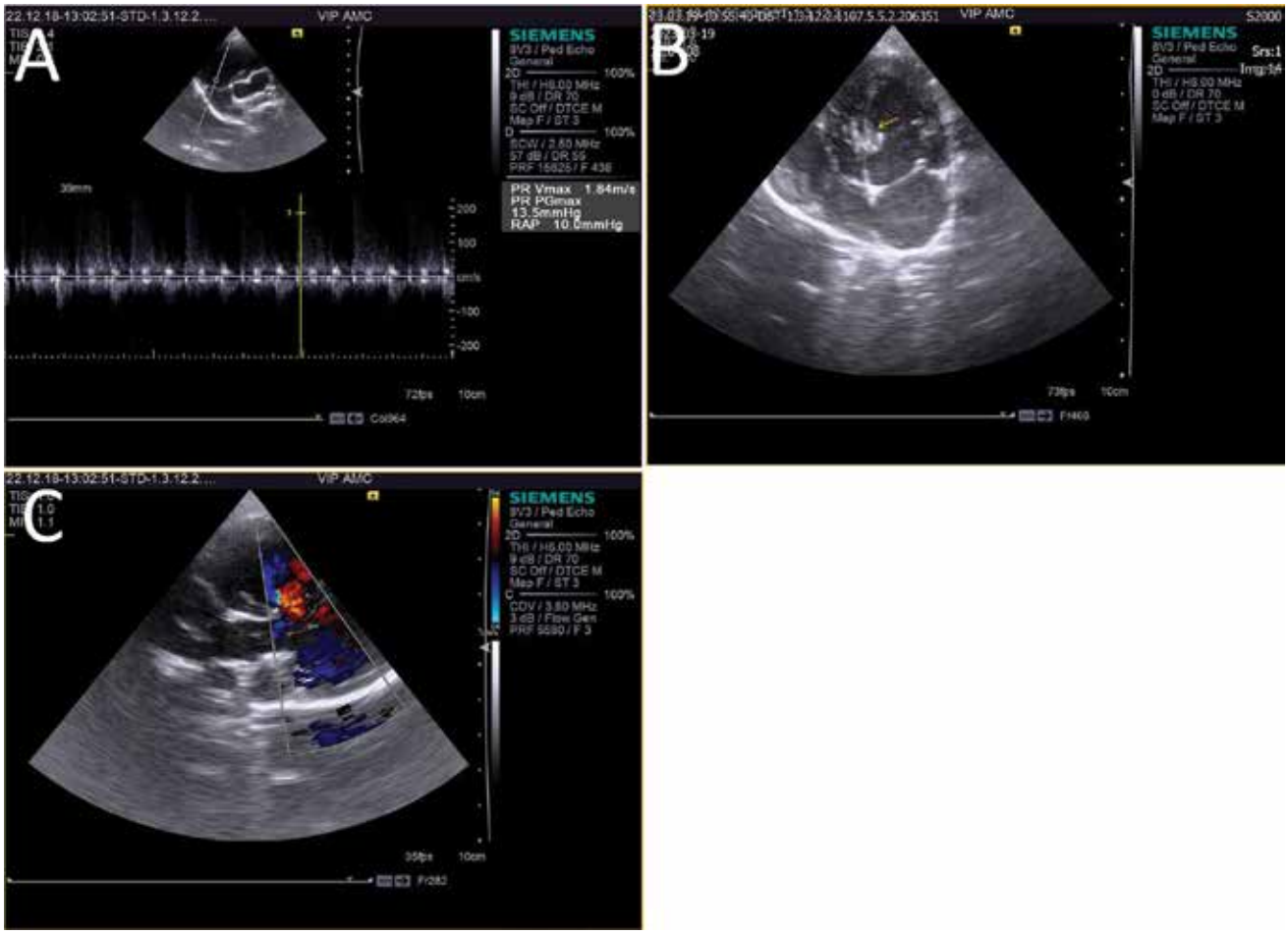


Figure 5. Echocardiography at 1 mo after intervention. A – Severity of pulmonary hypertension was remarkably reduced (pulmonary arterial pressure gradient was reduced from 74 to 13.5 mmHg). B and C – The occluder (arrow) was placed at the defect and successfully closed the shunt flow, with minimal residual flow at the occlusion site.

pulmonary hypertension, indicating the requirement for either surgical or interventional closure of VSD to improve the prognosis. Surgical (open-heart) closure of muscular VSD is a limited therapeutic option in dogs because it requires cardiopulmonary bypass and has a high risk of peri- and post-period complications associated with surgery (25–27). Therefore, transcatheter occlusion of the muscular VSD was a more attractive option for this dog, although this procedure has rarely been done in dogs.

Only 2 case reports have described successful transcatheter occlusion of muscular VSD in dogs (6,28). Those 2 studies used Amplatzer muscular VSD occluders (Amplatzer Muscular VSD Occluder; Abbott Medical, Abbott Park, Illinois, USA) designed for human patients. Applying the ready-made occlusion devices from Abbott was problematic because the desired diameter of occluder for this case (matched to the diameter of the defect and thickness of surrounded septum) was not available. Moreover, the diameter of the delivery system was too large to use in this dog since it requires a 6 to 9 Fr vascular sheath. Therefore, we decided to order a customized occluder from a commercial company (S&G Biotech, Seoul, Korea).

The occluder was designed with dimensions of 6 mm (waist diameter), 5 mm (waist length), and 10 mm (disc diameter), based on echocardiographic measurements at systole and diastole. Furthermore, the device was designed to be accommodated in a 5 Fr delivery system. Since the maximal diameter of the defect at diastole in this case was ~5 mm, the diameter of the disc was designed as 10 mm, to cover the defect more completely. In addition, the length of the waist was designed as 5 mm, to optimally occlude the defect, since the septal thickness around the defect was 5.8 mm at systole.

Suboptimal occlusion with persistent residual shunt around the occluder has been reported in a dog with a ready-made Amplatzer muscular VSD occluder (28). For ready-made occluders, the shortest waist length was 7 mm, making it too loose to fit and possibly resulting in suboptimal occlusion even though the diameter of the disc covered the defect. To prevent suboptimal occlusion in this case, the waist length was designed 0.8 mm smaller than the actual septal thickness around the VSD. With this design, residual shunt activity was minimal at 1 mo after intervention.

The interval from design to delivery of the occluder was only 2 wk, which was relatively shorter than the interval when purchasing an off-the-shelf occluder from the local distributor (usually takes 2 to 4 wk to import). However, delivery may take longer if the occluder must be imported, and this could be a limitation. In this case, the clinical condition and severity of

pulmonary hypertension were dramatically improved after the intervention, although normalization of cardiac remodeling took longer.

No short- or long-term complications associated with transcatheter occlusion of VSD have been detected to date in this dog (the last full examination was 6 mo after the procedure). Furthermore, no procedure- or device-related complications were observed. Complications (*i.e.,* hemolysis, conduction disorders, and valve dysfunction) have been associated with transcatheter occlusion of VSD in humans (8–10). According to the human literature, the most important risk with device closure of membranous VSD is complete heart block (14,15), which was also reported in dogs during and after the procedure (29). In the present case, noticeable heart blocks were not observed during or after the procedure, although catheter-triggered premature ventricular contractions were often noticed during the procedure.

The second-most important risks with device occlusion are device-related valvular dysfunction (especially mitral and tricuspid valves) and hemolysis (15–18). These complications were observed in an experimental canine study (29). The complications described above might be closely related to the type of VSD and occlusion devices, because membranous VSD have higher risks of complications in human studies. In this case, the absence of procedure- or device-related complications was attributed to the device being very well-fitted to the VSD and the fact that the VSD was muscular (located at the lower part of the interventricular septum).

In conclusion, this report described a minimally invasive interventional occlusion of a muscular VSD with a customized Amplatzer-type occluder in a dog. The VSD was almost completely closed with this customized occluder, which was designed based on echocardiographic measurements. This was apparently the first case of successful occlusion of a muscular VSD with a customized occluder in a dog.

Acknowledgment

The authors greatly appreciated the generous donation of the VSD occluder from S&G Biotech. CVJ

References

1. Tidholm A. Retrospective study of congenital heart defects in 151 dogs. J Small Anim Pract 1997;38:94–98.
2. Buchanan J. Prevalence of cardiovascular disorders. In: Fox PR, Sisson DD, Moise NS, eds. Textbook of Canine and Feline Cardiology: Principles and Clinical Practice. 2nd ed. Philadelphia, Pennsylvania: WB Saunders, 1999.
3. Hunt G, Church D, Malik R, Bellenger C. A retrospective analysis of congenital cardiac anomalies (1977–1989). Aust Vet Pract 1990;20: 70–75.
4. Mulvihill JJ, Priester WA. Congenital heart disease in dogs: Epidemiologic similarities to man. Teratology 1973;7:73–77.
5. Bomassi E, Misbach C, Tissier R, *et al.* Signalment, clinical features, echocardiographic findings, and outcome of dogs and cats with ventricular septal defects: 109 cases (1992–2013). J Am Vet Med Assoc 2015; 247:166–175.
6. Margiocco ML, Bulmer BJ, Sisson DD. Percutaneous occlusion of a muscular ventricular septal defect with an Amplatzer muscular VSD occluder. J Vet Cardiol 2008;10:61–66.
7. Kittleson MD, Kienle RD. Small Animal Cardiovascular Medicine. 1st ed. St. Louis, Missouri: Mosby, 1998.
8. Lock J, Block P, McKay R, Baim D, Keane J. Transcatheter closure of ventricular septal defects. Circulation 1988;78:361–368.
9. Landymore R, Marble A, Cameron C. Transvenous closure of acquired ventricular septal defects. Can J Cardiol 1988;4:277–280.
10. Latiff HA, Alwi M, Kandhavel G, Samion H, Zambahari R. Transcatheter closure of multiple muscular ventricular septal defects using Gianturco coils. Ann Thorac Surg 1999;68:1400–1401.
11. Tofeig M, Patel R, Walsh K. Transcatheter closure of a mid-muscular ventricular septal defect with an Amplatzer VSD occluder device. Heart 1999;81:438–440.
12. Carminati M, Butera G, Chessa M, *et al.* Transcatheter closure of congenital ventricular septal defect with Amplatzer septal occluders. Am J Cardiol 2005;96:52L–58L.
13. Michel-Behnke I, Le TP, Waldecker B, *et al.* Percutaneous closure of congenital and acquired ventricular septal defects — considerations on selection of the occlusion device. J Interven Cardiol 2005;18:89–99.
14. Fu YC, Bass J, Amin Z, *et al.* Transcatheter closure of perimembranous ventricular septal defects using the new Amplatzer membranous VSD occluder: Results of the U.S. Phase I trial. J Am Coll Cardiol 2006;47: 319–325.
15. Holzer R, de Giovanni J, Walsh KP, *et al.* Transcatheter closure of perimembranous ventricular septal defects using the Amplatzer membranous VSD occluder: Immediate and midterm results of an international registry. Catheter Cardiovasc Interv 2006;68:620–628.
16. Carminati M, Butera G, Chessa M, *et al.* Transcatheter closure of congenital ventricular septal defects: Results of the European Registry. Eur Heart J 2007;28:2361–2368.
17. Rao PS, Harris AD. Recent advances in managing septal defects: Ventricular septal defects and atrioventricular septal defects. F1000Res 2018;7:498.
18. Stout KK, Daniels CJ, Aboulhosn JA, *et al.* 2018 AHA/ACC guideline for the management of adults with congenital heart disease: A report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. J Am Coll Cardiol 2019;73: 1494–1563.
19. Fujii Y, Fukuda T, Machida N, Yamane T, Wakao Y. Transcatheter closure of congenital ventricular septal defects in 3 dogs with a detachable coil. J Vet Intern Med 2004;18:911–914.
20. Shimizu M, Tanaka R, Hirao H, *et al.* Percutaneous transcatheter coil embolization of a ventricular septal defect in a dog. J Am Vet Med Assoc 2005;226:69–72.
21. Bussadori C, Carminati M, Domenech O. Transcatheter closure of a perimembranous ventricular septal defect in a dog. J Vet Intern Med 2007;21:1396–1400.
22. Serres F, Chetboul V, Tissier R, *et al.* Quantification of pulmonary to systemic flow ratio by a Doppler echocardiographic method in the normal dog: Repeatability, reproducibility, and reference ranges. J Vet Cardiol 2009;11:23–29.
23. Monnet E, Orton E, Gaynor J, *et al.* Diagnosis and surgical repair of partial atrioventricular septal defects in two dogs. J Am Vet Med Assoc 1997;211:569–572.
24. Eyster G. Atrial septal defect and ventricular septal defect. Sem Vet Med and Surg Small Anim 1994:9:227–233.
25. Houyel L, Vaksmann G, Fournier A, Davignon A. Ventricular arrhythmias after correction of ventricular septal defects: Importance of surgical approach. J Am Coll Cardiol 1990;16:1224–1228.
26. Hanna B, Colan SD, Bridges ND, Mayer JE, Castaneda A. Clinical and myocardial status after left ventriculotomy for ventricular septal defect closure. J Am Coll Cardiol 1991;17:A110.
27. Serraf A, Lacour-Gayet F, Bruniaux J, *et al.* Surgical management of isolated multiple ventricular septal defects: Logical approach in 130 cases. J Thor Cardiovasc Surg 1992;103:437–443.
28. Durham JA, Scansen BA, Bonagura JD, *et al.* Iatrogenic embolization and transcatheter retrieval of a ventricular septal defect occluder in a dog. J Vet Cardiol 2015;17:304–313.
29. Bu H, Yang Y, Hu S, *et al.* A novel biodegradable occluder for the closure of ventricular septal defects: Immediate and medium-term results in a canine model. Interact Cardiovasc Thorac Surg 2019;29:783–792.

Case Report Rapport de cas

Suspected malnutrition-induced reversible feline skin fragility syndrome in a cat with congenital axial deformities

Yoshihiko Yu, Tadashi Miyamoto, Yui Kimura, Kazuhito Itamoto, Masaki Michishita, Hitoshi Hatakeyama, Tomokazu Nagashima, Rikako Asada, Tomomi Yamaguchi, Daisuke Hasegawa, Yoshihiro Nomura, Leslie A. Lyons, Tomoki Kosho

Abstract — A stray cat, an intact female Japanese domestic shorthair cat of unknown age (suspected to be a young adult), was rescued. The cat was lethargic and thin and had marked skin fragility, delayed wound healing without skin hyperextensibility, and hind limb proprioceptive ataxia and paresis. Survey radiography, computed tomography, and magnetic resonance imaging revealed congenital vertebral anomalies, including thoracolumbar transitional vertebrae, scoliosis resulting from a thoracic lateral wedge-shaped vertebra, and a kinked tail, and a dilated spinal cord central canal. Through nutritional support, the cat's general condition normalized, followed by a gradual and complete improvement of skin features. Whole-genome sequencing was completed; however, no pathogenic genetic variant was identified that could have caused this phenotype, including congenital scoliosis. A skin biopsy obtained 7 y after the rescue revealed no remarkable findings on histopathology or transmission electron microscopy. Based on clinical course and microscopic findings, malnutrition-induced reversible feline skin fragility syndrome (FSFS) was suspected, and nutritional support was considered to have improved the skin condition.

Key clinical message:
This is the second reported case of presumed malnutrition-induced reversible FSFS and was accompanied by long-term follow-up.

Résumé — Syndrome de fragilité cutanée réversible induit par la malnutrition soupçonné chez un chat avec des difformités axiales congénitales. Un chat errant, une femelle intacte de race japonaise à poil court et d'âge inconnu (suspecté être une jeune adulte), a été secourue. La chatte était léthargique et maigre, et avait une fragilité marquée de la peau, un retard dans la guérison de plaies sans hyperextensibilité de la peau, et une ataxie proprioceptive et parésie des membres postérieurs. Des radiographies, un examen par tomodensitométrie, et de l'imagerie par résonnance magnétique ont révélé des anomalies congénitales des vertèbres, incluant des vertèbres transitionnelles thoraco-lombaires, une scoliose résultant d'une vertèbre thoracique en forme de coin, une queue pliée, et un canal central de la moelle épinière dilaté. Grâce à un soutien nutritionnel, la condition générale du chat s'est stabilisée, suivi d'une amélioration graduelle et complète des caractéristiques de la peau. Le séquençage du génome complet a été effectué; toutefois, aucune variation génétique pathogénique n'a été identifiée qui aurait pu causer ce phénotype, incluant la scoliose congénitale. Une biopsie cutanée obtenue 7 j après le sauvetage n'a

Laboratory of Veterinary Radiology (Yu, Asada, Hasegawa), Department of Veterinary Pathology (Michishita, Nagashima), and Laboratory of Comparative Cellular Biology (Hatakeyama), Nippon Veterinary and Life Science University, Musashino, Japan; Miyamoto Animal Hospital, Yamaguchi, Japan (Miyamoto, Kimura); Department of Veterinary Small Animal Clinical Science, Joint Faculty of Veterinary Medicine, Yamaguchi University, Yamaguchi, Japan (Itamoto); Center for Medical Genetics, Shinshu University Hospital, Matsumoto, Japan (Yamaguchi, Kosho); Department of Medical Genetics and Division of Clinical Sequencing, Shinshu University School of Medicine, Matsumoto, Japan (Yamaguchi, Kosho); Scleroprotein and Leather Research Institute, Tokyo University of Agriculture and Technology, Fuchu, Japan (Nomura); Department of Veterinary Medicine and Surgery, College of Veterinary Medicine, University of Missouri, Columbia, Missouri, USA (Lyons); Research Center for Supports to Advanced Science, Shinshu University, Matsumoto, Japan (Kosho).

Yoshihiko Yu's present address is Mitaka, Tokyo, Japan.

Address all correspondence to Dr. Yoshihiko Yu; email: yoshi.yu.vet@gmail.com and Dr. Tomoki Kosho; email: ktomoki@shinshu-u.ac.jp

Unpublished supplementary material (Appendix 1; Tables S1, S2, S3, S4, S5) is available online from: www.canadianveterinarians.net

révélé aucune trouvaille spéciale à l'histopathologie ou par microscopie électronique à transmission. Basé sur le déroulement clinique et l'examen microscopique, le syndrome de fragilité cutanée réversible félin induit par la malnutrition (FSFS) était suspecté, et le soutien nutritionnel a été considéré comme ayant amélioré la condition cutanée.

Message clinique clé :
Ce cas est le deuxième cas rapporté de FSFS induit par la malnutrition soupçonné et a fait l'objet d'un suivi à long terme.

(Traduit par Dr Serge Messier)

Can Vet J 2024;65:227–233

Skin fragility is uncommon in cats (1); the skin may tear extensively and shed due to minimal trauma or handling for veterinary procedures. Differential diagnosis of skin fragility in cats is limited to a few uncommon or rare diseases, including feline skin fragility syndrome (FSFS; also known as acquired skin fragility) and Ehlers-Danlos syndromes (EDS; also known as feline cutaneous asthenia or dermatosparaxis) (1,2). Feline skin fragility syndrome has a multifactorial etiology (1,2). In contrast, EDS is a hereditary connective tissue disorder, and causative genetic variants have been reported in some cats (3,4). In humans, 14 subtypes of EDS have been recognized, and some have clinical signs such as skin fragility, easy bruising, kyphoscoliosis or scoliosis, or craniofacial features, with or without skin hyperextensibility (5).

Only a few cases of FSFS without an underlying disease have been reported (6,7). One FSFS case without concurrent diseases other than malnutrition was reported, with histopathological normalization of the skin after recovery (7).

This report presents a cat with skin fragility and congenital vertebral abnormalities, ultimately diagnosed as suspected acquired and reversible FSFS secondary to malnutrition. Long-term follow-up of the cat demonstrated improved clinical status with unremarkable histopathological and transmission electron microscopic findings.

Case description

A stray cat, an intact female Japanese domestic shorthair cat of unknown age (suspected to be a young adult), was rescued by veterinarians at a local veterinary clinic (Miyamoto Animal Hospital, Yamaguchi, Japan). At the time of rescue, the cat was lethargic and thin (weight: 1.4 kg, body condition score: 1 out of 5). Hematology and plasma chemistry revealed moderate anemia (PCV: 16.9%) and increased aspartate aminotransferase (138 IU/L, reference range: 18 to 51 IU/L). Other laboratory end points, including liver and renal panels and electrolytes, were unremarkable. Serological screening tests for feline leukemia virus antigen and feline immunodeficiency virus antibody were both negative. However, hind limb proprioceptive ataxia and paresis were observed.

Radiographs indicated scoliosis of the thoracic vertebrae and thoracolumbar transitional vertebrae. Although the images had poor contrast of abdominal organs due to limited abdominal fat, no other abnormalities were apparent in thoracic or abdominal areas. While the cat was hospitalized, the skin was vulnerable and easily torn (Figure 1). Skin tears were closed using a medical stapler but sometimes tore again. The cat also had mild ocular hypertelorism (Figure 1). The cat's short, kinked tail was also noted, although this phenotype is occasionally seen in Japanese domestic cats. Hyperextensibility of the skin and joint hypermobility were not observed. Palpation did not induce pain. Since this was a stray cat, pedigree information, history, and exact age were unavailable. The cat was maintained at the local veterinary clinic for ongoing care, including nutritional support.

Two months after the rescue, detailed radiography, computed tomography (CT), and magnetic resonance imaging were conducted under general anesthesia at a referral hospital (Yamaguchi University Animal Medical Center, Yamaguchi, Japan). Radiographs of the thorax, abdomen, skull, neck, thoracic limbs, and pelvic limbs were obtained. The abdominal organs had limited poor contrast due to minimal abdominal fat. Computed tomography imaging of the whole body was obtained with an 8-slice CT scanner (ECLOS 8; Hitachi Medical Corporation, Tokyo, Japan). Radiographs and CT imaging confirmed the 9th thoracic lateral wedge-shaped vertebra, causing scoliosis of the thoracic vertebrae and the thoracolumbar transitional vertebrae. The cat had 12 thoracic and 8 lumbar vertebrae, causing the thoracolumbar transitional vertebrae, whereas normal cats have 13 thoracic and 7 lumbar vertebrae. These abnormalities were well-visualized by CT 3-dimensional volume-rendering reconstruction (Figure 2). The short, kinked tail was also confirmed on radiographs and had abnormal-shaped coccygeal vertebrae that were outside the range of CT (Figure 2). Magnetic resonance imaging of the brain and spinal cord were obtained using a 0.4-T scanner (APERTO Inspire; Hitachi Medical Corporation), with sequences summarized in Appendix 1 (available online from: www.canadianveterinarians.net). No abnormalities were apparent in the brain parenchyma. Magnetic resonance imaging of the thoracic and lumbar spine revealed a longitudinal, T2-hyperintense lesion from T4 to T12 in the gray matter around the central canal of the spinal cord, whereas the longitudinal lesion had T1 iso- or hypointensity, implying a dilation of the central canal of the spinal cord (Figure 2) possibly associated with scoliosis. Hematology and plasma chemistry values were within normal limits.

At this time, the differential diagnosis included EDS or FSFS because skin fragility is a well-known clinical sign of those disorders in cats (2). Most reported FSFS cases occurred concurrent with various diseases present in middle-aged or older cats (2). In contrast, the cat in this case had no underlying disease but presented with vertebral deformity, one of the comorbidities in human EDS (5). Therefore, the possibility of a rare type of EDS was considered, although hyperextensibility of the skin is

Figure 1. Appearance of the cat in this case. The skin was vulnerable and easily torn, as indicated by lesions at the rump (A) and neck (B). C – The cat also had mild ocular hypertelorism.

a clinical feature of EDS in cats (2) that was not observed in this cat. Whole-genome sequencing (WGS) was completed to investigate the genetic variant(s) causing this phenotype in this cat. Histopathology was not available. Once the skin condition resolved, skin fragility was not observed, although caution was exercised during handling.

The WGS and subsequent data analysis were done as described in Appendix 1 (available online from: www.canadianveterinarians.net). Private homozygous and heterozygous genetic variants were filtered compared to data from 414 cats, including 362 cats with WGS and 52 cats with whole-exome sequencing data, for which the cat was privately homozygous; heterozygosity in up to 1 additional cat was permitted (see Tables S1, S2, S3, available online from: www.canadianveterinarians.net). In brief, a search for selected orthologous candidate genes (see Table S4, available online from: www.canadianveterinarians.net) in the data was conducted and included previously known causative genes of EDS, congenital scoliosis, or hereditary connective tissue disorders overlapping phenotype genes, based on literature for humans. A homozygous *COL6A1* genetic variant (XM_011285711.3:c.1678_1680del), predicted to result in 1 amino acid residue deletion (XP_011284013.1:p.Asn560del), was identified uniquely in this cat, although a heterozygous variant was present in 1 other cat in the dataset. Furthermore, a heterozygous *ZNF469* genetic variant (XM_023245050.1:c.4324G>A) was also detected as a unique variant to this case. No unique or (likely) pathogenic genetic variants were identified in any other candidate genes or known genes for the bobtailed or tailless phenotype in the Japanese bobtail *(HES7)* or in the Manx *(T)*, respectively (8,9).

Upon follow-up at 7 y after the cat was rescued, body weight had increased to 3.9 kg, with no apparent progression of clinical signs, such as neurological deficits, although care was exercised to avoid trauma and skin tearing. A skin biopsy of the caudal cervical area was performed under general anesthesia to evaluate the skin, obtain a definitive diagnosis, and obtain skin samples for fibroblast cell culture and transcriptional analysis.

Reverse-transcription polymerase chain reaction and Sanger sequencing were performed, and a homozygous *COL6A1* genetic variant (c.1678_1680del) was confirmed to cause a 3-bp in-frame deletion in the *COL6A1* transcript of the affected cat when compared to a normal cat. It was predicted to delete 1 amino acid residue (p.Asn560del; see Appendix 1 and Table S5, available online from: www.canadianveterinarians.net). Homozygous or compound heterozygous *ZNF469* genetic variants cause brittle cornea syndrome, a subtype of EDS in humans, when homozygous; however, this is clinically characterized by thin and fragile corneas (5,10). Thus, the heterozygous *ZNF469* genetic variant detected in this case was not further analyzed.

Findings from histopathological and transmission electron microscopic analyses, completed as described in Appendix 1 (available online from: www.canadianveterinarians.net), were unremarkable (Figures 3, 4). The biopsy wound-healing process was normal, along with prior evidence of skin fragility without skin hyperextensibility. This suggested a diagnosis of reversible FSFS, likely due to malnutrition before the rescue and similar to a previous single case (7), rather than a subtype of EDS seen in humans (5). Therefore, no further genetic analyses were done.

Discussion

This report describes a feline case characterized mainly by skin fragility, delayed wound healing, and congenital vertebral abnormalities. Although a rare subtype of EDS was initially suspected because of its unique phenotype, including skin fragility and vertebral deformity, the cat's skin condition improved clinically, and histopathology of a skin biopsy sample 7 y after the rescue was normal. In contrast to our case, cats with EDS reportedly have abnormalities in Masson's trichrome staining, with or without hematoxylin and eosin staining (6).

Unlike FSFS, the clinical hallmark of feline EDS is skin hyperextensibility and skin fragility recognized at a younger age (2). An accurate age and histopathology of the affected skin were not available in this case; however, because 7 y had passed, the cat was likely a young adult or juvenile at the time of the skin fragility and delayed wound healing. Epidermolysis bullosa is also a hereditary disease causing skin fragility in humans and animals; however, this disease was not considered likely as a differential diagnosis as skin sloughing is often limited to foot pads and integument lesions are unlikely in cats. Moreover, symptoms do not resolve (11).

There are various underlying causes of FSFS, including naturally occurring or iatrogenic hyperadrenocorticism, infectious diseases, neoplastic disease, non-neoplastic hepatopathies,

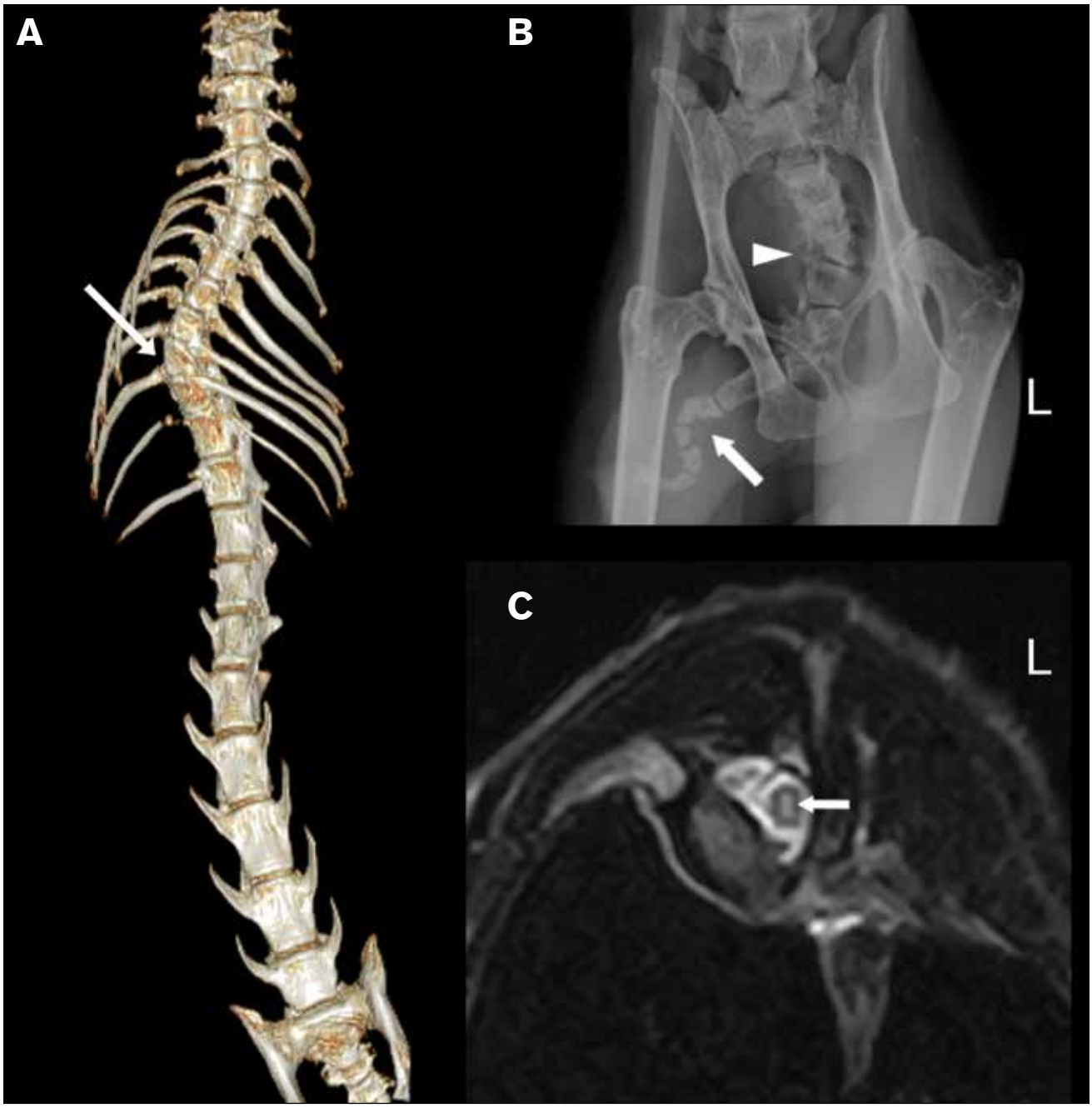


Figure 2. Imaging of the cat in this case. A – Ventral view of CT 3-dimensional volume rendering reconstruction of the thoracic and rostral lumbar spine of the cat. The arrow indicates a lateral wedge-shaped vertebra, causing scoliosis of the thoracic vertebrae. The numbers of thoracic and lumbar vertebrae are 12 and 8, respectively, causing thoracolumbar transitional vertebrae. B – Radiograph of the cat's pelvic region. The arrow indicates a markedly kinked tail area where abnormally shaped coccygeal vertebrae are present. The arrowhead indicates the presence of coccygeal hemivertebrae. C – Transverse T2-weighted magnetic resonance imaging at the level of C8 to C9, where scoliosis exists. A T2-hyperintense lesion is present in the middle of the spinal cord (arrow), suggesting dilation of the central canal of the spinal cord.

hyperprogesteronism, cachexia, and a history of drug administration (1,2). However, only 1 reversible FSFS case has been reported that involved not a progressive disease condition but malnutrition (7). That case had histopathological normalization after 6 mo of recovery.

At the time of rescue, the cat in the current case had moderate anemia, likely due to starvation (12). Increased aspartate aminotransferase may have been caused by muscle wasting or hemolysis, although creatine kinase was not measured to support this possibility.

The body condition score was 1 out of 5 when the cat was rescued, and abdominal radiography had poor contrast of organs due to limited fat. Since a worsening of clinical signs and symptoms was not observed during the 7-year follow-up, and the cat had FSFS without underlying diseases, we suspect the FSFS was caused by malnutrition.

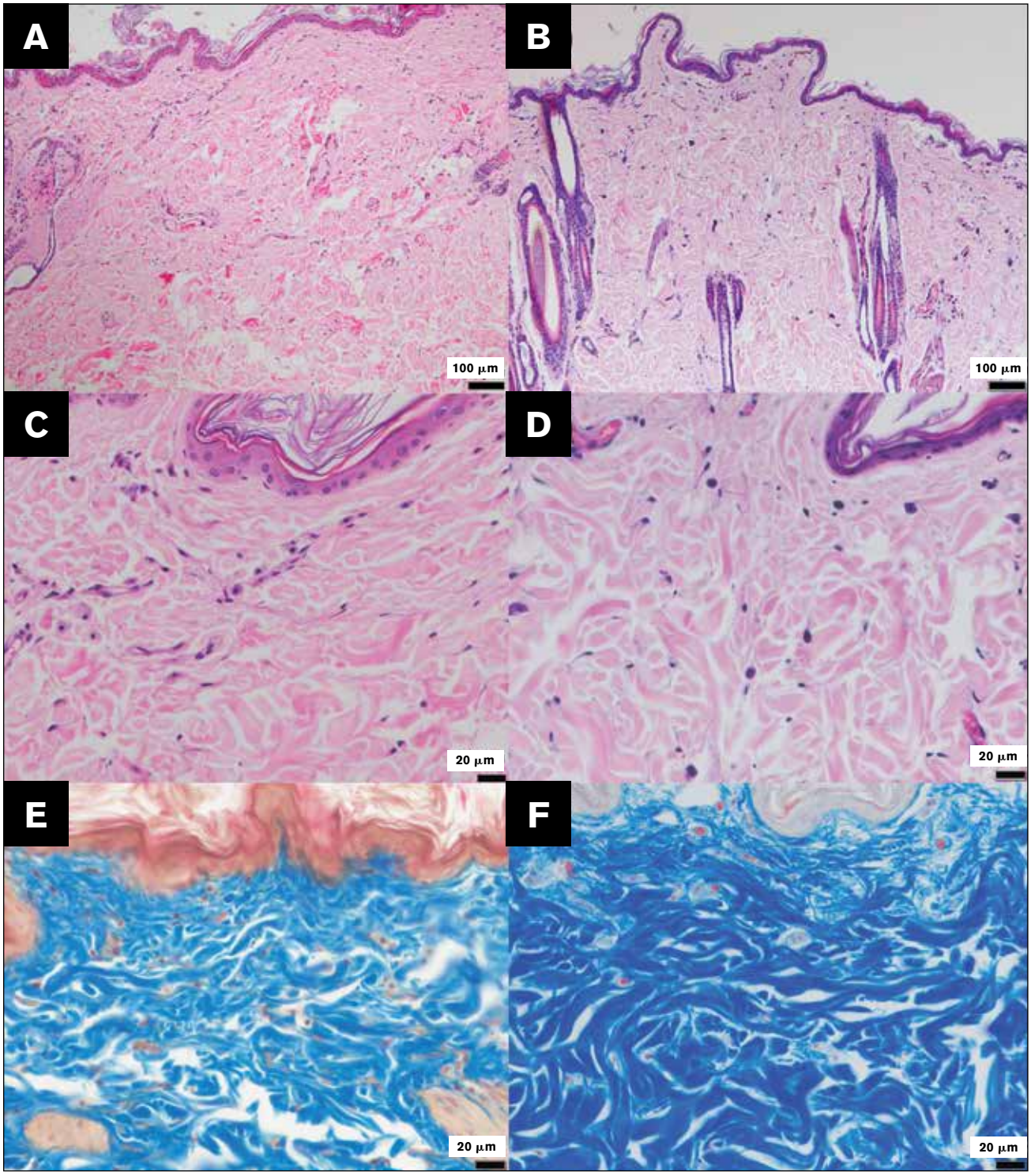


Figure 3. Histologic sections of the affected cat's cervical dorsal skin and those of a normal cat's caudal cervical skin, for comparison. The control cat used for comparative histopathology of the skin was an intact female aged 8 y and 10 mo. A to D – Hematoxylin and eosin-stained sections of skin biopsy samples from the affected cat (A, C) and a control cat (B, D), with magnifications of 100× (A, B) and 400× (C, D), appear unremarkable. E and F – Masson's trichrome staining of skin sections from the affected cat and a control cat, respectively (magnification: 400×). No abnormalities were apparent in histologic sections from the affected cat compared to those from a control cat. In panel E, note that the presence of larger space within the dermis is an artifact.

Interestingly, protein deficiency was suggested to affect synthesis and degradation of Types-I and -III collagen in rats (13). Although histopathology was not available when the skin fragility was present in our case, histopathology of the only previous case reported as suspected malnutrition-induced FSFS showed an atrophic dermis and the Masson's trichrome abnormality (7). Furthermore, a low-protein diet was reported to induce thinning of the skin epidermis, decrease cell proliferative activity

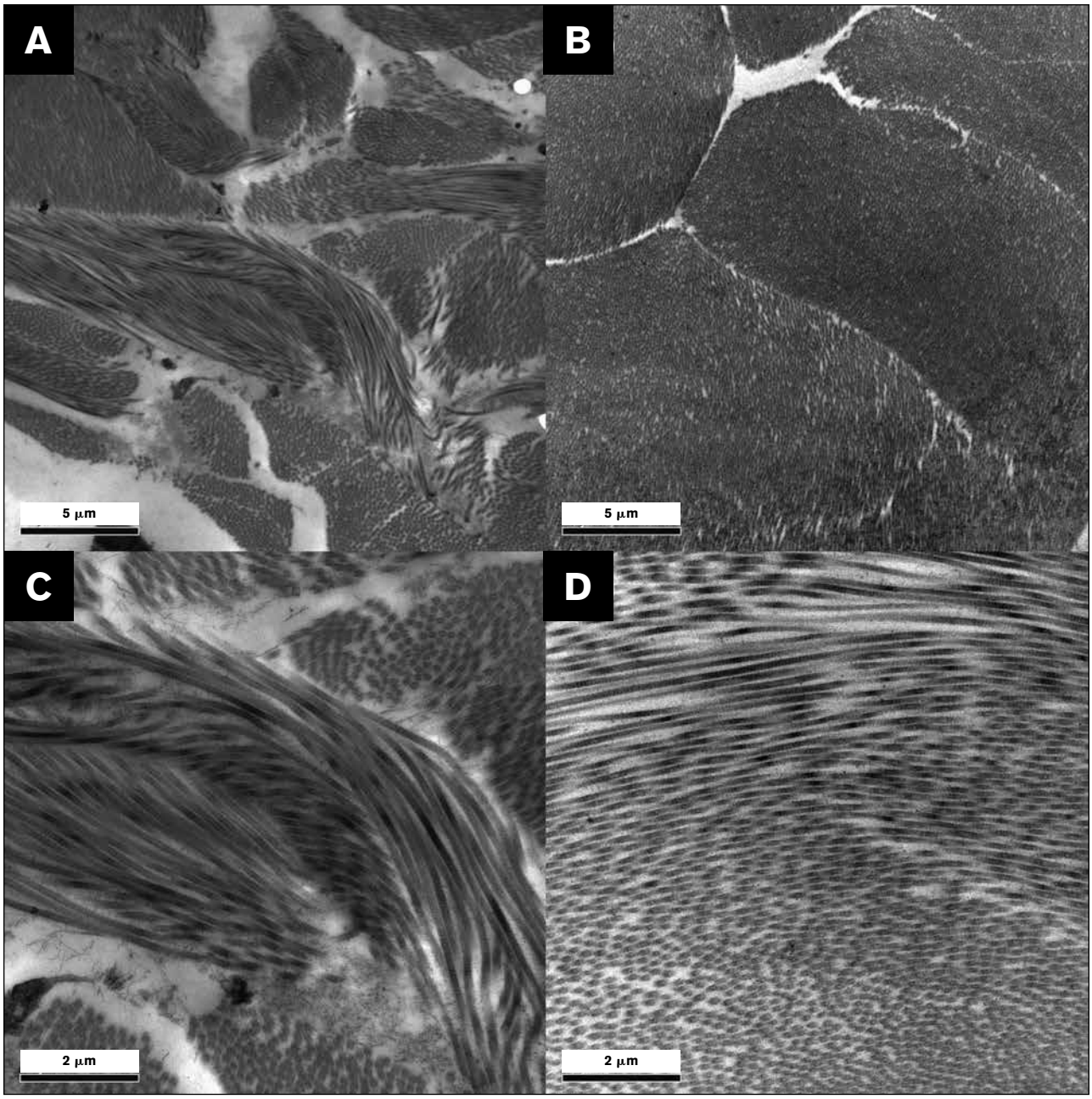


Figure 4. Transmission electron micrographs of the affected cat's cervical dorsal skin (A, C) and those of a normal cat's caudal cervical skin (B, D), for comparison. The control cat used for comparative transmission electron micrographs of the skin was an intact female aged 8 y and 10 mo. Magnifications are 6000× (A, B) and 15 000× (C, D). Collagen fibrils are well-organized and have uniform diameters and circular profiles in both the affected cat and a control cat. No abnormalities were apparent in transmission electron micrographs from the affected cat compared to those from a control cat.

in epidermal cells, and decrease stratum corneum hydration in mice (14). Although epidermal atrophy was not mentioned in the only case report to-date on suspected malnutrition-induced FSFS (7), epidermal atrophy is another histological sign in FSFS (15,16). Lack of protein intake might also contribute to malnutrition-induced FSFS.

The cat in this case had congenital vertebral abnormalities, and magnetic resonance imaging revealed dilation of the central canal of the spinal cord (Figure 2). Although it remains inconclusive whether this was secondary to scoliosis or congenital and independent of scoliosis, syringomyelia is the second-most common anomaly in human patients with congenital scoliosis (17). Hind limb proprioceptive ataxia and paresis was likely caused by scoliosis and a dilated spinal cord central canal.

An *HES7* genetic variant (c.5A>G; p.Val2Ala) reportedly causes a kinked-tail phenotype in Japanese bobtail cats (8). Japanese bobtail cats are also known to have variations in the normal feline vertebral formula (including transitional vertebra and abnormal vertebral formula), similar to the cat in our case (18). However, the *HES7* genetic variant was not detected in this case, even though the cat was a Japanese domestic cat, suggesting that other factors were involved in the phenotype.

Unique genetic variants in protein-coding regions detected by WGS included homozygous *COL6A1* genetic variant (c.1678_1680del; p.Asn560del), although 1 heterozygous variant was detected in 1 of 414 cats. Interestingly, a human patient with severe scoliosis and congenital vertebral deformity alone was reportedly diagnosed histopathologically with collagen VI-related myopathy, which had a heterozygous missense *COLA6A2* genetic variant and 2 splicing variants in *COL6A1* and *COL6A2* (19). Both *COL6A1* and *COL6A2* encode a collagen alpha-1 (VI) chain and collagen alpha-2 (VI) chain, respectively, which partially composes collagen VI. Although the presence of the *COL6A1* genetic variant might have been involved in the congenital vertebral deformity in our case, including scoliosis, the *COL6A1* genetic variant currently has uncertain significance.

This report has some limitations. First, histopathological and transmission electron microscopic analyses for the skin biopsy sample were conducted 7 y after the rescue, when the cat appeared healthy. Although those analyses were not available when skin fragility was observed, skin fragility without skin hyperextensibility supported the FSFS diagnosis. Second, the cat was originally a stray, and medical information was available only after the rescue. Therefore, the possibility that some factors causing skin fragility were present cannot be completely excluded. In addition, the circumstances that led to the cat's malnutrition are unknown, and the possibility that an underlying disease may have existed when it was rescued cannot be excluded. Finally, genetic variants present in regions other than the candidate genes we targeted may have influenced the phenotype of this case. This shortcoming also reflects the fact that this was a single case. Structural variants were also not evaluated. Nevertheless, the cat had skin fragility and delayed wound healing when rescued, and a favorable long-term outcome for 7 y was achieved through nutritional support, including a clinically and histopathologically normal skin condition.

In this report, we described a cat with FSFS presumably caused by malnutrition (only the second reported case supporting this connection) and accumulated evidence for 1 aspect of the etiology of FSFS. Further, a favorable long-term outcome with improved clinical status was achieved.

Acknowledgments

This study was partially supported by the MU Gilbreath McLorn Endowment for Comparative Medicine and EveryCat Health Foundation (formerly the Winn Feline Foundation) (L.A.L.). The authors thank the 99 Lives Cat Genome Consortium (felinegenetics.missouri.edu) for sharing domestic cat variant frequency information; its members are listed in Appendix 1 (available online from: www.canadianveterinarians.net). CVJ

References

1. Englar RE. Skin Fragility. In: Englar RE, ed. Common Clinical Presentations in Dogs and Cats. Hoboken, New Jersey: John Wiley & Sons, 2019:125–133.
2. Gross TL, Ihrke PJ, Walder EJ, Affolter VK, eds. Degenerative, Dysplastic and Depositional Diseases of Dermal Connective Tissue. In: Skin Diseases of the Dog and Cat. Oxford, UK: Blackwell Science, 2005:373–403.
3. Spycher M, Bauer A, Jagannathan V, Frizzi M, De Lucia M, Leeb T. A frameshift variant in the *COL5A1* gene in a cat with Ehlers-Danlos syndrome. Anim Genet 2018;9:641–644.
4. Kiener S, Apostolopoulos N, Schissler J, *et al.* Independent *COL5A1* variants in cats with Ehlers-Danlos syndrome. Genes 2022;13:797.
5. Malfait F, Castori M, Francomano CA, Giunta C, Kosho T, Byers PH. The Ehlers–Danlos syndromes. Nat Rev Dis Primer 2020;6:64.
6. Fernandez CJ, Scott DW, Erb HN, Minor RR. Staining abnormalities of dermal collagen in cats with cutaneous asthenia or acquired skin fragility as demonstrated with Masson's trichrome stain. Vet Dermatol 1998;9:49–54.
7. Furiani N, Porcellato I, Brachelente C. Reversible and cachexia-associated feline skin fragility syndrome in three cats. Vet Dermatol 2017;28:508–e121.
8. Lyons LA, Creighton EK, Alhaddad H, *et al.* Whole genome sequencing in cats, identifies new models for blindness in *AIPL1* and somite segmentation in *HES7*. BMC Genomics 2016;17:265.
9. Buckingham KJ, McMillin MJ, Brassil MM, *et al.* Multiple mutant *T* alleles cause haploinsufficiency of brachyury and short tails in Manx cats. Mamm Genome 2013;24:400–408.
10. Rohrbach M, Spencer HL, Porter LF, *et al. ZNF469* frequently mutated in the brittle cornea syndrome (BCS) is a single exon gene possibly regulating the expression of several extracellular matrix components. Mol Genet Metab 2013;109:289–295.
11. Medeiros GX, Riet-Correa F. Epidermolysis bullosa in animals: A review. Vet Dermatol 2015;26:3–13.
12. Weiss DJ. Aplastic anemia in cats: Clinicopathological features and associated disease conditions 1996–2004. J Feline Med Surg 2006;8:203–206.
13. Oishi Y, Fu Z, Ohnuki Y, Kato H, Noguchi T. Effects of protein deprivation on α1(I) and α1(III) collagen and its degrading system in rat skin. Biosci Biotechnol Biochem 2002;66:117–126.
14. Sugiyama A, Fujita Y, Kobayashi T, *et al.* Effect of protein malnutrition on the skin epidermis of hairless mice. J Vet Med Sci 2011;73:831–835.
15. McKnight CN, Lew LJ, Gamble DA. Management and closure of multiple large cutaneous lesions in a juvenile cat with severe acquired skin fragility syndrome secondary to iatrogenic hyperadrenocorticism. J Am Vet Med Assoc 2018;52:210–214.
16. Tamulevicus AM, Harkin K, Janardhan K, Debey BM. Disseminated histoplasmosis accompanied by cutaneous fragility in a cat. J Am Anim Hosp Assoc 2011;47:e36–e41.
17. Ghandhari H, Tari HV, Ameri E, Safari MB, Fouladi DF. Vertebral, rib, and intraspinal anomalies in congenital scoliosis: A study on 202 Caucasians. Eur Spine J 2015;24:1510–1521.
18. Pollard RE, Koehne AL, Peterson CB, Lyons LA. Japanese bobtail: Vertebral morphology and genetic characterization of an established cat breed. J Feline Med Surg 2015;17:719–726.
19. Li JY, Liu SZ, Zheng DF, Zhang YS, Yu M. Collagen VI-related myopathy with scoliosis alone: A case report and literature review. World J Clin Cases 2021;9:5302–5312.

Case Report Rapport de cas

Obstructive cardiac myxosarcoma of the right ventricular outflow tract with pulmonary embolism and concurrent right atrial hemangiosarcoma in a dog

Pini Zvionow, Daniel Moreno Reyes, Enrique Aburto

Abstract — A 13-year-old spayed female rottweiler crossbreed dog was presented with an 8-day history of abnormal gait and collapse associated with excitement or physical activity. A cardiac gallop was noticed on thoracic auscultation, and a 1st-degree atrioventricular block and sinus tachycardia were noted on an electrocardiogram. Echocardiography identified a hypoechoic, irregularly marginated luminal mass in the right ventricle at the level of the pulmonic valves. Postmortem gross examination confirmed the presence of a soft, polypoid, and botryoid mass (9 × 3 × 3 cm) with a smooth and glistening surface attached to the endocardium of the right ventricular outflow tract and extending to the pulmonary artery. The histological findings were consistent with the diagnosis of myxosarcoma with pulmonary embolism. In addition, the dog in this report had a right atrial hemangiosarcoma and a cutaneous hemangioma unrelated to her clinical findings.

Key clinical message:
Cardiac myxosarcomas are very rare neoplasms in dogs and concomitant primary heart tumors of different histogenesis are even rarer in dogs. To the authors' knowledge, this is the first report of coexistent myxosarcoma and hemangiosarcoma in the heart of a dog. Cardiac myxosarcomas should be considered in the differential diagnosis of intracavitary heart masses associated with signs of cardiac obstruction and failure.

Résumé — Myxosarcome cardiaque obstructif de la voie d'éjection du ventricule droit avec embolie pulmonaire et hémangiosarcome auriculaire droit concomitant chez un chien. Une chienne croisée rottweiler stérilisée âgée de 13 ans a été présentée avec une histoire de démarche anormale et d'effondrement associés à l'excitation ou à l'activité physique depuis 8 jours. Un galop cardiaque a été noté à l'auscultation thoracique, un bloc auriculo-ventriculaire du 1er degré et une tachycardie sinusale ont été notés à l'électrocardiogramme. L'échocardiographie a permis d'identifier une masse luminale hypoéchogène et irrégulièrement marginalisée dans le ventricule droit au niveau des valvules pulmonaires. L'examen macroscopique post-mortem a confirmé la présence d'une masse molle, polypoïde et botryoïde (9 × 3 × 3 cm) avec une surface lisse et brillante attachée à l'endocarde de la voie d'éjection du ventricule droit et s'étendant jusqu'à l'artère pulmonaire. Les résultats histologiques concordaient avec le diagnostic de myxosarcome avec embolie pulmonaire. De plus, la chienne dans ce rapport présentait un hémangiosarcome auriculaire droit et un hémangiome cutané sans rapport avec ses résultats cliniques.

Message clinique clé :
Les myxosarcomes cardiaques sont des néoplasmes très rares chez le chien et les tumeurs cardiaques primaires concomitantes d'histogenèse différente sont encore plus rares chez le chien. À la connaissance des auteurs, il s'agit du premier rapport de myxosarcome et d'hémangiosarcome coexistant dans le cœur d'un chien. Les myxosarcomes cardiaques doivent être pris en compte dans le diagnostic différentiel des masses cardiaques intracavitaires associées à des signes d'obstruction et d'insuffisance cardiaque.

(Traduit par Dr Serge Messier)

Can Vet J 2024;65:234–240

Department of Veterinary Pathology, Western College of Veterinary Medicine, University of Saskatchewan, 52 Campus Drive, Saskatoon, Saskatchewan S7N 5B4.

Address all correspondence to Dr. Pini Zvionow; email: Pini.zvionow@usask.ca

Cardiac tumors in dogs have a prevalence of 0.12 to 3.1% (1–3). The most common type is hemangiosarcoma of the right atrium, followed by chemodectoma at the base of the heart (2–5). In dogs, cardiac myxomas are rare tumors and cardiac myxosarcomas are even rarer (6–10). Cardiac myxomas and myxosarcomas primarily arise from the endocardium of any of the cardiac chambers or from the cardiac valves (6). These intracavitary, space-occupying neoplasms may obstruct the flow of blood and generate neoplastic emboli (6,11). Cardiac myxosarcomas can also invade the underlying myocardium (7) and produce metastases (9,10,12). A case of cardiac myxosarcoma obstructing the right ventricular outflow tract and causing pulmonary embolism is described in this report. A concomitant right atrial hemangiosarcoma was also seen incidentally in this case. To the authors' knowledge, this is the first report of coexistent myxosarcoma and hemangiosarcoma in the heart of a dog.

Case description

A 13-year-old spayed female rottweiler crossbreed dog was presented to the Western College of Veterinary Medicine Veterinary Medical Centre (Saskatoon, Saskatchewan) with an 8-day history of collapse without losing consciousness, mostly noted after excitement or physical activity. The reported signs lasted for ~5 to 10 min and were characterized by restlessness and unsteady gait, primarily affecting the pelvic limbs, followed by collapse. When recovered, the animal showed normal behavior except for a slower-paced gait. At that time, the medical history included a non-treated, persistent otitis of the right ear and a cutaneous hemangiosarcoma that was removed 3 y before admission.

On physical examination, the animal was alert and responsive, with pale and moist mucous membranes, and weighed 29.1 kg. The respiratory rate (24 breaths/min) and body temperature (38.8°C) were within normal limits. Cardiac auscultation revealed a gallop sound and weak, but synchronous, femoral pulses. An electrocardiogram identified a 1st-degree atrioventricular block and sinus tachycardia with a rate of ~170 beats/min. The animal was sedated with butorphanol (Torbugesic; Pfizer, Kirkland, Quebec), 0.4 mg/kg, IV, for imaging. Three-view thoracic radiographs were unremarkable (Figure 1). An echocardiogram revealed a large (W: 25 mm × L: 36 mm), hypoechoic, irregularly marginated, luminal mass within the right ventricle at the level of the pulmonic valve (Figure 2 A to D). The mass appeared to arise from the myocardium of the right ventricle (Figure 2 B) and occupied the right ventricular outflow tract. In addition, there was dilation of the right atrium and ventricle, marked tricuspid valve regurgitation (5.25 m/s; Figure 2 D), and impairment of the pulmonary circulation and left ventricular filling.

A presumptive diagnosis of myocardial neoplasia was given; hemangiosarcoma, rhabdomyosarcoma, and fibrosarcoma were considered as possible differential diagnoses. Due to the severity of clinical signs and poor prognosis associated with an intracardiac mass, euthanasia was elected.

On necropsy, the left side of the neck had an expansile, well-demarcated, round, dark-red tissue mass 3 cm in diameter. There were multiple, subcutaneous, variably sized, adipose tissue masses scattered over the thorax and abdomen. In the heart, there was moderate dilation of the right atrium and ventricle. The wall of the right atrium had a round, poorly demarcated, slightly raised, nodular lesion (1 cm in diameter; Figure 3 A). Within the right ventricular outflow tract and effacing the endocardium of the free ventricular wall and septum, there was a soft, polypoid, botryoid tissue mass (9 × 3 × 3 cm) with a smooth and glistening surface (Figure 3 B). The mass occupied the lumen of the *conus arteriosus,* effaced the pulmonic valve, and extended to the proximal portion of the pulmonary trunk. On cut section, the mass was solid with a gelatinous appearance and extended into the underlying myocardium. The liver was diffusely congested. No other abnormalities were observed on necropsy.

On histological examination, the right ventricular mass appeared to originate from the endocardium. It was poorly demarcated, highly cellular, and infiltrative, and invaded the adjacent myocardium. The growth was composed of sheets and streams of neoplastic spindle-shaped, stellate, and oval cells supported by loose fibrovascular stroma containing abundant bluish-grey, mucinous extracellular matrix (Figure 4 A). This matrix was positive with Alcian blue special stain, consistent with glycosaminoglycans. The tumor cells contained moderate amounts of poorly defined, eosinophilic, and vacuolated cytoplasm; their nuclei were oval-to-elongated with finely stippled chromatin and usually single, prominent basophilic or magenta nucleoli (Figure 4 B). There was mild-to-moderate anisocytosis and anisokaryosis. A total of 22 mitotic figures were counted in an area 2.37 mm^2. Binucleation was occasionally seen within the neoplastic population. Multifocal areas of necrosis, hemorrhage, and fibrin deposits were present within the mass. The lining endothelium of the endocardium was missing or effaced by fibrin deposits in some areas.

In the lung, 1 section displayed a single blood vessel occluded by neoplastic cells embedded in mucinous matrix as described in the right ventricular tumor (Figure 4 C, D). The adjacent lung parenchyma was effaced and infiltrated by small numbers of similar neoplastic cells separated by mucinous matrix, erythrocytes, and fibrin. Sections of the red nodular lesion in the right atrium revealed focal expansion and effacement of the epicardium and myocardium by a poorly demarcated, densely cellular, and infiltrative neoplasm with histologic features consistent with those of a hemangiosarcoma. The cutaneous mass on the left side of the neck was a cavernous hemangioma. The liver tissue was diffusely congested and moderately autolyzed.

Discussion

This report describes a case of obstructive cardiac myxosarcoma with pulmonary embolism in a 13-year-old rottweiler crossbreed dog. Concurrent vascular neoplasms, a right atrial hemangiosarcoma, and a cutaneous hemangioma were also seen incidentally in this case. Primary cardiac tumors are extremely rare in humans (13), with a prevalence of ~0.02% (14); metastatic lesions of the heart are more common than primary cardiac neoplasms (15). Myxomas are the most common primary type, representing ~85% of human cardiac neoplasms in 1 case series (16). Primary malignant tumors reported in the human

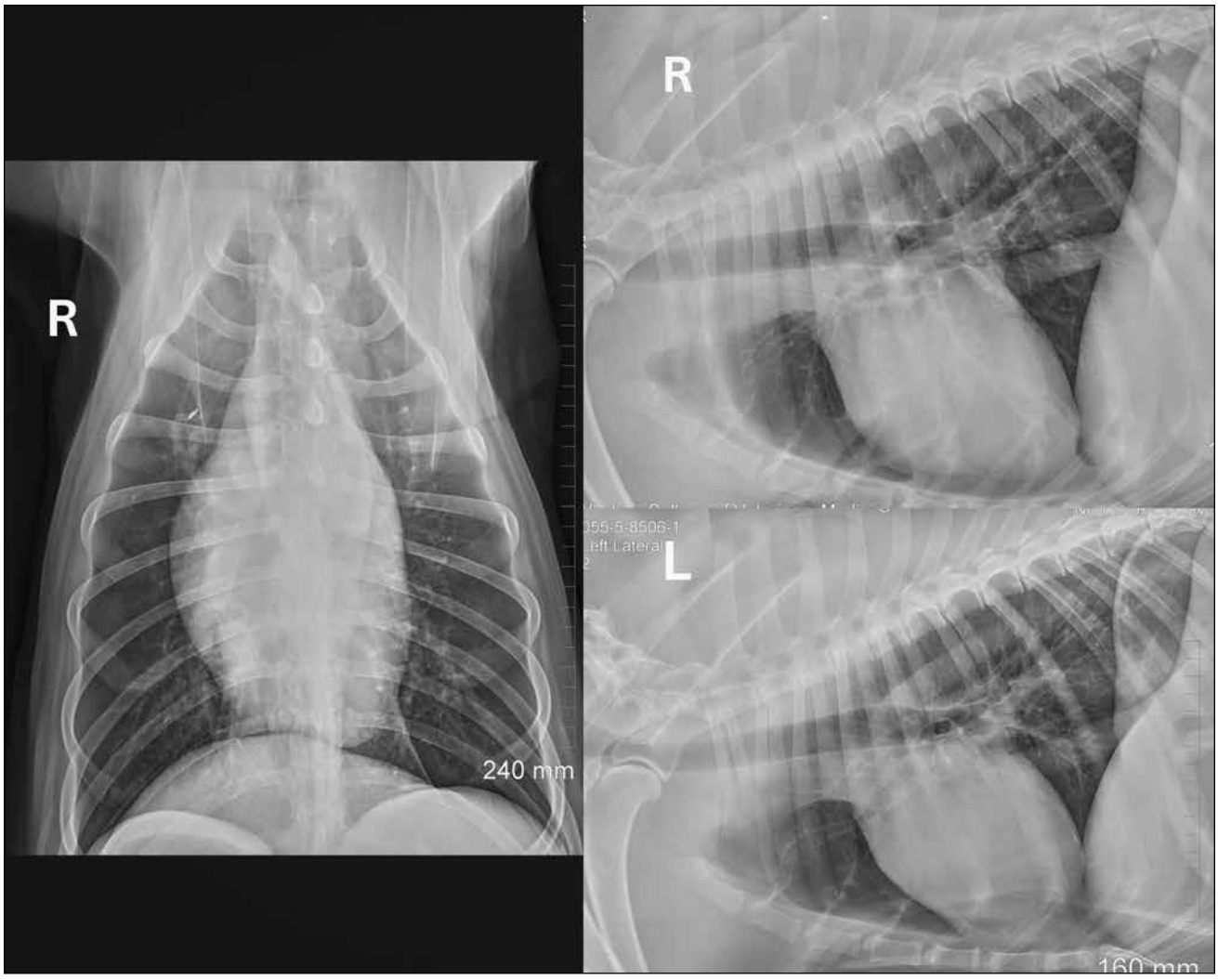


Figure 1. Chest X-ray images from a 13-year-old female rottweiler crossbreed dog. Unremarkable 3-view thoracic radiographs. There is mild rounding of the cranioventral aspect of the cardiac silhouette on the right lateral view; however, this is not appreciated in the rest of the study.

heart include angiosarcoma, rhabdomyosarcoma, undifferentiated sarcoma, leiomyosarcoma, fibrosarcoma, liposarcoma, osteosarcoma, malignant fibrous histiocytoma, pericardial mesothelioma, lymphoma, and myxosarcoma. Human primary cardiac sarcomas, including myxosarcomas, appear to have a predilection for the left atrium (12,15). Primary heart tumors are more frequent in dogs, with a prevalence of 0.12 to 3.1% (1–3). The most commonly reported type is hemangiosarcoma, which represents 69% of cardiac tumors in this species (5). Other types of cardiac tumors include aortic body tumor, lymphoma, ectopic thyroid carcinoma, mesothelioma, myxoma, myxosarcoma, undifferentiated sarcoma, fibrosarcoma, rhabdomyosarcoma, leiomyosarcoma, chondrosarcoma, osteosarcoma, and metastatic tumors (*e.g.,* adenocarcinoma and melanoma) (2–5,7–11). Most cardiac neoplasms originate in the heart; the rest are metastatic. However, as cardiac hemangiosarcomas may originate from bone marrow-based stem cells (17), the question of whether primary heart tumors are more common than metastatic lesions should be reconsidered. The occurrence of simultaneous neoplasms of different types has seldom been described in the canine heart. There is 1 report regarding the coexistence of a presumably primary sarcoma and a metastatic adenocarcinoma in the heart of a dog (18). To the authors' knowledge, simultaneous cardiac myxosarcoma and hemangiosarcoma have not been previously reported in dogs.

Primary canine cardiac myxosarcomas are extremely rare and usually arise from the endocardium of the cardiac chambers or the heart valves, similar to cardiac myxomas (7–11,19); however, myocardial and pericardial myxosarcomas have also been described in dogs (9,20). The histogenesis of cardiac myxomas and myxosarcomas has not been identified. These tumors appear to originate from the proliferation of primitive vasoformative cells in the heart with potential to differentiate into different mesenchymal tissues (6,21). Cardiac myxosarcomas represent the malignant form of myxoma. In contrast to cardiac myxomas, myxosarcomas should display histological features of malignancy, local invasion into the adjacent myocardium, or metastasis (7–10,12,19). In this case, the diagnosis of myxosarcoma

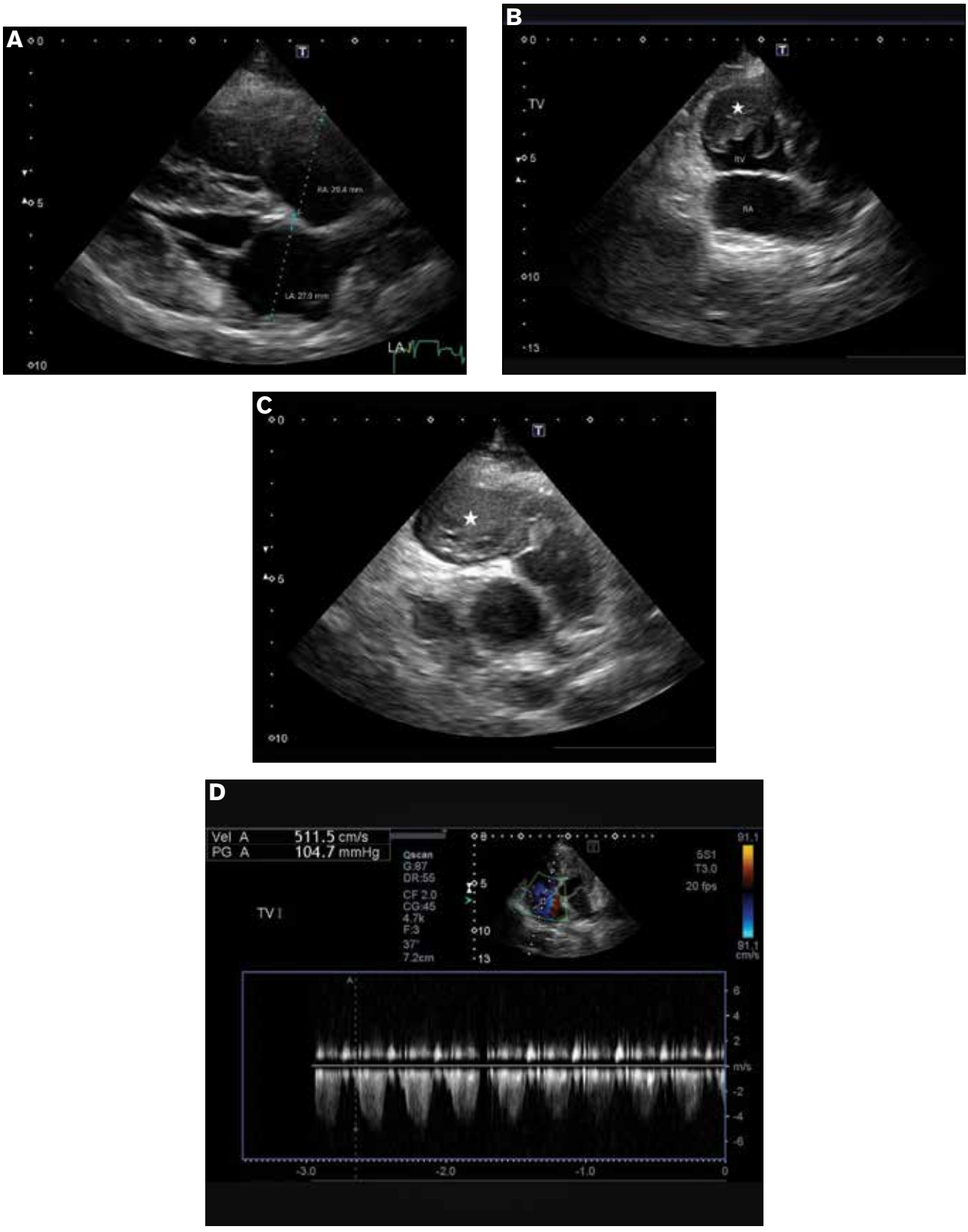


Figure 2. Echocardiogram from a 13-year-old female rottweiler crossbreed dog. A – Four-chamber right-sided parasternal long-axis view with measurements for left atrial (LA) and right atrial (RA) diameter. B – Left apical 4-chamber view modified to show the large mass effect (star) inside the right ventricle (RV). The left side of the heart is not shown in this picture. C – Non-traditional 2-dimensional echocardiogram view showing the same intracardiac mass effect (star) in the right ventricle causing a right outflow tract obstruction. D – Doppler echocardiography showing severe tricuspid valve regurgitation. Velocity is used to calculate pressure gradient through the tricuspid valve.

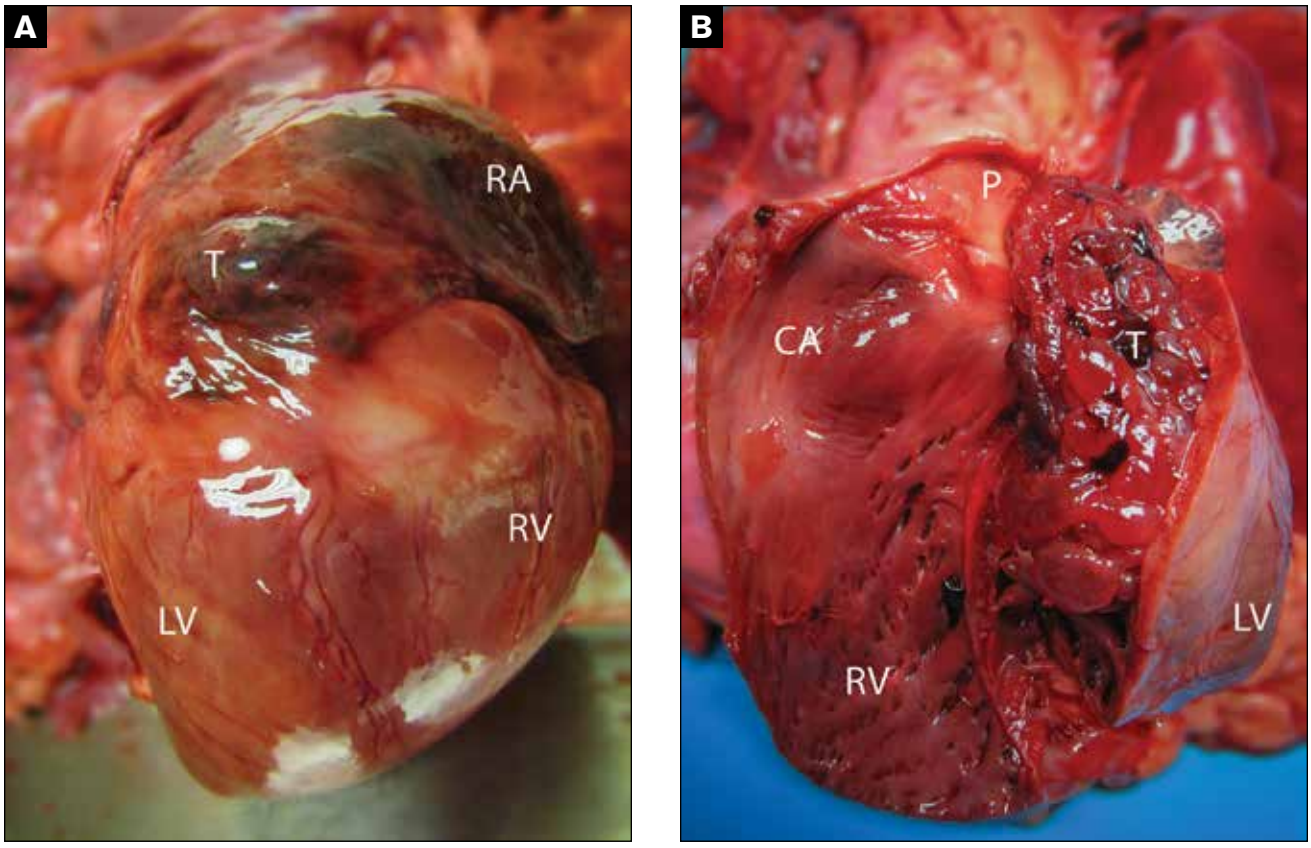


Figure 3. Gross cardiac images of the hemangiosarcoma and myxosarcoma in a 13-year-old female rottweiler crossbreed dog. A – The right ventricle is distended and there is a plaque-like mass (T) on the right atrium. LV – Left ventricle; RA – Right atrium; RV – Right ventricle; T – Hemangiosarcoma. B – There is a multilobular mass occupying the right ventricular outflow tract; *i.e., conus arteriosus,* and extending into the pulmonary artery. CA – *Conus arteriosus;* LV – Apex of the left ventricle; P – Pulmonary artery; RV – Right ventricle; T – Myxosarcoma.

was established based on the high cellularity of the mass and the presence of cellular atypia, pleomorphism, frequent mitotic figures, and necrosis. In addition, the neoplastic population invaded the adjacent myocardium and the pulmonary parenchyma was focally infiltrated by small numbers of similar spindle cells separated by mucinous matrix, which is consistent with metastasis. Adjacent to the affected pulmonary parenchyma, there was a neoplastic embolus occluding the lumen of a blood vessel. Cardiac myxomas and myxosarcomas can become fragmented and embolize to distant sites such as the pulmonary vasculature (1,13,22). Neoplastic emboli originating from cardiac myxomas do not invade the walls of the affected vessels and the adjacent tissues; *i.e.,* they do not generate metastasis (22).

The clinical outcome of intracardiac myxoma and myxosarcoma depends on the size of the mass and its location. In humans, these tumors may cause symptoms related to heart failure and embolization, among others (7,11). Cardiac myxomas and myxosarcomas may interrupt the blood flow *via* a space-occupying effect in the heart chambers that prevents their complete filling and reduces the anterograde flow of blood. Abnormal blood flow may also result from physical impairment of the valvular function, causing valvular regurgitation or occlusion, which increases venous pressures and leads to congestive heart failure (6,7,11,20). In the present case, the tumor occupied and obstructed much of the right ventricular outflow tract and effaced/occluded the pulmonic valve, causing marked tricuspid valve regurgitation, impairment of the pulmonary circulation, and reduced left ventricular filling. In addition, we saw evidence of pulmonary embolism affecting a microscopic blood vessel that did not have a clinical effect in this case. However, widespread pulmonary embolization, as was previously described in a case of cardiac myxoma (22), can have a marked clinical effect, such as *cor pulmonale,* when large branches of the pulmonary artery are obstructed (23).

Life expectancy in humans and dogs with heart tumors relies on the type of tumor and the therapeutic options available. In humans, surgical removal is the recommended therapy for cardiac myxoma, and complete removal is often curative (24); however, the prognosis for patients with cardiac myxosarcoma is poor due to the development of metastasis (25). In 1 case report of left ventricular myxosarcoma in a dog, the neoplasm was surgically removed without additional therapies; the dog made a full recovery and survived 11 mo after the surgery, but the tumor recurred and developed metastasis soon after that (9). In this case, surgery was not attempted due to the dog's grave prognosis.

In dogs, hemangiosarcomas are frequently observed in the heart, spleen, and skin. Hemangiosarcomas may occur in

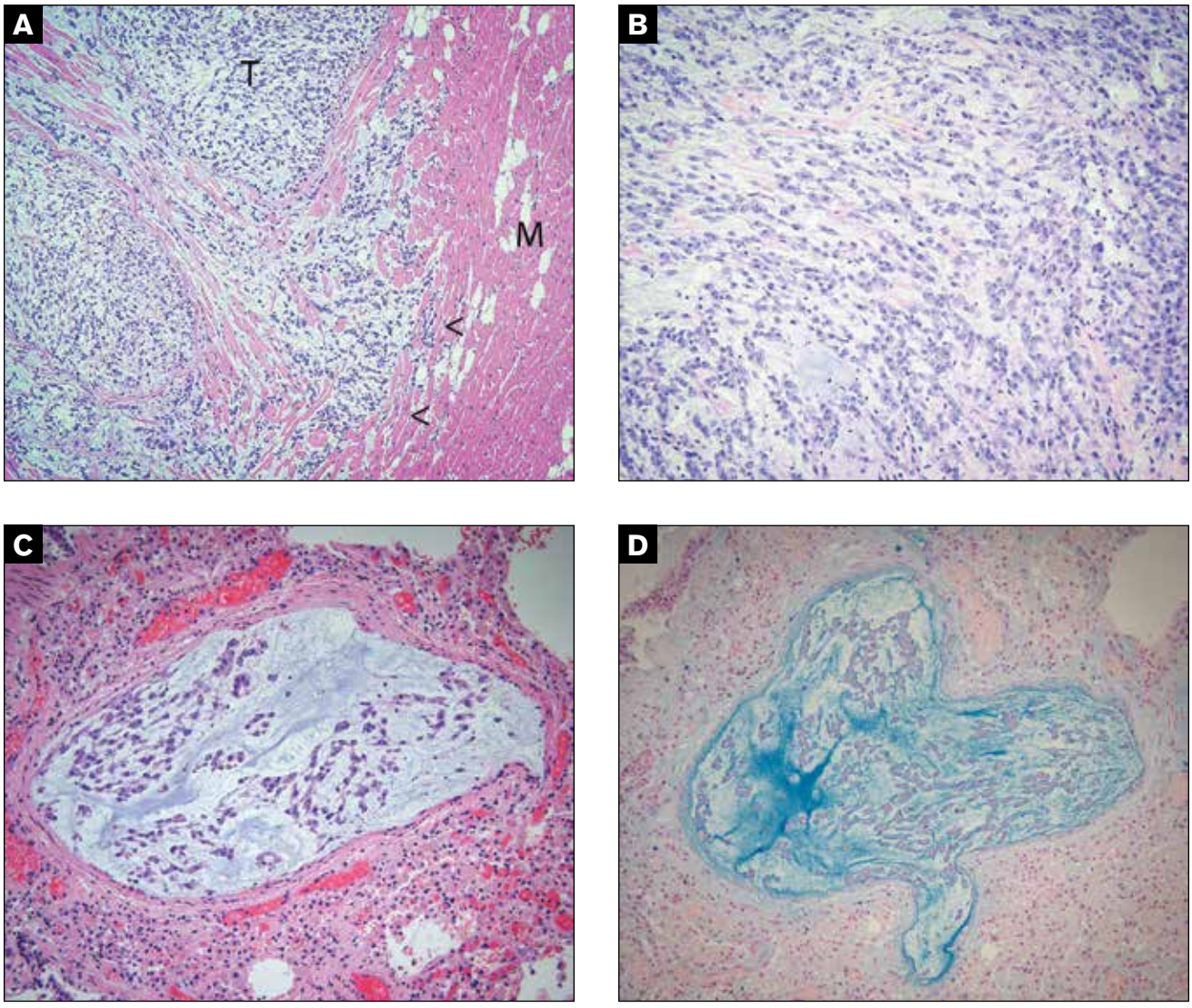


Figure 4. Histological examination of cardiac myxosarcoma in a 13-year-old female rottweiler crossbreed dog (A to D). A – Highly cellular myxomatous neoplasm is invading the endocardium and myocardium of the right ventricular septal wall. The "<" symbol denotes the invasion front. M – Myocardium; T – Myxosarcoma. Hematoxylin and eosin stain, magnification: 10×. B – Note the loose myxoid matrix, the numerous mitotic figures, and cellular pleomorphism. Hematoxylin and eosin stain, magnification: 20×. C – The neoplastic cells are occluding a pulmonary vessel; *i.e.,* embolus. Hematoxylin and eosin stain, magnification: 20×. D – The myxoid matrix of the neoplastic embolus within the occluded pulmonary vessels is positive with Alcian blue stain. Magnification: 20×.

the heart (right atrium) and spleen of the same animal. It is unknown if this simultaneous occurrence represents a *de novo* multicentric occurrence or metastasis (5). In the current case, a cutaneous hemangiosarcoma had been removed 3 y before we examined the dog, with signs attributable to cardiac disease. In addition, this animal had a cutaneous hemangioma and a concurrent right atrial hemangiosarcoma that were not related to the clinical manifestations.

Acknowledgment

The authors thank the University of Saskatchewan for covering the cost of this publication. CVJ

References

1. Detweiler DK, Patterson DF. The prevalence and types of cardiovascular disease in dogs. Annals NY Acad Sci 1965;127:481–516.
2. Ware WA, Hopper DL. Cardiac tumors in dogs: 1982–1995. J Vet Intern Med 1999;13:95–103.
3. Walter JH, Rudolph R. Systemic, metastatic, eu- and heterotope tumors of the heart in necropsied dogs. Zentralbl Veterinarmed A 1996;43:31–45.
4. Aupperle H, März I, Ellenberger C, Buschatz S, Reischauer A, Schoon HA. Primary and secondary heart tumors in dogs and cats. J Comp Path 2007;136:18–26.
5. Treggiari E, Pedro B, Dukes-McEwan J, Gelzer AR, Blackwood L. A descriptive review of cardiac tumours in dogs and cats. Vet Comp Oncol. 2017;15:273–288.
6. Robinson WF, Robinson NA. Cardiovascular system. In: Maxie MG, ed. Jubb, Kennedy, and Palmer's Pathology of Domestic Animals. 6th ed. Vol 3. St. Louis, Missouri: Elsevier, 2016:2–101.

7. Scurtu I, Taulescu M, Scurtu L, *et al.* Obstructive right ventricular outflow tract myxosarcoma in an adult dog. J Vet Cardiol. 2020;29:47–53.
8. Machida N, Hoshi K, Tanaka R, Yamane Y, Katsuda S, Mitsumori K. Cardiac myxosarcoma of the tricuspid valve in a dog. Anim Cardiol 2003;36:110–116. Available from: https://www.jstage.jst.go.jp/article/jsvc/36/2/36_2_110/_article/-char/ja/ Last accessed January 10, 2024.
9. Foale RD, White RAS, Harley R, Herrtage ME. Left ventricular myxosarcoma in a dog. J Small Anim Pract 2003;44:503–507.
10. Briggs OM, Kirberger RM, Goldberg NB. Right atrial myxosarcoma in a dog. JSAVA 1997;68:144–146. Available from: https://journals.co.za/doi/abs/10.10520/EJC99190 Last accessed January 10, 2024.
11. Mellish C, Cote E, Aburto E, Lichtenberger J. Mineralized, obstructive cardiac myxoma with chondroid differentiation in a cocker spaniel. Can Vet J 2022;63:411–415.
12. Hekmat M, Farzin AO, Aval ZA, Fanu K, Heidarpour A. Cardiac myxosarcoma: A case report. Caspian J Intern Med 2021;12:228–231.
13. Tyebally S, Chen D, Bhattacharyya S, *et al.* Cardiac tumors: JACC CardioOncology state-of-the-art review. JACC CardioOncol 2020;2:293–311.
14. Reynen K. Frequency of primary tumors of the heart. Am J Cardiol 1996;77:107.
15. Casavecchia G, Lestuzzi C, Gravina M, *et al.* Cardiac tumors. J Cardiovasc Echogr 2020;30:S45–S53.
16. Wu HM, Chen Y, Xiao ZB, *et al.* Clinical and pathological characteristics of cardiac tumors: Analyses of 689 cases at a single medical center. Chin J Pathol 2019;48:293–297.
17. Lamerato-Kozicki AR, Helm KM, Jubala CM, Cutter GC, Modiano JF. Canine hemangiosarcoma originates from hematopoietic precursors with potential for endothelial differentiation. Exp Hematol 2006;34:870–878.
18. Grieco V, Locatelli C, Riccardi E, Brambilla P. A case of two different tumors in the heart of a dog. J Vet Diagnostic Investig 2008;20:365–368.
19. Adissu HA, Hayes G, Wood GA, Caswell JL. Cardiac myxosarcoma with adrenal adenoma and pituitary hyperplasia resembling Carney complex in a dog. Vet Pathol 2010;47:354–357.
20. Karlin ET, Yank VK, Prabhakar M, Gregorich SL, Hahn S, Rush JE. Extracardiac intrapericardial myxosarcoma causing right ventricular outflow tract obsruction in a dog. J Vet Cardiol 2018;20:129–135.
21. Di Vito A, Mignogna C, Donato G. The mysterious pathways of cardiac myxomas: A review of histogenesis, pathogenesis and pathology. Histopathology 2015;66:321–332.
22. Machida N, Hoshi K, Kobayashi M, Katsuda S, Yamane Y. Cardiac myxoma of the tricuspid valve in a dog. J Comp Path 2003;129:320–324.
23. Caswell JL, Williams KJ. Respiratory system. In: Maxie MG, ed. Jubb, Kennedy, and Palmer's Pathology of Domestic Animals. 6th ed. Vol 1. St. Louis, Missouri: Elsevier, 2016:465–591.
24. Centofanti P, Di Rosa E, Deorsola L, *et al.* Primary cardiac tumors: Early and late results of surgical treatment in 91 patients. Ann Thorac Surg 1999;68:1236–1241.
25. Liu S, Wang Z, Chen AQ, Zhou GH, Jiang ZB, Xiao MD. Cardiac myxoma and myxosarcoma: Clinical experience and immunohistochemistry. Asian Cardiovasc Thorac Ann 2002;10:8–11.

Industry News
Nouvelles de l'industrie

Revolutionizing pet financing in Canada. Instant approval with no credit impact

Welcome to a world where caring for your furry companions' health is not only simpler but also more accessible. Petcard by iFinance introduces its revolutionary Instant Approval tech, a true game-changer in the world of pet financing. This innovative system streamlines the loan application process, allowing pet owners to check their eligibility within minutes, all without impacting their credit score.

Explore how Petcard is transforming the landscape of pet financing at www.ifinancecanada.com

Contact: Petcard by iFinance, 60 Bloor Street West, Suite 605, Toronto, Ontario; phone: 1-888-689-9876.

Case Report Rapport de cas

Gallbladder carcinoid in a cat

Tania Shaw

Abstract — Carcinoids are rare tumors that originate from neuroendocrine system cells. There has apparently only been 1 report in the veterinary medical literature of a cat with a gallbladder carcinoid, with no long-term follow-up information available from that case. Furthermore, apparently only 9 dogs with gallbladder carcinoids have been reported, again with no long-term follow-up. This case report describes the clinical presentation, surgical appearance, histopathologic and immunohistochemical findings, postoperative adjuvant chemotherapy treatment, and long-term outcome of a domestic longhair cat with a gallbladder carcinoid. The diagnosis of a gallbladder carcinoid in the present case was based on histologic and immunohistochemical findings. Clinical signs of a gallbladder carcinoid are nonspecific and ultrasonographic findings may not be definitive; however, it should be considered as a potential differential diagnosis in cats with lesions of the gallbladder or in the region of the gallbladder. The prognosis is poor, with a potentially high metastatic rate. In the present case, metastasis occurred 7 mo postoperatively despite adjuvant therapy, and the survival time was only 10 mo from the time of diagnosis.

Key clinical message:
This case report describes the clinical presentation, surgical appearance, histopathologic and immunohistochemical findings, postoperative adjuvant treatment, and long-term outcome of a cat with a gallbladder carcinoid, which should be considered as a potential differential diagnosis in cats with lesions of the gallbladder or in the region of the gallbladder.

Résumé — Carcinoïde de la vésicule biliaire chez un chat. Les carcinoïdes sont des tumeurs rares qui prennent leur origine des cellules du système neuroendocrinien. Dans la littérature médicale vétérinaire il n'y aurait qu'un seul cas rapporté d'un chat avec un carcinoïde de la vésicule biliaire, sans aucune information de suivi à long terme disponible pour ce chat. Également, il y aurait 9 cas rapportés de chiens avec des carcinoïdes de la vésicule biliaire, mais encore là aucun suivi à long terme. Le cas présenté ici décrit la présentation clinique, l'apparence chirurgicale, les trouvailles histopathologiques et immunohistochimiques, le traitement post-opératoire par chimiothérapie adjuvante, et le devenir à long terme d'un chat domestique à poil court avec un carcinoïde de la vésicule biliaire. Dans le cas présent, le diagnostic de carcinoïde de la vésicule biliaire était basé sur les trouvailles histologiques et immunohistochimiques. Les signes cliniques d'un carcinoïde de la vésicule biliaire sont non-spécifiques et les trouvailles échographiques pourraient ne pas être concluantes; toutefois, il devrait être considéré comme un diagnostic différentiel possible chez des chats avec des lésions à la vésicule biliaire ou dans la région de la vésicule biliaire. Le pronostic est mauvais, avec un risque élevé de métastases. Dans le cas présent, des métastases sont apparues 7 mo post-chirurgie malgré une chimiothérapie adjuvante, et le temps de survie a été de 10 mo à compter du moment du diagnostic.

Message clinique clé :
Ce rapport de cas décrit la présentation clinique, l'apparence chirurgicale, les trouvaille histologiques et immunohistochimiques, la thérapie adjuvante postopératoire, et le résultat à long-terme pour un chat avec un carcinoïde de la vésicule biliaire, qui devrait être considéré comme un diagnostic différentiel potentiel chez les chats avec des lésions à la vésicule biliaire ou dans la région de la vésicule biliaire.

(Traduit par Dr Serge Messier)

Can Vet J 2024;65:241–244

Surgery Department, Animal Referral Hospital Melbourne, 72 Hargrave Avenue, Essendon Fields, VIC 3041, Australia.
Address all correspondence to Dr. Tania Shaw; email: t.shaw@arhvets.com

Primary hepatobiliary tumors are uncommon in cats and dogs, representing only ~2.6 and 5.5% of canine and feline tumors, respectively (1). Primary tumors of the extrahepatic biliary tract can be differentiated into adenomas and carcinomas; when the latter originate from neuroendocrine system cells, they are known as neuroendocrine tumors or carcinoids (2). These neuroendocrine cells belong to 1 of 2 functional groups: the amine precursor uptake and decarboxylation (APUD) cells that produce serotonin and adrenocorticotrophic hormone, and cells that are capable of synthesizing low-molecular-weight polypeptide or protein hormones such as chromogranin, cholecystokinin, and secretin (3,4). Carcinoids are thought to arise from embryonal neural crest cells (argentaffin cells) that migrate to sites within the respiratory and gastrointestinal tracts during embryonal development.

There is, however, some debate regarding the most accurate terminology for these tumors, with an umbrella term of "neuroendocrine neoplasm" (NEN) encompassing neuroendocrine tumors and neuroendocrine carcinomas. In human pathology, based on the World Health Organization classification system for NENs in 2010, NENs are graded from 1 to 3, with Grades-1 and -2 NENs classified as neuroendocrine tumors, and Grade-3 NENs classified as carcinomas. Within this classification system, Grade-1 NENs are known as carcinoids (5). Unfortunately, there is no specific classification system for veterinary pathologists when diagnosing these neoplasms.

In dogs and cats, neuroendocrine carcinoma has been reported in the intestine, liver, bile duct, lungs, gallbladder, stomach, esophagus, nasal cavity, nasopharynx, and skin (6). Neuroendocrine carcinoma arising from the gallbladder is uncommon in humans and extremely rare in dogs and cats (4,7). In humans, primary gallbladder and biliary duct system carcinoids constitute $< 1\%$ of all carcinoid tumors arising from any tissue or organ (4). Clinical signs are nonspecific and can include anorexia, ascites, weight loss, diarrhea, and icterus.

This case report describes the clinical presentation, surgical appearance, histopathologic and immunohistochemical findings, postoperative adjuvant chemotherapy treatment, and long-term outcome of a domestic longhair cat with a gallbladder carcinoid. An extensive literature search identified only 1 other report of a gallbladder carcinoid in a cat, and there was no long-term follow-up for that case due to euthanasia shortly after surgery. The veterinary medical literature reports only 9 dogs with gallbladder carcinoids, again without postoperative chemotherapy or long-term outcomes reported. The objective of this case report is to bring awareness to the diagnosis and possible long-term outcome for such cases.

Case description

A 4-year-old neutered male domestic longhair cat weighing 5.01 kg was presented with a 1-week history of intermittent vomiting, weight loss, and lethargy. Initial examination was unremarkable apart from tacky mucous membranes and a capillary refill time of 2 s. Results from complete hematology and biochemistry were unremarkable apart from mild stress hyperglycemia (10.37 mmol/L; reference interval: 4.11 to 8.84 mmol/L) and mild hyperglobulinemia (53 g/L; reference interval: 28 to 51 g/L). Two-view (lateral and ventrodorsal) radiographs of the abdomen revealed moderate gas accumulation in the small intestine, possible bunching of the small intestines, and no discrete intestinal foreign body. The cat was treated initially with intravenous (IV) fluid therapy (5 mL/kg per hour) and buprenorphine (0.01 mg/kg, IV, q8h). The cat developed a mild pyrexia overnight (39.1°C) but ate small amounts and appeared more comfortable in the abdomen. Abdominal radiographs were repeated 12 h later and revealed a reduction in gas accumulation in the small intestine. The cat continued to receive IV fluid therapy and IV buprenorphine.

The following day, abdominal ultrasonography, performed by a board-certified internist, revealed an incidental finding of a multinodular mass (32 × 26 mm) within the mesentery caudal to the stomach and ventral to the kidneys, in the region of the pancreas. The mass had an overall low echogenicity, and color flow Doppler revealed blood flow present within the center of the mass. The gallbladder was empty and the liver appeared normal. There was a small amount of free peritoneal fluid around and between hepatic lobes. The remainder of the abdominal cavity was unremarkable, with no evidence of a gastrointestinal foreign body obstruction. Ultrasound-guided fine-needle aspiration of the mass was completed, and in-house cytologic evaluation revealed sheets of epithelial cells. Further aspirates were obtained, and cytologic assessment by a veterinary pathologist revealed moderate-to-large numbers of spindle cells in large tissue clumps dispersed by a small amount of eosinophilic matrix. Cellular morphology was most suggestive of a spindle cell origin, with suspicion for a leiomyoma or sarcoma. Based on these findings, an exploratory celiotomy was recommended for excision of the mass.

Preoperative computed tomography (CT) or thoracic radiography was not performed for staging; however, the caudal thorax was included in the cat's original abdominal radiographs and was unremarkable on those radiographs.

The cat was returned for surgery 4 d after the abdominal ultrasound. The pyrexia had resolved, and the cat had only had a single episode of vomiting in the previous week. A ventral midline celiotomy was completed and the abdomen was explored. The liver, spleen, kidneys, adrenal glands, pancreas, urinary bladder, and gastrointestinal tract appeared normal. Intra-abdominal lymph nodes and peritoneum also appeared normal. The gallbladder was empty and fibrosed and was firmly attached to the adjacent right lateral hepatic lobe. There was a firm, lobulated mass arising from the gallbladder. The common bile duct was of a normal diameter and patent. A cholecystectomy was completed, along with a partial liver lobectomy of the right lateral lobe that was firmly adhered to the gallbladder. The partial liver lobectomy was achieved with a bipolar vessel-sealing device (LigaSure; Medtronic, Minneapolis, Minnesota, USA). The cholecystectomy was completed by double ligation of the cystic duct using 4-0 polydioxanone suture and transection of the cystic duct distal to the ligatures.

Histologic examination by a board-certified veterinary pathologist revealed a mass composed of small, neoplastic cells that were separated into nests and packets by a delicate fibrovascular matrix. The cells generally had scant eosinophilic cytoplasm and

fairly distinct cell boundaries, with small, oval-to-rounded nuclei containing fine-stippled chromatin and small basophilic nucleoli. There was some scattered single-cell necrosis, and mitotic figures were common. The mitotic rate exceeded 5 per high-power field on average, which, based on the World Health Organization's 2010 classification in humans, was consistent with a Grade-3 neoplasm (5). The lesion did not appear to arise from the gallbladder epithelium but was evident within the wall, covered by attenuated epithelium, and displaced the mural tissues of the gallbladder. Tracts of necrosis were present, but many areas had a typical neuroendocrine pattern. The lesion was occasionally surrounded by a delicate compressed capsule. Histomorphology was most consistent with a primary neuroendocrine tumor, possibly arising from nests of endocrine cells within the gallbladder wall. Immunohistochemical analysis demonstrated diffuse positive cytoplasmic immunolabelling for neuron-specific enolase (NSE), supporting the diagnosis of a carcinoid.

The cat recovered well from surgery and was eating well at home, with no further episodes of vomiting. Incisional staples were removed 10 d postoperatively. At 14 d postoperatively, the cat began receiving adjuvant therapy with the tyrosine kinase inhibitor toceranib phosphate (Palladia; Pfizer Australia, West Ryde, NSW, Australia), 10 mg, PO, 3 times per week. At reexamination 7 mo after starting adjuvant therapy, repeat abdominal ultrasonography conducted by a board-certified internist revealed multiple mesenteric masses and lymphadenomegaly. Adjuvant therapy was continued until the patient started developing seizures 2 mo later and was euthanized. The cause of the seizures is unknown, as neither advanced imaging of the brain nor necropsy was performed, and may or may not have been related to intracranial metastatic lesions. However, the cat was known to already have metastatic lesions within the abdomen.

Discussion

In humans, extrahepatic carcinoids are extremely rare, accounting for 0.1 to 0.2% of all carcinoids of the gastrointestinal tract, and only 4% of epithelial tumors of the gallbladder are carcinoids (6). Gallbladder neoplasms are uncommon in domestic animals, and gallbladder carcinoids in particular are extremely rare in dogs and cats. An extensive literature search identified only 9 dogs and 1 cat reported in the veterinary medical literature with gallbladder carcinoids (2–4,6–9). In this case, the tumor was diagnosed as a NEN and has been referred to as a carcinoid in this paper, as there is no specific classification system for these tumors in veterinary species.

In dogs, carcinoids account for 13% of primary hepatobiliary tumors and most commonly involve hepatic parenchyma and, sporadically, biliary tissue (1). No breed or sex predilection has been described; however, these tumors typically affect younger dogs (average: 8 to 9.8 y) (1). In cats, hepatobiliary carcinoids have a male predilection, and the average age of diagnosis is 9 y (1). This is in contrast to the present case, which involved a 4-year-old cat. Hepatobiliary carcinoid tumors in dogs are often diffuse in nature and affect most of the hepatic parenchyma. The metastatic potential of hepatic carcinoids in dogs has been reported to be high, and at necropsy, nearly all animals had evidence of metastasis, most frequently to the lymph nodes, peritoneum, and lungs (1,7). The lack of thoracic imaging in this case was a limitation because pulmonary metastases may have been present at the time of surgery and may have affected the animal's prognosis. If there is no evidence of intraperitoneal or distant metastasis at the time of diagnosis, and the tumor is localized to the gallbladder, the prognosis is considered good. In the present case, the mass had a high mitotic rate but no known regional or distant metastasis at the time of surgery. Therefore, adjuvant therapy was recommended based on the assumption of a likely high metastatic potential, despite the absence of published recommendations for adjuvant therapy for hepatobiliary carcinoids in veterinary patients.

An extensive search identified only 1 other cat reported in the veterinary medical literature with a gallbladder carcinoid. In the study by Patnaik *et al* (2005) describing 17 cats with hepatobiliary neuroendocrine carcinomas, only 1 of the 17 cats had a carcinoid affecting the gallbladder (6). The cat in that study was an 11-year-old neutered male domestic shorthair cat. That cat had a 3-centimeter intraluminal mass infiltrating the wall of the gallbladder and adjacent liver. In contrast, the cat described here was much younger, and the mass was extraluminal but infiltrating the wall of the gallbladder.

In the present case, abdominal ultrasonography was a diagnostic tool that identified the mass as an incidental finding, unrelated to the patient's presenting signs. Ultrasonographically, the mass was described as a mesenteric mass caudal to the stomach in the region of the pancreas, with a multinodular appearance and low echogenicity. Color flow Doppler ultrasonography identified the presence of blood flow within the center of the mass. In 2 previous case reports of gallbladder carcinoids in dogs, abdominal ultrasonography failed to clearly identify masses within the gallbladder, with 1 suggestive of cholelithiasis instead (2,3). The lack of visualization of the tumor was hypothesized to be due to the presence of a large volume of dense biliary sludge. The presence of echogenic material within the gallbladder can represent inspissated bile or gallbladder debris, cholecystoliths, gallbladder mucocele, or gallbladder neoplasia (benign or malignant), and color flow Doppler ultrasonography has been advocated for differentiating among these differential diagnoses to determine the need for treatment or surgical intervention (7). In the present case, whereas color Doppler ultrasonography identified blood flow within the center of the mass, it was not used to differentiate between gallbladder debris and solid tissue because the mass was external to the gallbladder lumen.

Despite an absence of reports comparing the diagnostic accuracy of ultrasonography, CT and MRI for gallbladder carcinoids, a recent case report provided a description of the CT appearance of a gallbladder carcinoid in the dog (9). In that animal, the gallbladder carcinoid was strongly contrast-enhancing in the arterial phase of the post-contrast CT, which can also be useful for differentiating gallbladder neoplasia from cholecystoliths (9).

Preoperative fine-needle aspiration cytology of the mass in the present case confirmed a malignant tumor and resulted in the recommendation for an exploratory celiotomy and surgical excision. The tumor was only discovered to be associated with the gallbladder intraoperatively.

The histologic appearance of the tumor in the present case report was very similar to that described for the cat in the study by Patnaik *et al* (2005), as well as those in other reports in dogs, except for the mitotic rate (6). The cat in the Patnaik *et al* (2005) study had a low mitotic rate of 0 to 1 per high-power field; this is in contrast to the high mitotic rate observed in the present case, which exceeded 5 per high-power field on average (6).

In previous reports of gallbladder carcinoids in dogs and cats, immunohistochemically, these tumors historically stained positive for NSE and synaptophysin. Although chromogranin A is the most commonly used neuroendocrine marker in human medicine, it was not particularly useful in the Patnaik *et al* (2005) study, in which tumors from only 2 of the 17 cats stained positive for chromogranin A (neither of which was the cat with the gallbladder carcinoid) (6). In the present case, the tumor stained positive for NSE but negative for synaptophysin. Positive staining for NSE is consistent with a neuroendocrine tumor (carcinoid).

In humans, extrahepatic carcinoids tend to be slow-growing, with a 5-year survival rate of 94% for localized disease, 64% if regional metastasis is present at the time of diagnosis, and 18% if distant metastasis is present at the time of diagnosis (10). In the present case, the cat had localized disease with no evidence of regional or distant metastasis; however, the disease-free interval was only 7 mo despite adjuvant therapy, and the survival time was only 10 mo after diagnosis.

The diagnosis of a gallbladder carcinoid in the present case was based on histologic findings. Gallbladder carcinoid is a rare neoplasm in cats, and to the author's knowledge, this is only the second report in a cat. Although clinical signs are nonspecific, and ultrasonographic findings may not be definitive, it should be considered as a potential differential diagnosis in cats with lesions of the gallbladder or in the region of the gallbladder. The prognosis is poor, with a potentially high metastatic rate. In the present case, metastasis occurred 7 mo postoperatively despite adjuvant therapy, and the survival time was only 10 mo from the time of diagnosis.

Acknowledgments

I thank Dr. John Jardine for his assistance with the histologic and immunohistochemical analyses in this case, and Dr. Robert Labuc and Dr. David Lurie for their input on chemotherapy. This case was not funded and has not been presented at a meeting. CVJ

References

1. Wypij J, Fan TM, de Lorimier LP. Primary hepatic and biliary tract tumors in dogs and cats: An overview. Vet Med 2006;101:384–394.
2. Birettoni F, Porciello F, Caivano D, Arcelli R, Sforna M, Antognoni M. Primary neuroendocrine carcinoma of the gallbladder in a dog. Vet Res Commun 2008;32:S239–S242.
3. Morrell CN, Volk MV, Mankowski JL. A carcinoid tumor in the gallbladder of a dog. Vet Pathol 2002;39:756–758.
4. Lippo NJ, Williams JE, Brawer RS, Sobel KE. Acute hemobilia and hemocholecyst in 2 dogs with gallbladder carcinoid. Vet Intern Med 2008;22:1249–1252.
5. Cavalcanti MS, Gonen M, Klimstra DS. The ENETS/WHO grading system for neuroendocrine neoplasms of the gastroenteropancreatic system: A review of the current state, limitations and proposals for modifications. Int J Endocr Oncol 2016;3:203–219.
6. Patnaik AK, Lieberman PH, Erlandson RA, Antonescu C. Hepatobiliary neuroendocrine carcinoma in cats: Clinicopathologic, immunohistochemical, and ultrastructural study of 17 cases. Vet Pathol 2005;42:331–337.
7. Bhandal J, Head LL, Francis DA, Foster RA, Berrington A. Use of color flow Doppler ultrasonography to diagnose a bleeding neuroendocrine tumor in the gallbladder of a dog. J Am Vet Med Assoc 2009;235:1326–1329.
8. Argenta FF, Pereira PR, Bertolini M, *et al.* Carcinoid of the gallbladder in two dogs. Ciênc Rural 2020;50:e20190445.
9. Tanaka T, Akiyoshi H, Hirata S, Shimada D, Nishida H. CT findings of bleeding from a canine gall bladder carcinoid tumour. Vet Rec Case Rep 2022;10:e420.
10. Modlin IM, Sandor A. An analysis of 8305 cases of carcinoid tumors. Cancer 1997;79:813–829.

The impact of skin preparation method on electrocardiogram quality in horses

Persephone McCrae, Hannah Spong, Amin Mahnam, Yana Bashura, Wendy Pearson

Abstract

Objective

Several skin preparation techniques are used in electrocardiogram (ECG) monitoring of horses. The objective of this study was to determine which methods produce the greatest signal quality using textile electrodes and standard silver/silver chloride (Ag/AgCl) electrodes.

Animals and samples

Electrocardiogram data were collected using textile and Ag/AgCl electrodes simultaneously for 4 skin preparation techniques in 6 horses.

Procedure

The effects of skin preparation (cleansing with isopropyl alcohol, with or without shaving the hair) and the effects of the application of a conductive gel were assessed using metrics of signal quality.

Results

Shaving and cleansing with alcohol had no effect on signal quality for either electrode type. The Ag/AgCl electrodes contain a solid gel, and the application of additional gel did not affect signal quality. Data quality was significantly improved when gel was applied to textile electrodes. Furthermore, there was no difference in signal quality between electrode types when gel was used.

Conclusion and clinical relevance

This study suggests that skin preparation by cleansing and/or shaving does not have a significant effect on equine ECG signal quality. When gel is used, textile electrodes are a practical alternative for Ag/AgCl electrodes, as they produce ECG recordings of the same quality.

Résumé

Impact de la méthode de préparation de la peau sur la qualité de l'électrocardiogramme chez le cheval

Objectif

Plusieurs techniques de préparation de la peau sont utilisées lors de la surveillance électrocardiographique (ECG) des chevaux. L'objectif de cette étude était de déterminer quelles méthodes produisent la meilleure qualité de signal en utilisant des électrodes textiles et des électrodes standard argent/chlorure d'argent (Ag/AgCl).

Animaux et échantillons

Les données d'électrocardiogramme ont été obtenues simultanément à l'aide d'électrodes textiles et d'électrodes Ag/AgCl pour 4 techniques de préparation cutanée chez 6 chevaux.

Procédure

Les effets de la préparation de la peau (nettoyage à l'alcool isopropylique, avec ou sans rasage des cheveux) et les effets de l'application d'un gel conducteur ont été évalués à l'aide de métriques de qualité du signal.

Department of Animal Biosciences, University of Guelph, 50 Stone Road East, Guelph, Ontario N1G 2W1 (McCrae, Spong, Pearson); Department of R&D, Myant Inc., 200 Ronson Drive, Suite 500, Etobicoke, Ontario M9W 5Z9 (Mahnam, Bashura).

Address all correspondence to Dr. Wendy Pearson; email: wpearson@uoguelph.ca

Résultats

Le rasage et le nettoyage à l'alcool n'ont eu aucun effet sur la qualité du signal pour les deux types d'électrodes. Les électrodes Ag/AgCl contiennent un gel solide et l'application de gel supplémentaire n'a pas affecté la qualité du signal. La qualité des données a été considérablement améliorée lorsque le gel a été appliqué sur des électrodes textiles. De plus, il n'y avait aucune différence dans la qualité du signal entre les types d'électrodes lorsque du gel était utilisé.

Conclusion et pertinence clinique

Cette étude suggère que la préparation de la peau par nettoyage et/ou rasage n'a pas d'effet significatif sur la qualité du signal ECG équin. Lorsque du gel est utilisé, les électrodes textiles constituent une alternative pratique aux électrodes Ag/AgCl, car elles produisent des enregistrements ECG de même qualité.

(Traduit par Dr Serge Messier)

Can Vet J 2024;65:245–249

Equine cardiac health is typically assessed using electrocardiography, auscultation, and echocardiography, although definitive diagnoses of arrhythmias require high-quality electrocardiogram (ECG) recordings (1). However, ECGs can be difficult to interpret due to the presence of motion artifacts (MAs), which are caused by changes in the electrode/skin potential, where the electrode moves against the skin or the skin stretches, affecting the distribution of charges between the electrolyte and electrode (2). The primary approach for minimizing the occurrence of MAs in ECGs is to improve the application of electrodes to the skin to reduce electrode movement and improve electrical conduction (2).

There are a variety of electrode types used to collect ECGs in horses, including crocodile clips, adhesive electrodes, and smart textile electrodes. Crocodile clips are attached directly to the skin, which can cause discomfort and are only appropriate for short-term use (1). Adhesive silver/silver chloride (Ag/AgCl) electrodes are more commonly used. These electrodes contain a solid gel and may require shaving of the hair depending on coat length (1). During prolonged recordings, Ag/AgCl electrodes may become detached from the skin and the solid gel may dry. To address these issues, textile electrodes, in which conductive yarns are knit directly into textiles, have been developed. Work previously conducted on horses at rest (3,4) and during exercise (5,6) has shown that textile electrodes can produce data of the same quality as Ag/AgCl electrodes, indicating that they are a practical alternative if designed and used properly. However, these studies used various methods of skin preparation and, perhaps as a result, reported a wide range of data quality.

Standard preparation in human cardiovascular monitoring includes shaving the hair, cleansing the skin, and drying (7). Preparation may also include abrasion using a fine sandpaper to remove the stratum corneum (7). Finally, Ag/AgCl electrodes are applied with a conductive gel for optimal signal quality (7). Similarly in dogs and cats, the hair is shaved, the skin is cleansed using alcohol, and an adhesive electrode (containing gel) is adhered to the skin (8). A combination of cast padding and adhesive bandages are applied to minimize electrode movement and detachment (8). In horses, preparation methods include using conductive gel and/or alcohol, both with and without shaving of the hair (1,9). Elastic and/or adhesive bandages or foam patches are often applied for extended recordings (1). However, there are no standard skin preparation methods for equine ECG data collection, and the most appropriate methods may vary with electrode type. Therefore, the objective of this study was to assess different skin preparation techniques for short-duration, resting ECGs obtained using standard Ag/AgCl electrodes and novel textile electrodes. Based on sample size calculations done using a confidence level of 0.05 and a power of 0.80 from pilot data, 6 healthy horses [5 standardbred, 1 Morgan; mares; median age: 15.5 y (range: 9 to 19 y)] without a history of cardiac abnormalities were recruited. The study was done in accordance with the University of Guelph Animal Utilization Protocol (reference No. 4705). Horses were housed separately in standard box stalls (3.66 m × 3.66 m) and were permitted to freely move around the stalls, as is standard for non-exercising ECGs. Horses were provided *ad libitum* access to hay and water throughout the study.

The ECGs were simultaneously collected using adhesive Ag/AgCl electrodes containing a solid gel (SKINTACT W-601; Leonhard Lang GmbH, Innsbruck, Austria) and dry textile electrodes composed of carbon- and silver-coated yarns (Skiin Equine; Myant, Toronto, Ontario). The 5 textile electrodes were integrated into a girth band in a modified base-apex configuration to construct a 3-lead trace (3,6). Five Ag/AgCl electrodes were placed immediately above the textile electrodes, under the band. Silver-coated yarns were knit into the textile band to connect the textile electrodes to the recording device, and cable wires were snapped directly to the button of the Ag/AgCl electrodes. Identical devices (Skiin Equine; Myant) were used to record ECGs from both types of electrodes at a sampling frequency of 320 Hz. Both electrode types were tested on all horses, with 4 different skin preparation techniques in the following order: i) unshaved hair, isopropyl alcohol (control); ii) unshaved hair, alcohol, and conductive gel (Spectra 360; Parker Laboratories, Fairfield, New Jersey, USA); iii) shaved hair, alcohol (control); iv) shaved hair, alcohol, and gel. The techniques were completed one immediately after the other, separated only by the time needed to perform each technique. Alcohol was applied to gauze for cleansing of each electrode site. Following data collection with gel, the gel was wiped from the skin before shaving. Shaving was completed using electronic equine clippers without a guard comb, to achieve a close shave. In the case of Ag/AgCl electrodes, additional gel was applied to the silver connection of the electrode for the gel condition. Textile electrodes did not contain any conductive medium and were therefore considered dry electrodes. For the gel condition, the conductive gel was applied to the surface of

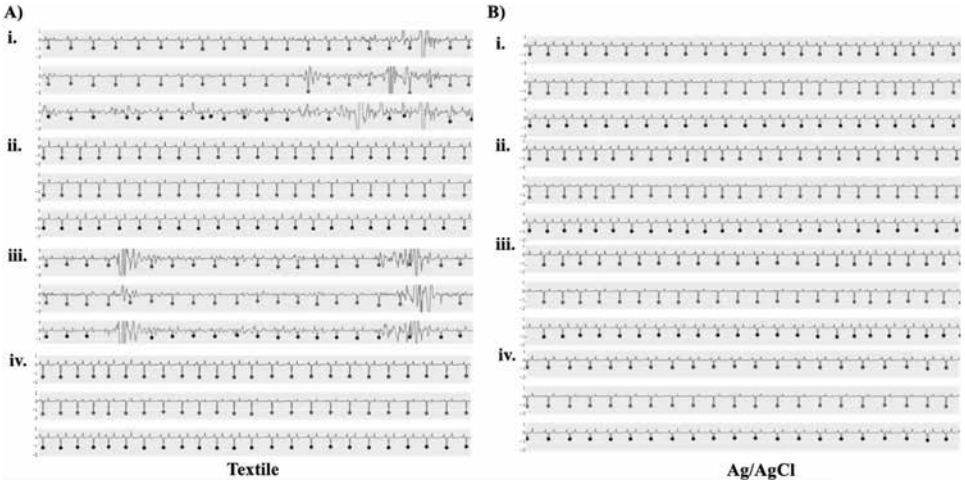


Figure 1. Three-lead electrocardiogram traces obtained from the same horse using textile electrodes (A) and Ag/AgCl electrodes (B), with preparation methods as follows: i) unshaved hair, isopropyl alcohol (control); ii) unshaved hair, isopropyl alcohol, and conductive gel; iii) shaved hair, isopropyl alcohol (control); iv) shaved hair, isopropyl alcohol, and conductive gel.

the textile electrode once the band was positioned on the horse. All electrodes (textile and Ag/AgCl) were replaced between testing conditions to prevent contamination. Data were collected for 10 min per condition and were transmitted *via* a Bluetooth connection to 2 mobile phones for later analysis. Electrocardiogram data were analyzed using a custom Python script; data were filtered to remove baseline, high-frequency, and power-line noise, as has previously been described (3,5). Signal quality was assessed using kurtosis (k), kurtosis signal quality index (kSQI), and the percentage of MAs (%MA). Kurtosis is an excellent indicator of ECG signal quality, as the distribution of peaks is compared to a Gaussian distribution (10). Kurtosis values > 5 indicate good signal quality, whereas k values < 5 indicate the presence of MAs (5,10). The kSQI was calculated by dividing the number of windows where the k value was > 5 by the total number of windows, for a maximum value of 1 (5,11,12). The %MA was calculated by manually counting the duration of segments where P-waves and/or QRS complexes were not identified. Data from each electrode type were averaged across the 3 channels for a single value. The assumptions of normality and equal variance were assessed using Kolmogorov-Smirnov tests. Kurtosis and kSQI data were determined to be normally distributed and are presented as mean $\pm$ standard deviation. Repeated measures 2-way ANOVAs with Tukey multiple comparison tests were run. Data considered not to be of diagnostic value ($> 10\%$ MAs) were excluded from statistical analysis. All tests were run using GraphPad Prism (9.1.0) software (Dotmatics, Boston, Massachusetts, USA) with statistical significance set at $P \leq 0.05$.

Overall, skin preparations of shaving and/or cleansing with alcohol did not significantly affect ECG signal quality for either electrode type when tested on unrestrained, resting horses (Figure 1 A, B). Shaving of the hair was not shown to have an effect for either electrode type for any of the metrics assessed. There was an effect of conductive gel for textile electrodes, where signal noise that obscured P-waves and/or QRS complexes was observed with dry electrodes (Figure 1 A). Good signal quality was observed, with median k values above the optimal value of 5 for all conditions tested, except when textile electrodes were used without gel (Figure 2 A, B). When values obtained for unshaved and shaved conditions were pooled, the average k values were 20.01 ± 4.46 and 6.31 ± 2.51 for textile electrodes used with and without conductive gel, respectively; and 17.10 ± 3.53 and 15.83 ± 5.79 for Ag/AgCl electrodes used with and without additional gel, respectively. Similarly, average pooled kSQI values were close to the maximum value of 1 when conductive gel was used for both electrode types (textile: 0.96 ± 0.05, Ag/AgCl: 0.96 ± 0.06) but were significantly lower when gel was not used with textile electrodes (0.44 ± 0.15) (Figure 2 C). However, no differences in kSQI were observed with Ag/AgCl electrodes when no additional gel was applied to the electrode (0.95 ± 0.07) (Figure 2 D). The %MA was very low for both electrode types when conductive gel was used: 0.25% (range: 0 to 1.05%) and 0% (range: 0 to 0.73%) for textile and Ag/AgCl electrodes, respectively. However, when textile electrodes were used without gel, the %MA was greater than 10% and was deemed not to be of diagnostic value. In comparison, when Ag/AgCl electrodes were used without additional gel, the %MA was much lower, at 0% (range: 0 to 0.49%).

No significant differences were appreciated between the 2 electrode types for any of the 3 metrics when gel was used. However, when gel was not used, the k values for textile electrodes were 56% ($P = 0.03$) and 64% ($P = 0.02$) lower than those for Ag/AgCl in the unshaved and shaved conditions, respectively. Similarly, textile kSQI values without gel were 49% ($P = 0.001$) and 59% ($P = 0.01$) lower for unshaved and shaved conditions, respectively. For all horses, ECGs obtained with dry textile electrodes were considered not to be of diagnostic value, with %MA values exceeding 10%, whereas all ECGs obtained with Ag/AgCl electrodes had low degrees of MAs when additional gel was not used.

The results of this study indicate that the preparation methods that produce high-quality ECGs are dependent on the

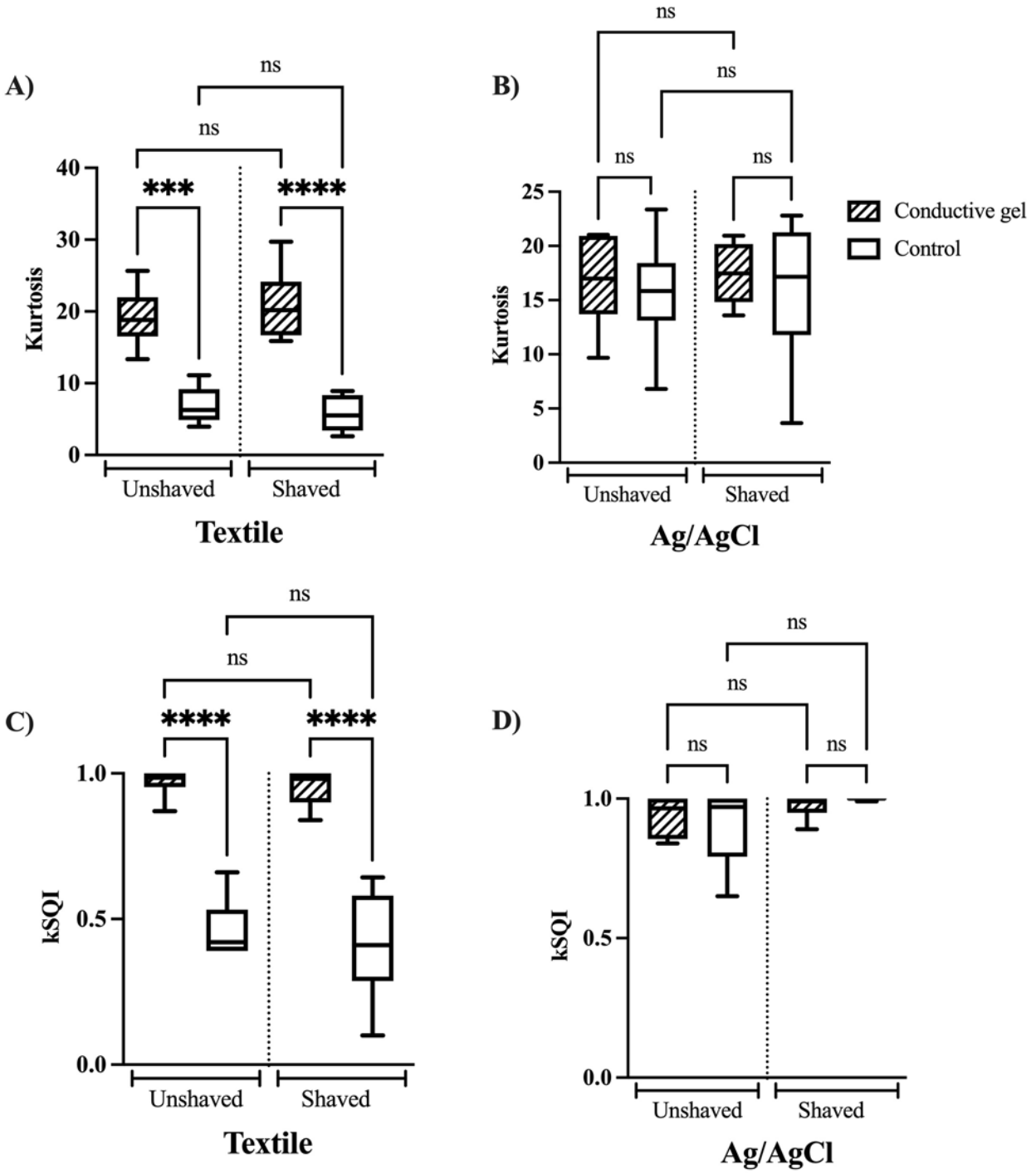


Figure 2. Kurtosis (A, B) and kSQI (C, D) values for electrocardiograms obtained from horses using smart textile and Ag/AgCl electrodes, with no conductive medium (control; white bars) and electrically conductive gel (hatched bars), with and without shaving of the hair.

ns – No statistical significance ($P > 0.05$).
*** $P < 0.001$, **** $P < 0.0001$.

type of electrode used. With textile electrodes, the presence of a conductive medium had a strong effect on signal quality. Application of additional gel to Ag/AgCl electrodes did not affect any of the metrics assessed, indicating that gel already present in the electrode was sufficient, as has previously been suggested by Petrie for canine and feline ECGs (8). In comparison, textile electrodes are manufactured without any conductive medium, and the medium added must be able to sufficiently saturate both the skin and the electrode during recording. Previous work with textile electrodes has been conducted on horses, where alcohol was applied between the skin and electrode without shaving (9). However, variable data quality was observed, with kSQI values ranging from 0.3 to 0.9 during exercise on a treadmill (walk, trot, gallop) (5) and an average of

35% of the data corrupted by MAs at rest (4). In comparison, we previously observed < 0.5% of data being corrupted by MAs when gel was used with textile electrodes in resting horses (3). These differences in data quality are likely attributed to multiple factors. The present results indicate that, although skin preparation techniques of shaving and cleansing may not be required, dry textile electrodes are not suitable for equine ECG recordings. Therefore, it is recommended that alcohol alone not be used with textile electrodes, as evaporation leads to a dry electrode, resulting in reduced signal quality over time. It is important to note that this study did not evaluate ECG quality over an extended duration and was conducted only in resting horses. Further work is necessary to understand how signal quality may change over time or in the context of exercise. Additionally, no effect of shaving was observed for either electrode type when data were collected from horses with medium-length coats (autumn in Canada). Therefore, although we did not observe an effect of shaving, a difference may be appreciated when a very thick coat is present, particularly for certain breeds, such as Icelandic horses (1). In these cases, shaving may be warranted to ensure sufficient contact between the skin and electrode. However, when a thin-to-moderate haircoat is present, shaving is not necessary when using textile or Ag/AgCl electrodes.

As we previously observed in horses at rest and during submaximal exercise (3,6), there were no significant differences in signal quality between textile and Ag/AgCl electrodes when conductive gel was used. This indicates that textile electrodes are a practical and reliable alternative to adhesive Ag/AgCl electrodes for short-duration resting ECGs. Further work is required to determine if this is also the case for prolonged recordings and during exercise.

Acknowledgment

The authors thank Myant Inc. for providing the equine smart textile equipment. CVJ

References

1. Mitchell KJ. Equine electrocardiography. Vet Clin North Am Equine Pract 2019;35:65–83.
2. Lanata A, Guidi A, Baragli P, Valenza G, Scilingo EP. A novel algorithm for movement artifact removal in ECG signals acquired from wearable systems applied to horses. PLoS One 2015;10:e0140783.
3. McCrae P, Spong H, Rutherford AA, Osborne V, Mahnam A, Pearson W. A Smart textile band achieves high-quality electrocardiograms in unrestrained horses. Animals 2022;12:3254.
4. Guidi A, Lanata A, Valenza G, Scilingo EP, Baragli P. Validation of smart textile electrodes for electrocardiogram monitoring in free-moving horses. J Vet Behav 2017;17:19–23.
5. Felici M, Nardelli M, Lanatà A, Sgorbini M, Scilingo EP, Baragli P. Smart textiles biotechnology for electrocardiogram monitoring in horses during exercise on treadmill: Validation tests. Equine Vet J 2021; 53:373–378.
6. McCrae P, Spong H, Golestani N, Mahnam A, Bashura Y, Pearson W. Validation of an equine smart textile system for heart rate variability: A preliminary study. Animals 2023;13:512.
7. Oster CD. Proper Skin Prep Helps Ensure ECG Trace Quality. St. Paul, Minnesota: 3M Health Care, 2005. Available from: http://multimedia.3m.com/mws/media/358372O/proper-skin-prep-ecg-trace-quality-white-paper.pdf Last accessed January 3, 2024.
8. Petrie JP. Practical application of holter monitoring in dogs and cats. Clin Tech Small Anim Pract 2005;20:173–181.
9. Gatti L, Holmes JR. ECG recording at rest and during exercise in the horse. Equine Vet Educ 1990;2:28–30.
10. Li Q, Mark RG, Clifford GD. Robust heart rate estimation from multiple asynchronous noisy sources using signal quality indices and a Kalman filter. Physiol Meas 2008;29:15–32.
11. Clifford GD, Behar J, Li Q, Rezek I. Signal quality indices and data fusion for determining clinical acceptability of electrocardiograms. Physiol Meas 2012;33:1419–1433.
12. Scilingo EP, Gemignani A, Paradiso R, Taccini N, Ghelarducci B, De Rossi D. Performance evaluation of sensing fabrics for monitoring physiological and biomechanical variables. IEEE Trans Inf Technol Biomed 2005;9:345–352.

Article

Comparison of virus-neutralizing and virus-specific ELISA antibody responses among bovine neonates differentially primed and boosted against bovine coronavirus

Nathan E.N. Erickson, Stacey Lacoste, Michelle Sniatynski, Cheryl Waldner, John Ellis

Abstract

Objective

This study addressed the current gap in knowledge of neonatal prime-boost immune responses for the control of bovine coronavirus (BCoV) respiratory disease in weaning-age beef cattle.

Animals

Study 1 and Study 2 had 33 and 22 commercial cross neonatal beef calves, respectively.

Procedures

Study 1 compared BCoV-neutralizing antibody concentrations of control calves with 3 groups of calves differentially vaccinated with mucosal and/or systemic BCoV modified live virus (MLV) vaccines. Study 2 compared specific and neutralizing antibody concentrations among mucosally BCoV primed groups of calves that were differentially systemically boosted.

Results

In Study 1, calves that were mucosally primed and systemically boosted had higher BCoV-neutralizing antibody concentrations than the control group at weaning. In Study 2, boosting mucosally primed calves by injecting inactivated or MLV vaccine resulted in anamnestic BCoV-specific antibody responses at weaning.

Conclusion

Neonatal mucosal priming and systemic boosting resulted in anamnestic BCoV antibody responses at weaning.

Clinical relevance

Prime-boost vaccination should be considered for control of BCoV respiratory disease.

Résumé

Comparaison des réponses en anticorps ELISA neutralisant le virus et spécifiques du virus chez des nouveau-nés bovins vaccinés par amorces-rappels différenciés contre le coronavirus bovin

Objectif

Cette étude a abordé le manque actuel de connaissances sur les réponses immunitaires néonatales de stimulation pour maitriser la maladie respiratoire à coronavirus bovin (BCoV) chez les bovins de boucherie en âge de sevrage.

Animaux

Les études 1 et 2 portaient respectivement sur 33 et 22 veaux de boucherie néonatals croisés commerciaux.

Procédures

L'étude 1 a comparé les concentrations d'anticorps neutralisant le BCoV de veaux témoins avec 3 groupes de veaux vaccinés de manière différentielle avec des vaccins à virus vivant modifié (MLV) contre le BCoV pour administration par voie mucosale et/ou systémique. L'étude 2 a comparé les concentrations d'anticorps spécifiques et

Department of Large Animal Clinical Sciences (Erickson, Lacoste, Waldner) and Department of Microbiology (Sniatynski, Ellis), Western College of Veterinary Medicine, 52 Campus Drive, Saskatoon, Saskatchewan S7N 5B4; Vaccine and Infectious Disease Organization, 120 Veterinary Road, Saskatoon, Saskatchewan S7N 5E3 (Sniatynski).

Address all correspondence to Dr. Nathan Erickson; email: Nathan.erickson@usask.ca

Sources of support: Government of Saskatchewan Department of Agriculture, Saskatchewan Cattlemen's Association, Alberta Beef Producers, Western College of Veterinary Medicine.

neutralisants parmi des groupes de veaux sensibilisés au BCoV par voie mucosale et qui ont eu un rappel par voie systémique différentielle.

Résultats

Dans l'étude 1, les veaux qui avaient reçu une amorce au niveau des muqueuses et un rappel systémique présentaient des concentrations d'anticorps neutralisant le BCoV plus élevées que le groupe témoin au sevrage. Dans l'étude 2, le rappel des veaux amorcés par voie mucosale par l'injection d'un vaccin inactivé ou MLV a entraîné une réponse anamnestique en anticorps spécifiques du BCoV au sevrage.

Conclusion

En période néonatale, l'amorce par voie mucosale et le renforcement systémique ont entraîné des réponses anamnestiques en anticorps BCoV au sevrage.

Pertinence clinique

La vaccination de rappel doit être envisagée pour maitriser la maladie respiratoire causée par le BCoV.

(Traduit par Dr Serge Messier)

Can Vet J 2024;65:250–258

Introduction

Bovine coronavirus (BCoV) is strongly associated with bovine respiratory disease (BRD) in calves near the weaning phase of their production cycle (1–5). Calves shedding BCoV upon feedlot arrival are more likely to require treatment for BRD and to have lung lesions at slaughter than nonshedders (2,6). There are limited data that serum antibody titers to BCoV might be a marker for protection against BCoV respiratory disease, indicating that induction of humoral immunity could be important for control of BCoV respiratory disease (3). The importance of BCoV was further supported by evidence that intranasal administration of a modified live virus BCoV vaccine conferred a reduced risk of BRD treatment among calves vaccinated at arrival to the feedlot (2).

Although ELISA and virus neutralization (VN) tests are both commonly used to measure antibody concentrations when studying responses to vaccination (7–9), they potentially measure immune responses differently. In previous reports, ELISA for BCoV generally had higher antibody concentrations than VN (10). This could be because ELISA, using whole virus as the antigen, generally detects the total virus-specific antibody, including antibodies to internal structural and nonstructural proteins, whereas VN tests primarily measure responses to envelope glycoproteins that are targets for neutralizing antibody (11,12). Therefore, whereas ELISA will indicate whether a virus-specific antibody response to an exposure such as vaccination occurred, it does not provide information regarding the functional nature of the antibody or whether the antibody measured by ELISA was protective or not. Using both types of assays can provide a better understanding of response to vaccination.

Understanding the nature of antibody responses is important due to potential negative consequences associated with ineffective or muted antibody responses. For example, antibody-dependent enhancement of disease (ADE) can result when antibody concentrations are either not specific to protective epitopes or not in sufficient concentration to provide protection, facilitating virus entry or enhancing inflammatory responses (13,14). These ADE-associated phenomena have been observed in human responses to respiratory syncytial virus and Dengue fever virus infections, and in cats with the coronavirus that causes feline infectious peritonitis (FIPV) (14).

Immunization of neonatal beef calves is complicated by the presence of high concentrations of circulating maternal antibodies that interfere with immune response to systemically delivered vaccines (15,16). Recently developed and adopted, mucosal vaccines successfully induce protective immunity when administered to neonatal calves, even in the face of maternal antibodies (17). However, whereas the protective immunity engendered in mucosally vaccinated seropositive neonatal calves aids in the control of disease at a young age, duration of protective immunity does not necessarily persist to the high-risk preweaning or weaning periods (18,19). Although protection offered by mucosal vaccination is probably short in duration (20), mucosal priming is important for development of immunity toward viral BRD pathogens such as bovine respiratory syncytial virus (BRSV) and bovine herpes virus type 1 (BoHV-1) (18,21). The use of injectable vaccines to boost mucosal priming results in more robust immunity at weaning than vaccination with injectable vaccines alone (21). However, the magnitude of the humoral response in mucosally primed-systemically boosted calves varies among viruses based on the choice of an inactivated *versus* modified live virus booster vaccine (9,21).

Evidence regarding protection from BRD associated with vaccination against BCoV is limited, specifically regarding the effectiveness of various approaches to prime-boost vaccination of neonatal calves. The current study addressed these deficiencies by comparing differential virus-specific and -neutralizing antibody responses between control calves and calves administered various regimes using commercially available BCoV vaccines.

Materials and methods

Calves and enrollment

Calves were spring-born to beef herds managed commercially in western Canada.

Study 1. Neonatal Red Angus–Simmental cross calves were enrolled, at ~24 h of age, into 1 of 4 groups: control (no vaccine) (CON, $n = 8$); intranasal (IN) birth only (IN-BO, $n = 9$); intramuscular (IM) prime at turnout — boost (IM, $n = 8$)

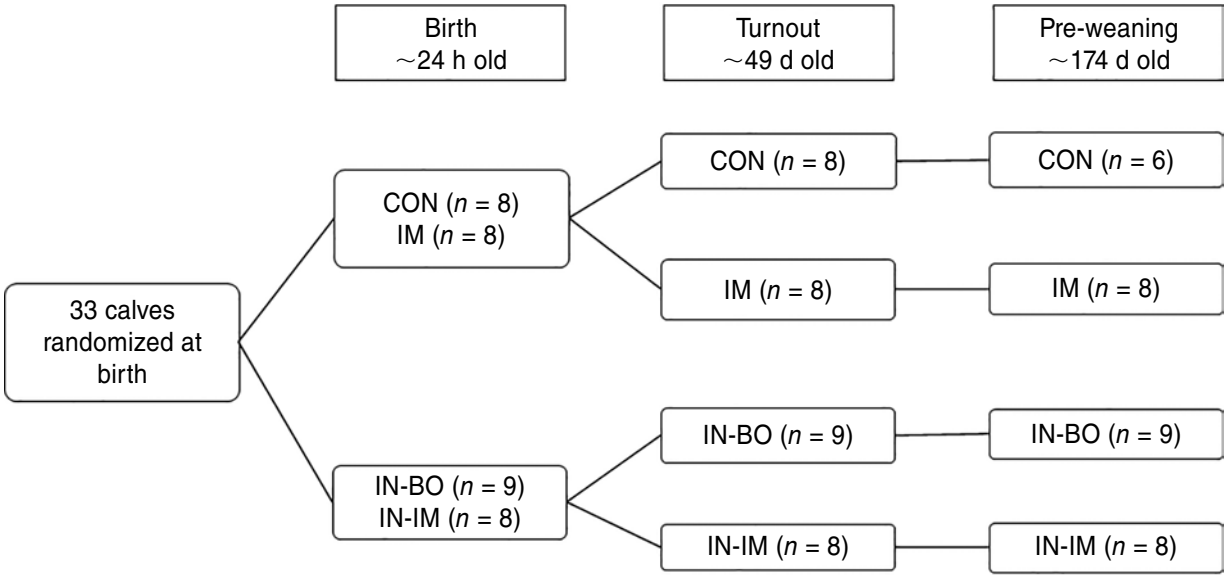


Figure 1. Study group outline for Study 1.
CON – Control group; IM – Intramuscular only group; IN-BO – Intranasal only group; IN-IM – Intranasal prime-intramuscular boost group.

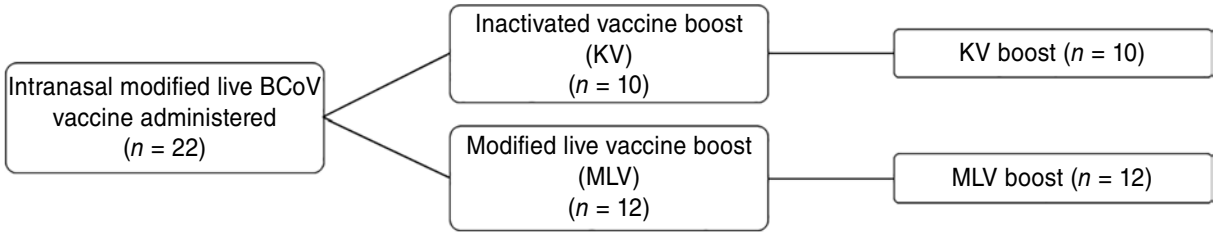


Figure 2. Study group outline for Study 2.
BCoV – Bovine coronavirus; KV – Inactivated vaccine; MLV – Modified live vaccine.

pre-weaning (no vaccine at birth); IN prime at birth — IM boost at turnout and pre-weaning (IN-IM, *n* = 8) (Figure 1). Calves were randomly assigned to a treatment group through use of a random number generator (Excel; Microsoft Corporation, Redmond, Washington, USA). Calves were enrolled sequentially by birth order into the treatment list sequence. The vaccines were administered at times when commercial operations typically vaccinate calves, including within the first day of birth, turnout (22,23) (when cow-calf pairs are moved to summer pasture), and pre-weaning.

Calves and their dams were managed as a single group from birth to weaning. Two calves were removed from the CON group: 1 calf was removed after turnout when the dam became lame and the pair had to be moved to another facility for the remainder of the summer, and the other was unaccounted for at weaning and is believed to have died unobserved on pasture; therefore, at the peri-weaning collection points, the CON group sample size was *n* = 6.

Study 2. Twenty-two commercial Black Angus neonatal heifer calves were enrolled at ~24 h of age. Calves were randomized into treatment groups (Figure 2) using a random number tool (Excel; Microsoft Corporation). Eleven calves were assigned to either an inactivated vaccine (KV) group or a modified live vaccine (MLV) boost group. One calf in the KV group was administered the wrong vaccine and was moved to the MLV group. The calves and their dams were managed as a single group and were comingled on pasture throughout the summer pasture season with pairs of cattle that were not included in the trial.

Vaccination and sample collection

Study 1. An IN vaccine containing modified live bovine coronavirus (BCoV) and bovine rotavirus (Calfguard; Zoetis Canada, Kirkland, Quebec), 3 mL, was administered into the left nostril of calves enrolled in the IN-BO and IN-IM groups within 24 h after birth *via* a nasal cannula attached to a 5-milliliter syringe (Figure 1). The vaccine administered is commercially available for oral and IM routes; therefore, this was a novel route of administration for this vaccine.

The second vaccine administration occurred when the calves were 49 d of age (turnout) [standard deviation (SD): 11 d]. Calves enrolled in the IM and IN-IM groups had 3 mL of the same vaccine administered by IM injection into the neck. The final vaccine was administered to the IM and IN-IM groups pre-weaning, when the calves' average age was 174 d [SD: 10 d] (Figure 1). At turnout, the calves also were administered 2-milliliter doses of MLV vaccine containing BRSV, BoHV-1,

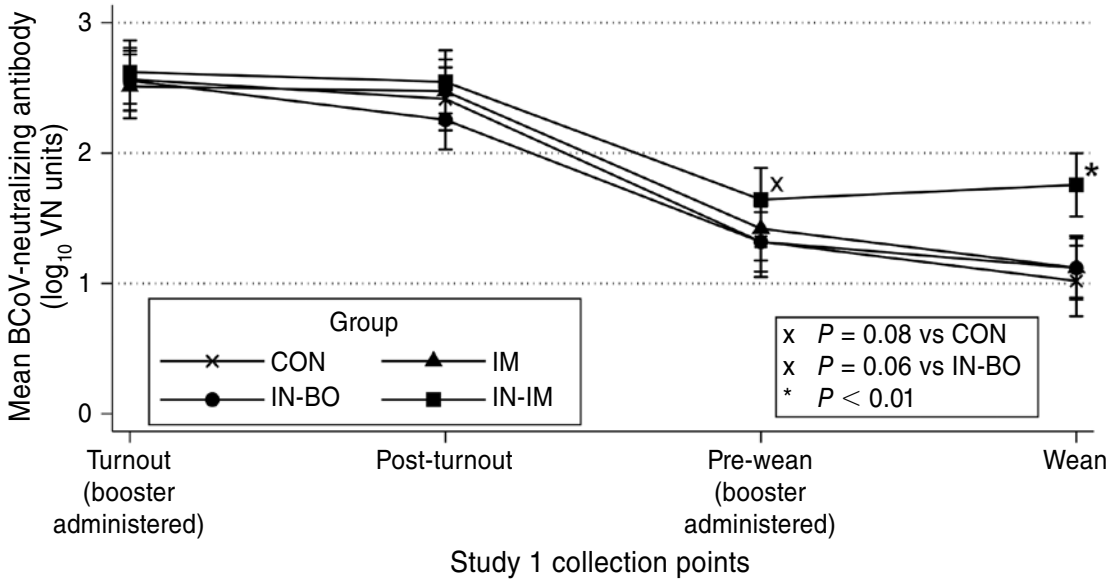


Figure 3. Comparison of Study 1 predicted mean bovine coronavirus (BCoV)-neutralizing antibody concentration, with 95% confidence intervals, for a model that included group, collection point, and day of birth BCoV antibody concentration as cofactors.

CON – Control group; IM – Intramuscular only group; IN-BO – Intranasal only group; IN-IM – Intranasal prime-intramuscular boost group; VN – Virus neutralization.

BPI3, BVDV Types-1 and -2, and inactivated *Mannheimia haemolytica* (Bovi-shield Gold Oneshot; Zoetis Canada), by subcutaneous injection, as part of the herd-management protocol.

Venous blood was collected from each calf by jugular venipuncture into a 5-milliliter serum tube within 24 h after birth, at turnout vaccination, 14 d post-turnout vaccination, at preweaning vaccination, and 14 d after preweaning vaccination. Blood samples were stored in a refrigerator until they were centrifuged at between 900 and 1127 × *g* for 10 min. Serum was collected and stored at −20°C.

Study 2. Within 24 h after birth, all 22 calves were vaccinated IN with the same BCoV vaccine used in Study 1 (Figure 2). As part of the herd-management protocol, the calves also received an IN dose (2 mL) of MLV vaccine containing BRSV, BoHV-1, and BPI3 (Inforce 3; Zoetis Canada).

Calves were next vaccinated at turnout, when they were an average age of 42 d (SD: 7 d). Calves assigned to the KV group (n = 10) received a dose of inactivated vaccine containing antigens for BCoV, bovine rotavirus, *E. coli* K99, and *Clostridium perfringens* (Scourguard 4KC; Zoetis Canada), 2 mL by IM injection; calves in the MLV group (n = 12) received a 3-milliliter dose of an MLV vaccine (Calfguard; Zoetis Canada). At weaning, calves (mean age: 170 d) were boosted a second time using the same vaccine and route that they received at turnout. At turnout and weaning, calves received a dose of MLV vaccine containing BRSV, BoHV-1, BPI3, BVDV Types-1 and -2, and inactivated *Mannheimia haemolytica* (Bovi-shield Gold Oneshot; Zoetis Canada), 2 mL by subcutaneous injection, as part of the regular herd-management protocol.

Blood samples were collected in the same manner as for Study 1, from all calves, at turnout vaccination, day of weaning vaccination, and 14 d post-weaning vaccination.

Virus microneutralization (VN) assay (Study 1 and Study 2)

A microneutralization assay to detect BCoV-neutralizing antibodies was completed using a field isolate of BCoV and standard procedures (9), with validated, in-house protocols, at the Animal Health Laboratory, University of Guelph (Guelph, Ontario). In Study 1, VN was the only method used to measure antibody responses, whereas Study 2 used this method only for the 14 d post-weaning sera, to enable comparison with antibody (IgG) concentrations determined by ELISA.

ELISA for bovine coronavirus-reactive antibodies (Study 2)

An indirect ELISA for BCoV-reactive antibodies was completed following standard procedures (9) on sera collected from calves in Study 2 at 3 collection points. Briefly, BCoV antigen was sucrose density-gradient-purified from infected human rectal carcinoma (HRT) cells infected with a field isolate of BCoV from Saskatchewan. Tissue culture control antigen was similarly prepared from uninfected HRT cells. Optimal concentrations of antigens coated on to 96-well ELISA plates (Immunlon-4HBX; Thermo Fisher Scientific, Waltham, Massachusetts, USA) were determined in a checkboard analysis using positive and negative control sera. Sera were tested at a dilution of 1/50. Binding of primary antiserum was detected using a 1/5000 dilution of peroxidase-conjugated *(Staphylococcus)* protein G (Invitrogen, Waltham, Massachusetts, USA), that binds to IgG of numerous species, including cattle and humans (13). This was followed by reaction with an ABTS [2,2′-azino-bis(3-ehtylbenzothiazoline-6-sulfonic acid)] substrate (SeraCare Life Sciences, Milford, Massachusetts, USA). Optical densities (OD) were read at 415 nm on an automated ELISA reader (iMark; Bio-Rad

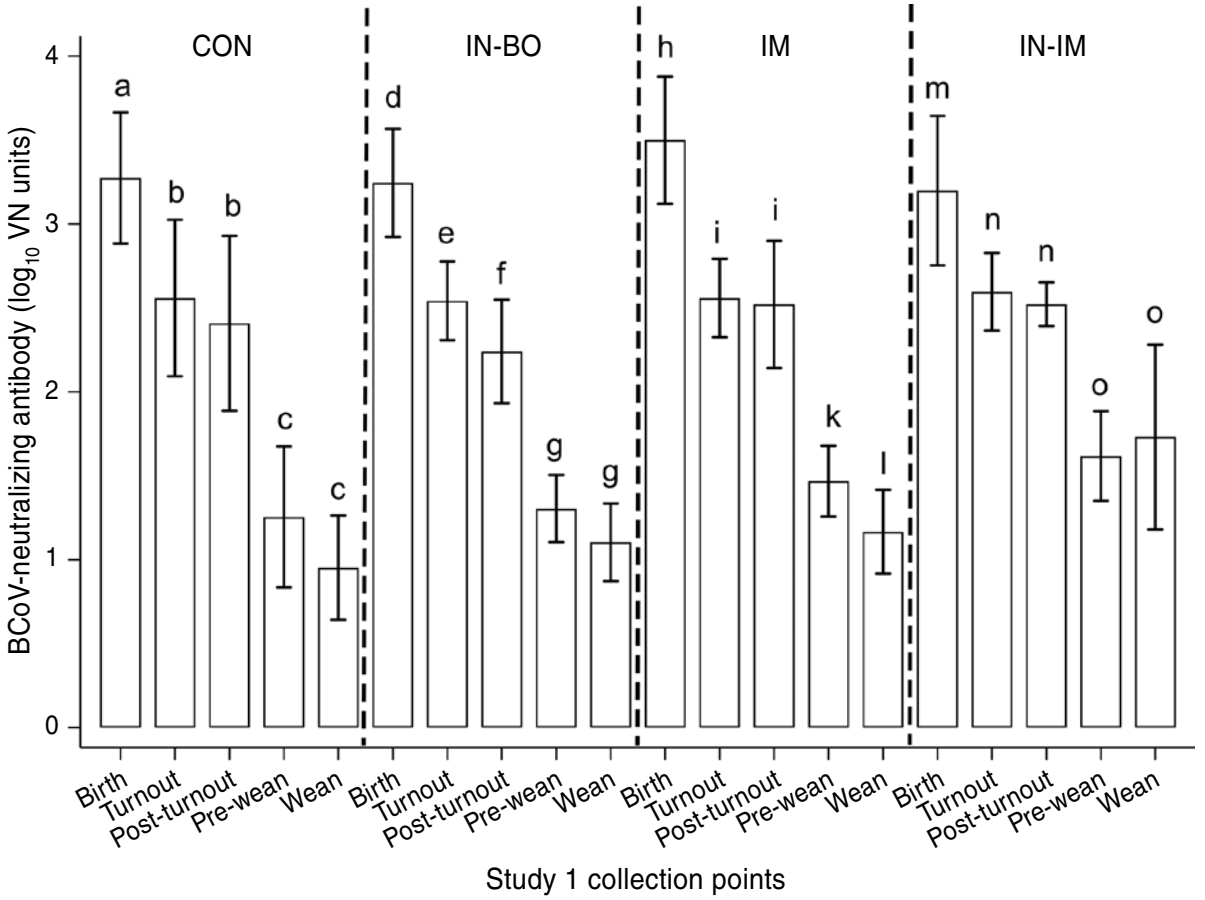


Figure 4. Comparison of Study 1 within-groups change in mean bovine coronavirus (BcoV)-neutralizing antibody concentration by collection point.

CON – Control group; IM – Intramuscular only group; IN-BO – Intranasal only group; IN-IM – Intranasal prime-intramuscular boost group; VN – Virus neutralization.

[a–o] Within each group, letters indicate a difference ($P \leq 0.05$) from the previous data point.

Laboratories, Mississauga, Ontario). The ELISA "units" were calculated as follows (9):

$$\frac{\text{Net OD test sample (OD antigen} - \text{OD tissue culture control)}}{\text{Net OD positive control serum (OD antigen} - \text{OD tissue culture control)}} \times 100 = \text{units}$$

The positive control serum (A/S) from a mature cow with high reactivity in ELISA for BCoV was considered as 100 units.

Statistical methods

Data were evaluated using a commercial software program (Stata 15; StataCorp, College Station, Texas, USA). The Shapiro-Wilk test of normality was applied to BCoV-reactive antibodies, as determined from ELISA and VN assays, and indicated the data were not normally distributed. Both ELISA and VN antibody concentrations were transformed by $\log_{10}$ before statistical analysis. Interaction terms between treatment and collection time were included in all models as design variables, reflecting study objectives.

Study 1. Differences in mean $\log_{10}$ BCoV VN antibody concentration among treatments and collection times were compared using generalized estimating equations (GEE). The GEE included treatment, collection time point, and a treatment*collection time interaction term as main effects; mean $\log_{10}$ BCoV antibody concentration on the day of birth was used as a cofactor. The GEE used a Gaussian distribution, identity link, and exchangeable correlation; calf ID was used as the repeating subject. The relative differences between the control group and each vaccine group were observed by collection point (turnout, post-turnout, pre-wean, and wean) using pairwise comparison. Estimations of relative difference between the IN-IM group and both IN-BO and IM groups were also made for the weaning collection point. The relative differences between collection points from birth to weaning were also estimated for each treatment group. Differences with a *P*-value ≤ 0.05 were considered statistically significant.

Pearson correlation was used to investigate the relationship between BCoV VN antibody concentration on day of birth and post-weaning booster vaccination by treatment group. Negative or positive correlations with *P*-values ≤ 0.05 were considered statistically significant. Correlations were considered strong if > 0.5.

Study 2. Differences among the mean $\log_{10}$ BCoV-specific ELISA antibody concentration were compared between KV and MLV groups using GEE as in Study 1, with the same main

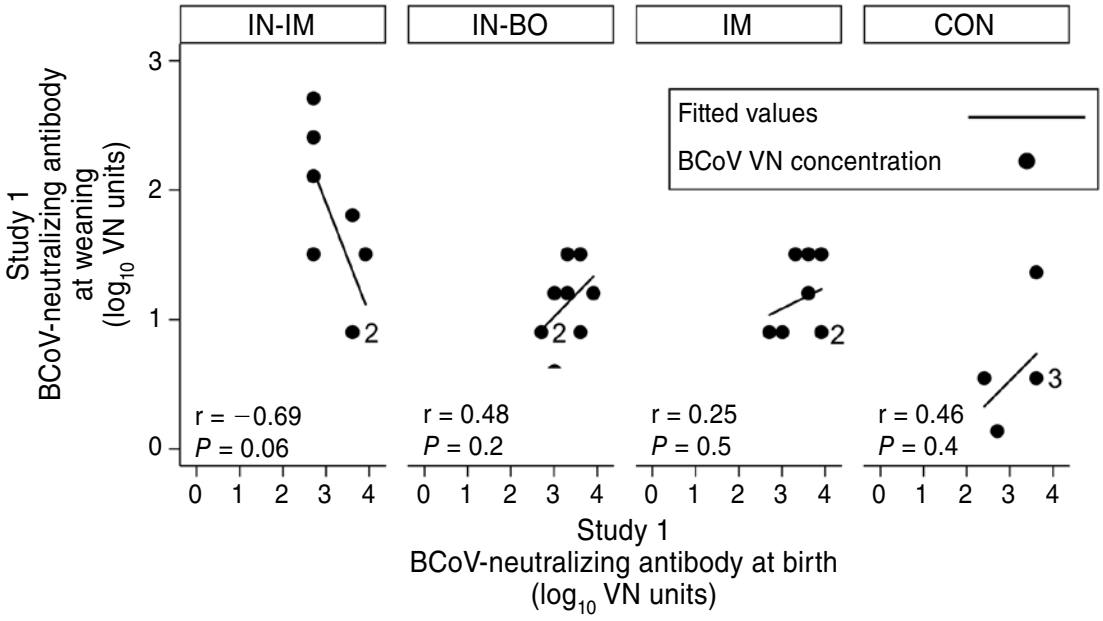


Figure 5. Scatter matrix of Study 1 bovine coronavirus (BCoV)-neutralizing antibody concentration at birth and weaning.

CON – Control group; IM – Intramuscular only group; IN-BO – Intranasal only group; IN-IM – Intranasal prime-intramuscular boost group; VN – Virus neutralization.

Numbers beside data point markers indicate numbers of calves represented by the data points.

effects but no additional cofactors. Within-group changes in mean $\log_{10}$ BCoV-specific ELISA antibody concentration were also compared using the same equation. The difference in mean $\log_{10}$ BCoV VN antibody concentration between the KV and MLV groups at 2 wk post-weaning vaccination was estimated using simple linear regression.

The relationship between BCoV-reactive ELISA and BCoV VN antibody concentration was investigated using Kendall's tau-b, based on a rank correlation with a Bonferroni adjustment for significance levels. A positive value of Kendall's tau-b indicates that, as one test's result increases, so does the other test's; and the closer to 1, the greater the correlation. Tests were considered correlated when $P \leq 0.05$.

Results

Study 1

The mean antibody BCoV VN concentrations for the treatment groups were not significantly different from those for the CON group at turnout, post-turnout, or pre-weaning (Figure 3). The absence of differences in antibody concentrations at turnout indicated that there was likely no induction or minimal induction of a systemic antibody production by neonatal IN vaccination. However, the BCoV VN antibody concentration for the IN-IM group was higher ($P < 0.01$) than for the CON group at weaning, indicating that a mucosal prime-systemic boost combination might be effective in priming neonates for subsequent boosting responses at weaning. Also, at weaning, the IN-IM group had higher BCoV VN concentration than both the IN-BO and IM groups ($P < 0.01$).

The highest mean BCoV VN antibody concentrations for all 4 groups were observed at birth, likely indicating maternal antibody transfer (Figure 4). The antibody concentration decreased between birth and turnout (mean age: 49 d) in all 4 groups. However, trends of within-group response began to diverge after turnout. Post-turnout, only the IN-BO group had a significant ($P = 0.03$) reduction in BCoV VN antibody concentration. Pre-weaning (mean calf age: 174 d), each group had a decrease ($P < 0.01$) in BCoV VN antibody concentration from post-turnout. At weaning, the IM group had a decrease in BCoV VN antibody concentration ($P = 0.05$).

Within the IN-IM group, calves with lower BCoV VN antibody concentrations at birth appeared to have higher BCoV VN concentrations at weaning (Figure 5). However, this same relationship between day of birth and weaning BCoV VN concentration was not present among calves in the CON, IN-BO, or IM groups. The BCoV VN antibody concentration at birth did not differ among the 4 treatment groups ($P > 0.3$). The day of birth and day of weaning BCoV VN antibody concentrations were not correlated for any treatment group. However, interestingly, the IN-IM group differed from the other treatment groups with regard to direction of the Pearson correlation (r) value; specifically, the IN-IM group had a strong negative r value (−0.69, $P = 0.06$), whereas the CON, IM, and IN-BO groups had small or medium positive r values [0.46 ($P = 0.4$), 0.25 ($P = 0.5$), and 0.48 ($P = 0.2$), respectively].

Study 2

In Study 2, mean BCoV-specific ELISA antibody concentrations did not differ between KV and MLV groups at any of the 3 collection points (Figure 6). When within-treatment group change in mean $\log_{10}$ BCoV-specific antibody concentrations were observed, both treatment groups increased ($P < 0.01$)

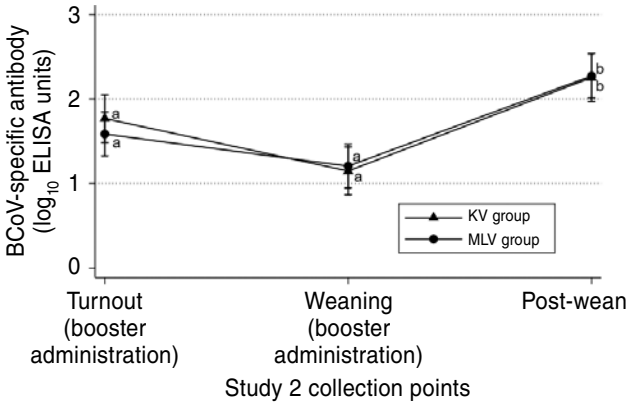


Figure 6. Comparison of Study 2 predicted mean bovine coronavirus (BCoV) ELISA antibody concentration, with 95% confidence intervals, for a model that included group and collection point as cofactors, between calves primed with intranasal vaccine at birth and differentially boosted with either a modified live vaccine (MLV) or an inactivated vaccine (KV).

[a,b] Within each group, letters indicate a difference ($P \leq 0.05$) from the previous data point.

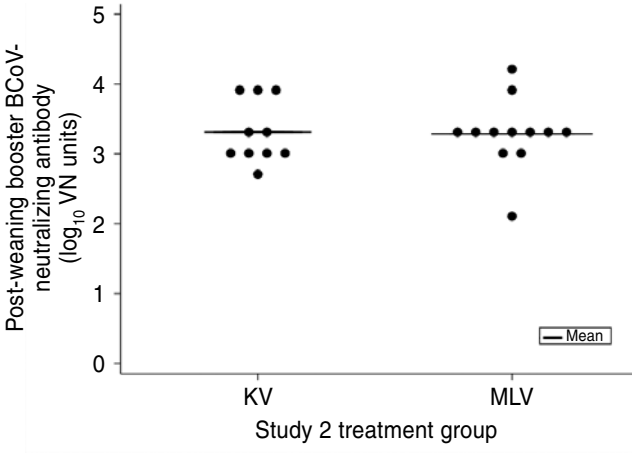


Figure 7. Comparison of Study 2 bovine coronavirus (BCoV)-neutralizing antibody concentration between calves primed with intranasal vaccine at birth and differentially boosted with systemic modified live vaccine (MLV) or inactivated vaccine (KV).

VN – Virus neutralization.

post-weaning. The increase in specific antibody concentration post-weaning indicated that both groups were previously primed and had an anamnestic response to the booster vaccine administered at weaning. Further to the ELISA results, both treatment groups had high concentrations of BCoV VN antibody at the postweaning collection point, indicating that both vaccine protocols induced functional antibody responses (Figure 7).

Antibody concentrations measured by BCoV-specific ELISA and VN were not correlated for either the KV (tau-b: 0.53, $P = 0.06$) or MLV (tau-b: 0.22, $P = 0.4$) groups (Figure 8). Altogether, these data suggested that both KV and MLV vaccines boosted IN-primed calves similarly, as indicated by similar anamnestic BCoV-specific antibody responses at weaning. Moreover, these data were consistent with those from Study 1, in which MLV systemic boosting of IN-primed calves was the

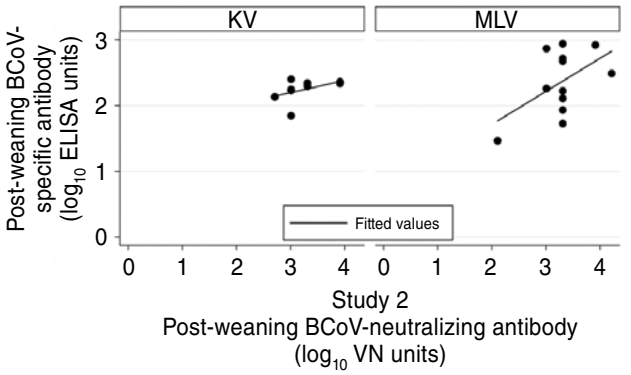


Figure 8. Scatter matrix comparing Study 2 bovine coronavirus (BCoV)-neutralizing (VN) and virus-specific (ELISA) antibody concentration 14 d after differentially boosting calves at weaning with either an inactivated vaccine (KV) or a modified live vaccine (MLV).

only protocol that resulted in a BCoV VN antibody response that was greater than that in the CON group.

Discussion

These data supported previous work showing that use of prime-boost vaccination, with a mucosal prime and systemic boosters, improved immune responses in seropositive neonatal calves (9,21). In a recent study, IN MLV priming vaccination of neonates induced an immune memory response that resulted in greater protection from disease challenge with BoHV-1 at weaning (18). In the BoHV-1 challenge study, groups primed with IN MLV and boosted at weaning age with either an IN or injectable MLV booster, had less weight loss and incidence of fever and greater survival than those not vaccinated at weaning age. It was reported that protection from BRSV challenge might be improved for neonates mucosally primed and boosted with either an MLV or KV vaccine compared to those not mucosally primed (9). Further support for IN neonatal prime-boost was observed in a study that considered differences in age and route of administration (19). Neonates with mucosal MLV vaccination had significantly higher neutralizing BVDV Type-1 antibody concentration after systemic MLV booster at weaning age than neonates MLV vaccinated systemically and boosted similarly at weaning age (19). Study 1 supported these previous findings, as the only treatment group in Study 1 that had a significant difference in BCoV VN antibody concentration was MLV mucosally primed and systemically boosted (IN-IM). Clearly, the difference in antibody concentration between the IN-IM and IM groups was important and demonstrated that IN priming, in the face of maternal antibody, enhanced development of BCoV immunity out to the weaning phase of calf production. Note that the previous BVDV study had a vaccine protocol that also used 2 systemic booster vaccinations, but these were both administered peri-weaning. In the current study, the first booster was administered at turnout and the second booster peri-weaning.

In contrast to previously published neonatal prime-boost data, in Study 1, BCoV VN antibody concentration at birth might be important for the magnitude of antibody response after booster vaccination at weaning. Specifically, for the IN-IM

group, there was a strong negative correlation between day of birth BCoV VN antibody concentration and post-booster weaning concentration. Interestingly, calves with lower day of birth BCoV VN antibody concentration appeared to have had higher concentrations after a second booster vaccine was administered at weaning.

The sample size *(n)* of Study 1 was too small to determine if a specific day of birth antibody concentration limited the probability of inducing a higher magnitude weaning booster antibody response. Therefore, the relationship between day of birth antibody concentration and booster antibody response should be further explored. For the IM group, the absence of a similar correlation between day of birth and post-weaning booster BCoV antibody concentration may provide insights into neonatal vaccine responses. The only difference between the IN-IM and IM groups was neonatal administration of mucosal vaccine at birth; therefore, these data indicated that IN priming probably affected the booster antibody response at weaning. Based on these findings, in the future, IN priming should be considered as a method of improving overall humoral herd immunity among calves, even though these data suggested that the antibody response might vary individually depending on the concentration of antibody on day of birth/first exposure to IN vaccine. Possibly there is a threshold of antibody concentration at birth that allows for some systemic priming response to an IN-administered vaccine and early building of immune memory that persists to weaning.

Based on existing data from neonatal mucosal prime-boost studies, immune responses could, in part, depend on the natural history of the virus being studied. In previous work, calves primed with MLV IN vaccine and boosted twice SC, at times and ages similar to those used in the current studies, had different antibody responses with regard to specific virus type; *i.e.,* BRSV *versus* BoHV-1 (21). For example, specific BRSV antibody responses were greater in calves primed IN and boosted SC with a KV vaccine compared to those primed similarly and boosted with an SC MLV vaccine. Similar IN prime differential SC boost vaccination showed limited difference between boosting vaccine types for BoHV-1, indicating possible variability in immune response to specific viruses. Also, BCoV-specific antibody responses observed in Study 2 were more similar to previous BoHV-1 findings, in that BCoV-specific antibody concentrations did not differ with regards to booster vaccine type.

In addition, BCoV-specific antibody concentrations, as measured by ELISA, were high in both the KV and MLV treatment groups, indicating that both treatment groups had an anamnestic BCoV-specific antibody response after booster vaccination; however, these results do not necessarily represent a protective antibody response. In previous experiences with vaccination against viruses such as human respiratory syncytial virus (HRSV) and feline FIPV, relying solely on virus-specific ELISA antibody concentrations can be misleading (13,14). When antibody is produced, either subsequent to vaccination or infection, ADE can occur (13). In Study 2, the independence between BCoV-specific and BCoV VN antibody concentrations indicated that ELISA antibody concentration results should be interpreted with caution because the antibody measured by ELISA might not be neutralizing and could effectuate ADE. Similar to HRSV (13) and, importantly, FIPV (14), and perhaps SARS-CoV-2 and other coronaviruses, BCoV ELISA concentrations might not be predictive of virus neutralization. Clearly, the comparison of BCoV-specific and BCoV VN antibody can be affected by the ELISA method used to determine antibody concentration. In this study, lysate from BCoV-infected cells was used for the ELISA antigen. This may overestimate neutralizing function — for instance, by measuring responses to the N protein, an internal structural protein, thereby overestimating the similarity of results deriving from the 2 methods. However, in this study, the results of ELISA and VN were not correlated, indicating that overestimation of neutralizing components was not evident.

In Study 2, both treatment groups had similarly high mean concentrations of BCoV VN antibody, indicating that the antibody produced should inhibit infection of host cells either by blocking the interaction between envelope glycoprotein and cellular receptors, or by inhibiting fusion after attachment (24). High concentrations of BCoV VN antibody indicated that procedures used in the formulation of both vaccines largely preserved the epitopes associated with viral attachment and/or fusion.

Based on results from Study 1, we inferred that mucosal priming of BCoV-seropositive neonatal calves with an MLV BCoV and boosting with a systemic MLV can induce a neutralizing antibody response significantly greater than in non-vaccinated controls and mucosally unprimed IM-vaccinated calves. Study 2 indicated that IM booster vaccination of mucosally primed calves with either MLV or KV vaccine resulted in similar anamnestic BCoV-specific antibody responses at weaning. However, BCoV-specific antibody responses should be interpreted with caution, as they are not necessarily correlated with VN antibody concentrations. Immunization against BCoV through a neonatal IN prime and systemic boost approach appeared to engender a protective antibody response by virtue of high concentrations of neutralizing BCoV antibody. CVJ

References

1. Boileau M, Kapil S. Bovine coronavirus associated syndromes. Vet Clin North Am Food Anim Pract 2010;26:123–146.
2. Fulton R, d'Offay J, Landis C, *et al.* Detection and characterization of viruses as field and vaccine strains in feedlot cattle with bovine respiratory disease. Vaccine 2016;34:3478–3492.
3. Saif L. Bovine respiratory coronavirus. Vet Clin North Am Food Anim Pract 2010;26:349–364.
4. Vlasova A, Saif L. Bovine coronavirus and the associated diseases. Front Vet Sci 2021;8:643220.
5. Workman A, Kuehn L, McDaneld T, Clawson M, Loy J. Longitudinal study of humoral immunity to bovine coronavirus, virus shedding, and treatment for bovine respiratory disease in pre-weaned beef calves. BMC Vet Res 2019;15:161–175.
6. Workman A, Kuehn L, McDaneld T, Clawson M, Chitko-McKown C, Loy J. Evaluation of the effect of serum antibody abundance against bovine coronavirus on bovine coronavirus shedding and risk of respiratory tract disease in beef calves from birth through the first five weeks in a feedlot. Am J Vet Res 2017;78:1065–1076.
7. Chamorro MF, Walz PH, Haines DM, *et al.* Comparison of levels and duration of detection of antibodies to bovine viral diarrhea virus 1, bovine viral diarrhea virus 2, bovine respiratory syncytial virus, bovine herpesvirus 1, and bovine parainfluenza virus 3 in calves fed maternal colostrum or a colostrum-replacement product. Can J Vet Res 2014;78:81–88.

8. Chamorro MF, Walz PH, Passler T, *et al.* Efficacy of four commercially available multivalent modified-live virus vaccines against clinical disease, viremia, and viral shedding in early-weaned beef calves exposed simultaneously to cattle persistently infected with bovine viral diarrhea virus and cattle acutely infected with bovine herpesvirus 1. Am J Vet Res 2016;77:88–97.
9. Ellis J, Gow S, Berenik A, Lacoste S, Erickson N. Comparative efficacy of modified-live and inactivated vaccines in boosting responses to bovine respiratory syncytial virus following neonatal mucosal priming of beef calves. Can Vet J 2018;59:1311–1319.
10. Rodak L, Babiuk L, Acres S. Detection by radioimmunoassay and enzyme-linke immunosorbent assay of coronavirus antibodies in bovine serum and lacteal secretions. J Clin Microbiol 1982;16:34–40.
11. Corti D, Lanzavecchia A. Broadly neutralizing antiviral antibodies. Ann Rev Immunol 2013;31:705–742.
12. West K, Ellis J. Functional analysis of antibody responses of feedlot cattle to bovine respiratory syncytial virus following vaccination with mixed vaccine. Can J Vet Res 1997;61:28–33.
13. Arvin A, Fink K, Schmid M, *et al.* A perspective on potential antibody-dependent enhancement of SARS-CoV-2. Nature 2020;584:353–363.
14. Gartlan C, Tipton T, Salguero F, Sattentau Q, Gorringe A, Carroll M. Vaccine-associated enhanced disease and pathogenic human coronaviruses. Front Immunol 2022;13:882972.
15. Ellis J, Gow S, Bolton M, Burdett W, Nordstrom S. Inhibition of priming for bovine respiratory syncytial virus-specific protective immune responses following parenteral vaccination of passively immune calves. Can Vet J 2014;55:1180–1185.
16. Niewiesk S. Maternal antibodies: Clinical significance, mechanism of interference with immune responses, and possible vaccination strategies. Front Immunol 2014;5:446.
17. Ellis J, Gow S, West K, *et al.* Response of calves to challenge exposure with virulent bovine respiratory syncytial virus following intranasal administration of vaccines formulated for parenteral administration. J Am Vet Med Assoc 2007;230:233–243.
18. Hill K, Natasa A, Nordstrom S, Griebel P. Immune memory induced by intranasal vaccincation with a modified-live viral vaccine delivered to colostrum fed neonatal calves. Vaccine 2019;37:7455–7462.
19. Woolums A, Berghaus R, Berghaus L, *et al.* Effect of calf age and administration route of initial multivalent modified-live virus vaccine on humoral and cell-mediated immune responses following subsequent administration of a booster vaccination at weaning in beef calves. Am J Vet Res 2013;74:343–354.
20. Ellis J, Gow S, Mahan S, Leyh R. Duration of immunity to experimental infection with bovine respiratory syncytial virus following intranasal vaccination of young passively immune calves. J Am Vet Med Assoc 2013; 243:1602–1608.
21. Erickson N, Berenik A, Lardner H, *et al.* Evaluation of bovine respiratory syncytial virua (BRSV) and bovine herpesvirus (BHV) specific antibody responses between heterologous and homologous prime-boost vaccinated western Canadian beef calves. Can Vet J 2021;62:37–44.
22. Lazurko M, Erickson N, Campbell JR, Gow S, Waldner C. Vaccine use in Canadian cow-calf herds and opportunities for improvement. Front Vet Sci 2023;10:1235942.
23. Waldner C, Parker S, Campbell J. Vaccine usage in western Canadian cow-calf herds. Can Vet J 2019;60:414–422.
24. Klasse P, Sattentau Q. Mechanisms of virus neutralization. Curr Top Microbiol Immunol 2001;260:87–108.

Article

Effect of a *Lactococcus lactis* culture supernatant on diarrhea and performance parameters of piglets in the post-weaning period and on expression of the *faeG* gene *in vitro*

Ana Sophia Jaramillo-Jaramillo, Virginie Blanvillain-Rivera, Thomas J.D. Coulson, Vahab Farzan, Robert Friendship, Alain Labbe

Abstract

Objectives

To evaluate the effects of a cell-free supernatant from *Lactococcus lactis* (CFSM) on performance and diarrhea-related parameters and the presence of F4+ enterotoxigenic *E. coli* (ETEC) in piglets during post-weaning, and to evaluate the *in vitro* effect of the CFSM on *faeG* gene expression in an *E. coli* F4+.

Animals and procedure

In 3 trials with 90 piglets per trial, pigs were assigned to receive a placebo or 1 of 2 CFSM treatments and observed for diarrhea and performance. Fecal swabs were taken to determine the presence of ETEC. Quantitative RT-PCR was used to assess *faeG* gene expression in *E. coli* 21259 after treatment with CFSM at 50 mg/mL.

Results

The CFSM administered for 14 d at a dose of 24 mg/kg BW (2X) reduced diarrhea-related parameters compared to the placebo. Quantitative RT-PCR showed that, in *E. coli* 21259 treated with CFSM at 50 mg/mL, expression of the *faeG* gene was significantly repressed ($P < 0.0001$) relative to that in the untreated control.

Conclusion

The evaluated CFSM reduced the frequency and prevalence of diarrhea in a field situation. The *in vitro* treatment had an inhibitory effect on the expression of the *faeG* gene in F4+ *E. coli* 21259.

Résumé

Effet d'un surnageant de culture de *Lactococcus lactis* sur la diarrhée et les paramètres de performance des porcelets en période post-sevrage et sur l'expression du gène *faeG in vitro*

Objectifs

Évaluer les effets d'un surnageant acellulaire de *Lactococcus lactis* (CFSM) sur les paramètres de performance et de diarrhée et la présence d'*E. coli* entérotoxinogène F4+ (ETEC) chez les porcelets en post-sevrage, et évaluer l'effet *in vitro* du CFSM sur l'expression du gène *faeG* dans un *E. coli* F4+.

Animaux et procédure

Dans 3 essais portant sur 90 porcelets par essai, les porcs ont reçu un placebo ou 1 des 2 traitements CFSM et ont été observés pour détecter la diarrhée et leurs performances. Des prélèvements fécaux ont été effectués pour déterminer la présence d'ETEC. La RT-PCR quantitative a été utilisée pour évaluer l'expression du gène *faeG* dans *E. coli* 21259 après traitement avec CFSM à 50 mg/mL.

Résultats

Le CFSM administré pendant 14 jours à une dose de 24 mg/kg de poids corporel (2X) a réduit les paramètres liés à la diarrhée par rapport au placebo. La RT-PCR quantitative a montré que, chez *E. coli* 21259 traité avec CFSM à 50 mg/mL, l'expression du gène *faeG* était significativement réprimée ($P < 0{,}0001$) par rapport à celle du témoin non traité.

MicroSintesis, 797 Victoria Road, Victoria, Prince Edward Island C0A 2G0 (Jaramillo-Jaramillo, Blanvillain-Rivera, Coulson, Labbe); Department of Population Medicine, University of Guelph, 50 Stone Road East, Guelph, Ontario N1G 2W1 (Farzan, Friendship).

Address all correspondence to Dr. Thomas J.D. Coulson; email: tcoulson@microsintesis.com

Unpublished supplementary material (Tables S1, S2, S3, S4, S5) is available online from: www.canadianveterinarians.net

Conclusion

Le CFSM évalué a réduit la fréquence et la prévalence de la diarrhée sur le terrain. Le traitement *in vitro* a eu un effet inhibiteur sur l'expression du gène *faeG* chez F4+ *E. coli* 21259.

(Traduit par Dr Serge Messier)

Can Vet J 2024;65:259–266

ARTICLE

Introduction

In commercial swine production, the first 3 wk after weaning are critical because this period is often associated with depressed feed intake, poor growth, post-weaning health problems, and mortality. Social, dietary, and immunological stressors resulting from the weaning process, in combination with the challenge from endemic pathogens such as enterotoxigenic *Escherichia coli* (ETEC), may result in severe diarrhea and higher mortality rates (1,2). For example, after adherence to the epithelial cells, F4 fimbriae-positive enterotoxigenic *E. coli* (F4+ ETEC) will produce enterotoxins that disrupt the intestinal barrier function, causing tissue inflammation and abnormal electrolyte and water secretion, leading to diarrhea (3). Diarrhea causes dehydration, acidosis, and even death due to impaired intestinal absorption (4).

The F4 fimbriae include in their structure the major structural subunit and adhesin FaeG and several minor subunits (FaeF, FaeH, FaeC, probably FaeI, and FaeJ), which are encoded in a single operon within a large virulence plasmid (2). Other studies suggest that strains of ETEC in which the *faeG* locus is deleted show impaired colonization of porcine enterocytes (5). In addition, FaeG has been a target for vaccine development against ETEC colonization, indicating the importance of this major subunit in the pathogenesis of post-weaning diarrhea in pigs (6,7).

Pork producers have relied on mass medication with antibiotics and, more recently, zinc oxide. However, given the move by many European countries to ban pharmacological application of zinc oxide in swine, there is pressure to move to alternative approaches (8,9). Although much effort has been placed on providing diets that contribute to the gut microbiome balance and management steps to minimize challenges, post-weaning diarrhea persists on many farms (4).

Several alternatives and replacements for antibiotics and heavy metals have been proposed, including vaccination, probiotics, prebiotics, nutraceuticals, and organic acids. However, their efficacy has been inconsistent (8). An interesting new approach for controlling bacterial diseases is using quorum sensing inhibition (QSI) molecules. Quorum sensing is a form of bacterial communication that allows bacteria to detect changes in local population density by producing and detecting molecules called autoinducers. Quorum sensing allows for coordinated changes, including the expression of virulence genes required for bacterial pathogenesis. Some forms of QSI molecules include metabolites produced by probiotic bacteria, which have been shown to reduce the expression of virulence genes in *Salmonella enterica* Typhimurium, enterohemorrhagic *E. coli,* and methicillin-resistant *Staphylococcus aureus* (10–12). In the case of post-weaning diarrhea in piglets, QSI has been reported as a promising alternative for disrupting the *E. coli* virulence factors associated with colonization and enterotoxins production, contributing to reduced morbidity in the animals (13,14).

This study aimed to determine the effects of different doses of fermented cell-free supernatant from *Lactococcus lactis* on the frequency and prevalence of diarrhea, the presence of F4+ ETEC, and the performance and diarrhea-related parameters in piglets under field conditions (natural health challenges) in 3 clinical trials during the first 14 d after weaning. In addition, an *in vitro* experiment was done to evaluate the effect of cell-free supernatant treatment on the expression of *faeG* in F4+ ETEC 21259.

Materials and methods

Ethics declaration

The clinical component of the present study is divided into 3 trials. These trials occurred at the Arkell Swine Research Station, University of Guelph (Ontario). All procedures used in this study were approved by the University of Guelph Animal Care Committee and followed the guidelines set forth by the Canadian Council on Animal Care. All the piglets from the treated groups were euthanized upon study completion following animal welfare standards approved by the American Veterinary Medical Association.

General information

The piglets included in this study were provided by Arkell Swine Research Station, University of Guelph (Ontario). The studies took place at the Arkell Swine Research Station, and housing and management of the animals followed the station's standard operating procedures, with the following exception: to increase the likelihood of post-weaning diarrhea, the thermostats in the room were set at 18°C, and the pens were washed but not disinfected before the pigs were introduced. For each trial, the facility consisted of a room containing 9 pens. Each pen was equipped with a drinking water bowl and a feeder. Water was sourced from the city supply, free of any additive, delivered through a system set up so a single delivery would go from 1 20-liter container to the 3 respective pens in each group.

Piglet selection

Each trial was performed with a total of 90 pigs. The piglets were weaned at ~3 wk of age and randomly assigned to 1 of 3 treatment groups. Piglet selection allowed uniform population distribution within and between pens and groups. All piglets selected were in good health with a live weight close to the herd's average. Piglets were randomly assigned to reach a balanced design with 50% barrows and 50% gilts in each pen. Each piglet was ear-tagged so it could be identified to its sow and specific treatment. Pigs were individually weighed at the beginning of the trial on the day of weaning, at 2 wk post-weaning, and at 4 wk post-weaning (study completion).

Table 1. Study protocol and treatment distribution for each trial during the first 14-day post-weaning period in the first, second, and third trials.

Trial	Group	Treatment	Dose	Pens	Pigs
1	A	Placebo	2X[a]	3	10
	B	CFSM	0.5X[b]	3	10
	C	CFSM	2X	3	10
2	A	Placebo	2X	3	10
	B	CFSM	1X[c]	3	10
	C	CFSM	2X	3	10
3	A	Placebo	2X	3	10
	B	CFSM B11	2X	3	10
	C	CFSM FA	2X	3	10

CFSM — Cell-free spent media.
[a] 2X, 24 mg/kg of live body weight (BW).
[b] 0.5X, 6 mg/kg BW.
[c] 1X, 12 mg/kg BW.

Experimental design and protocol

The 3 trials in the study were conducted as completely randomized block designs. The experimental unit was the individual piglet. Each treatment group had 3 pens with 10 piglets per pen, randomly blocked as 3 pens per block. There were 3 blocks per trial. In each trial, 3 treatment groups were identified by letters: A, B, and C. Animals in group A received a placebo (control group), and those in groups B and C received dried cell-free spent media (CFSM) delivered *via* drinking water, for the first 14 d after weaning. All pigs were fed a transition feed containing 3000 ppm zinc oxide, followed by 3 starter diets with no antimicrobial content. The transition diet was fed for 7 d post-weaning. The 4 diets contained protein decreasing from 20% to 18%, and the diets' compositions decreased in complexity from the 1st phase to the 4th phase. The feeds contained non-starch polysaccharides and phytase enzymes. The age distribution of each feed phase was documented, and feed intake was recorded on a pen basis.

Treatment description and distribution

In the drinking water, each group was given either a placebo treatment (cellulose gum) or 1 of 2 CFSM treatments (2 doses of the same material or 2 different production batches) (Table 1). The first trial tested the material at 2 doses, 6 mg/kg (0.5X) or 24 mg/kg (2X) of live body weight; the second trial tested 2 doses, 12 mg/kg (1X) or 24 mg/kg (2X); the third trial included 2 different CFSM production batches (F and B), both at 24 mg/kg (2X). Every morning, at approximately the same time of day, the volume of water remaining in the container was recorded to allow daily water intake calculation per group.

Fecal scores and diarrhea-related parameter estimation

Individual pigs were observed for diarrhea daily for the first 14 d of each trial. Fecal scores were classified as 0 (normal), 1 (mild; pasty, or loose stool), 2 (moderate; stool quite liquid but coloured), and 3 (severe; watery, clear diarrhea with scalding on the skin), as described previously (7), with a fecal score of 2 or 3 diagnosed as diarrhea. The average daily fecal score was calculated from the individual fecal scores for each group between post-weaning day (PWD) 1 and PWD14 of each trial. The cumulative number of individuals diagnosed with diarrhea for at least 1 d was calculated per group to determine the percentage of sick animals during the observation period. When expressed as a percentage of individuals, this parameter was identified as diarrhea incidence. Diarrhea prevalence was calculated daily from PWD1 to PWD14 as the ratio of piglets with diarrhea divided by the number of living piglets in the pen. Diarrhea frequency was calculated on PWD14 as the cumulative number of days pigs within a group showed diarrhea divided by the total number of days living within a pen.

Performance parameter measurement

Daily weight gain and average daily weight gain corrected for mortality were calculated per group for PWD0 to PWD7, PWD0 to PWD12, PWD7 to PWD14, and for the entire period (PWD0 to PWD14). Average daily feed intake per pig was calculated as the difference between the total amount of feed distributed, minus feed withdrawal, divided by the number of living days. Feed conversion corrected for mortality was calculated as the ratio between cumulative feed intake and pen weight difference.

Fecal swab collection

Fecal swabs were taken from piglets with diarrhea to assess for the presence of hemolytic *E. coli.* All swabs from the first 2 trials were analyzed at the University of Guelph to confirm the presence of hemolytic *E. coli.* Swabs from the third trial were analyzed by Gallant Custom Laboratories (Cambridge, Ontario) for isolation and typing of F4+ ETEC.

Preparation of cell-free spent media (CFSM)

Cell-free spent media containing bioactive peptides was prepared as follows: A culture of *Lactococcus lactis* ATCC 11454 was inoculated into 30 L of a proprietary blend of whey and lactose and grown at 37°C with agitation in a 40-liter fermentation vessel. At the end of fermentation, cells were removed from the supernatant by continuous centrifugation to obtain the CFSM. The CFSM was spray-dried, and the dried powder was stored at 4°C until use.

E. coli challenge with cell-free spent media (CFSM)

Single-colony isolates of *E. coli* 21259 were inoculated into LB broth, grown aerobically overnight at 37°C, and shaken at 200 RPM. One milliliter of each overnight culture was pelleted by centrifugation, and the supernatant was discarded. Cells were resuspended in 1 mL PBS before adjusting to an OD600 of 1.0 ($\sim 10^7$ CFU/mL). Adjusted cultures were diluted 1:100 into LB or LB supplemented with CFSM and incubated at 37°C, 200 RPM. Media containing CFSM was prepared as follows: CFSM was weighed out and resuspended in LB broth to a final concentration of 50 mg/mL. The pH was adjusted to 7.0 $\pm$ 0.05, and then the solution underwent centrifugation at 3217 $\times$ *g* for 15 min to pellet insoluble material. From this solution, a CFSM solution of 5 mg/mL was also prepared by diluting 1:10 in LB broth. The CFSM medium was sterilized with a 0.22-micrometer-pore PES filter and left overnight at 37°C.

RNA extraction and cDNA synthesis

Isolation of RNA from *E. coli* 21259 was from cultures grown in LB alone or with CFSM, as described above. After 4 h of incubation, 0.5 mL of culture was transferred to a tube containing 2 culture volumes of RNAprotect Bacterial Reagent (Qiagen, Mississauga, Ontario), vortexed for 30 s and incubated at room temperature for 10 min, and then centrifuged at 5000 × *g* for 10 min. The supernatant was discarded and cell pellets were stored at −80°C until further use. Total bacterial RNA was extracted using the RNeasy Mini Kit (Qiagen), following the manufacturer's recommendations for Gram-negative bacteria with enzymatic lysis, with an on-could DNase digestion step to remove contaminating genomic DNA. The RNA purity and quantity were measured on a NanoDrop 2000 (Thermo Fisher Scientific). Only samples with a 260/280 nm ratio of 2.0 to 2.2 were used for cDNA synthesis. The RNA was stored at −80°C until further use. Total cDNA synthesis was performed using the BioRad iScript gDNA clear cDNA synthesis kit (Bio-Rad, Mississauga, Ontario). Contaminating genomic DNA was removed by treating 500 ng of total RNA with iScript DNase in a total volume of 16 μL and incubating at 25°C for 15 min, followed by DNase I heat inactivation at 75°C for 5 min. Reverse transcription was performed by adding 4 μL of iScript Reverse Transcription Supermix directly to each reaction tube, or 4 μL iScript No-RT Control Supermix for no-reverse-transcriptase controls. Reactions were run on an iCycler iQ thermocycler (Bio-Rad) with the following parameters: 25°C, 5 min; 46°C, 20 min; 95°C, 1 min; 4°C hold. Following cDNA synthesis, samples were diluted tenfold in RNase-free water to be used immediately or stored at −20°C.

Real-time quantitative PCR

Real-time qPCR reactions were set up in 96-well PCR plates, as follows: 5 μL of diluted cDNA was used in a 20-microliter qPCR reaction containing 10 μL of SsoAdvanced Universal SYBR Green Supermix (Bio-Rad) and 0.6 μL of each 10 μM forward and reverse primer (see Table S1, available online from: www.canadianveterinarians.net). Amplification was performed on a QuantStudio3 thermocycler (Applied Biosystems) running the following reaction parameters: 95°C for 2 min; followed by 40 cycles of 95°C for 10 s, 60°C for 15 s, 72°C for 15 s; and a final elongation step of 95°C for 15 s. A dissociation curve from 60 to 95°C was performed at the end of the run to ensure product specificity. The relative quantification of mRNA expression was normalized to the level of the housekeeping genes *tufA* and *recA*. The relative fold-change in gene expression was calculated using the comparative threshold cycle ($2^{-\Delta\Delta Ct}$) method (15).

Statistical analyses

The statistical analysis for this study was performed at the pen level with a combination of the 3 trials. Feed conversion and body weight gain were analyzed as follows: The distribution of each group was first assessed using the Shapiro-Wilk normality test. If all data sets were distributed normally, an ANOVA analysis was performed. If a significant difference was detected, further analysis applied the Tukey HSD test to detect which groups differed. The nonparametric Kruskal-Wallis rank-sum test was used if any groups were not normally distributed. If a significant difference was detected, pairwise comparisons were completed using the Wilcoxon rank-sum test to compare each treatment group to the placebo group. The Bernoulli correction for multiple comparisons was applied. Additional analysis of the CFSM 2X dose compared to the placebo in all 3 trials was applied using the pen as the statistical unit. The models included fixed effects (treatment, sex, the interaction between sex and treatment, and body weight at Day 0 as a covariable) and random effects [including trial, block used to distribute the litters (embedded in the trial), and the pen]. Statistical analyses of the clinical trials were completed using the software R (version 4.0.4) (R Foundation for Statistical Computing, Vienna, Austria). Diarrhea incidence analysis was performed with the epiR package (version 2.0.19) using a X^2 analysis using the Mantel-Haenszel test of homogeneity of the odds ratios. Statistical analysis of *faeG* gene expression was completed using 1-way ANOVA after assessing the data distribution and applying $\log_2$-transformation of the values using GraphPad Prism 9 software (version 9.5.0) (GraphPad Software, San Diego, California, USA).

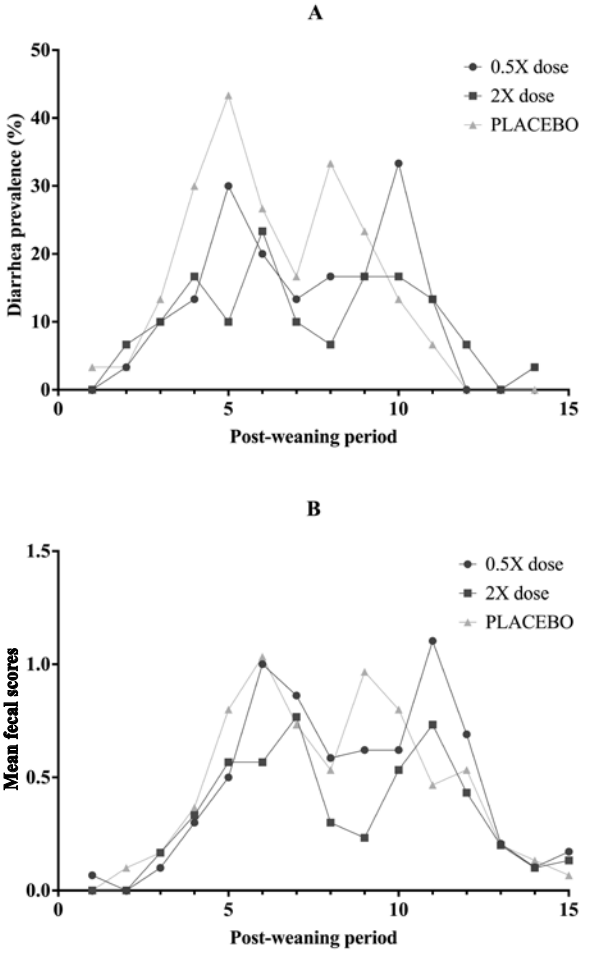


Figure 1. Diarrhea prevalence (A) and mean fecal scores (B) of piglets during the 14-day post-weaning period (PWD). In the first trial, the piglets were treated with 6 mg/kg (0.5X dose) (circles) or 24 mg/kg (2X dose) (squares) of live body weight, or with a placebo (triangles).

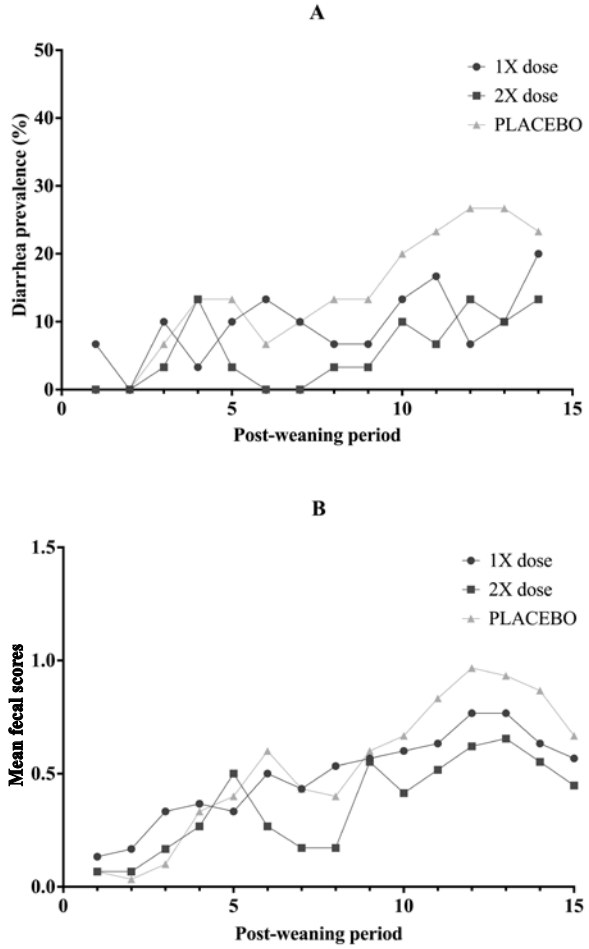


Figure 2. Diarrhea prevalence (A) and mean fecal scores (B) of piglets during the 14-day post-weaning period (PWD). In the second trial, the piglets were treated with 12 mg/kg (1X dose) (circles) or 24 mg/kg (2X dose) (squares) of live body weight, or with a placebo (triangles).

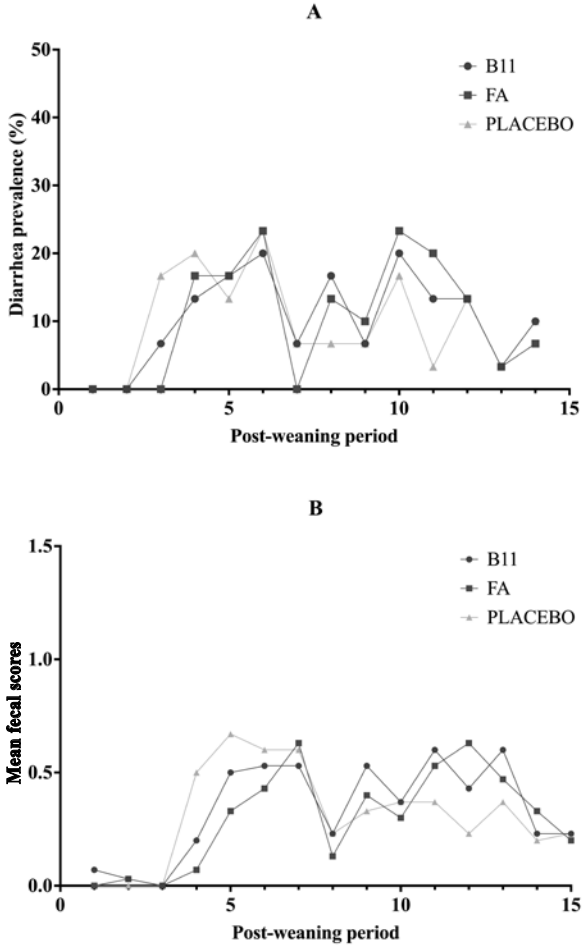


Figure 3. Diarrhea prevalence (A) and mean fecal scores (B) of piglets during the 14-day post-weaning period (PWD). In the third trial, the piglets were treated with 2 different production batches, B11 (circles) and FA (squares), both at 24 mg/kg of live body weight; or with a placebo (triangles).

Results

Fecal scores and diarrhea prevalence

For the first trial, the diarrhea diagnostic results showed 2 diarrhea peaks at PWD5 and PWD9. After PWD12, diarrhea prevalence was minimal. On PWD5, diarrhea prevalence reached 43% in the placebo group. In contrast, in the CFSM 2X dose group, the prevalence decreased by 77% and 80% during the 2 diarrhea peak days, respectively, relative to the placebo group (Figure 1). Average fecal scores are presented in Figure 1. In the second trial, the placebo group showed 2 diarrhea peaks on PWD4 to 5 and PWD12 to 13, with prevalences of 13% and 27%, respectively. Diarrhea prevalence in the 2X dose group was lower than in the placebo group after the prevalence began increasing. The 2X dose showed a 63% reduction in prevalence on PWD13 relative to the placebo (Figure 2). Average fecal scores for the second trial are presented in Figure 2. In the third trial, the maximum prevalence observed was 23% on PWD6. Prevalences reached 57 to 67% in the study groups, with a low average fecal score during treatment administration (PWD1 to PWD14). The low severity of the challenge was also reflected by the low average fecal scores in all groups (Figure 3).

Table 2 presents the frequency analysis of diarrhea during the trials. There was a significant reduction in the frequency of diarrhea for the 2X dose group in the first and second trials. Overall, the piglets in the 2X groups showed lower frequencies than the placebo group. Specifically, in the first trial, the 2X treatment reduced the diarrhea frequency by 35% during CFSM administration ($P = 0.02$), relative to the placebo group. This reduction was related to fewer individuals being affected by diarrhea (18 individuals in the 2X dose group *versus* 23 in the placebo group). The analysis of frequency for the second study further demonstrated a significant reduction in diarrhea frequency between the 2X group (4.8%) and the placebo group (12.2%) over the treatment period, for a reduction of 60% in the frequency ($P < 0.001$). The frequency analysis for the third study detected no differences between the placebo and the treatment groups, with an overall low frequency of 10%.

In the first trial, piglets in the placebo group were 4.33 times more likely to be sick at diarrhea peak (PWD5) than those in

Table 2. Effects of different treatments on piglets' diarrhea-related parameters during the first 14-day post-weaning period in the first, second, and third trials.

Trial	Group	Diarrhea frequency (%)	Diarrhea incidence	Diarrhea duration (d/pig)
1	A	15.2	23 (77%)	2.13
	B	12.9	21 (70%)	1.76
	C	10	18 (60%)	1.4
2	A	14	23 (77%)	1.97
	B	9.5	19 (63%)	1.33
	C	5.8	8 (27%)	0.80
3	A	10	17 (57%)	1.4
	B	10.5	19 (63%)	1.47
	C	10.5	21 (70%)	1.47

the 2X group — a significant difference (P = 0.02, adjusted P-value = 0.06). Additional statistical analysis consisted of testing the probability of the piglets having a fecal score of 0 (*i.e.,* an optimal fecal score) when given the CFSM at 2X dose compared with the placebo. The same logistic regression model was used to test the hypothesis $H(p,t) = 0$ if the fecal score on a given day was zero. The results indicated that piglets in the 2X dose group had a significantly higher chance of scoring zero during the second peak (PWD8; P = 0.02, adjusted P-value = 0.06) (see Table S2, available online from: www.canadianveterinarians.net).

In the second trial, the 2X dose significantly improved the chances, relative to the challenged placebo group, that the piglets would not get diarrhea on any day during the CFSM treatment administration period (PWD1 to PWD14; P = 0.05, adjusted P-value = 0.13) and the observation period (PWD1 to PWD14; P = 0.03, adjusted P-value = 0.08) (see Table S3, available online from: www.canadianveterinarians.net). That is, piglets in the challenged placebo group were 2.78 times more likely to be diagnosed with diarrhea than those in the 2X group during the 2 wk post-weaning (see Table S2, available online from: www.canadianveterinarians.net). A contrast analysis was performed for the third trial to compare the 2 2X test dose groups with the placebo group. No significant difference was observed between the placebo and the 2X dose group (see Table S4, available online from: www.canadianveterinarians.net).

Results of the analysis comparing the 2X dose to placebo in all 3 trials, using the pen as the statistical unit, showed that the effect of the treatment on the occurrence (proportion of sick animals) was 17.6% higher in the placebo group — a difference that was almost statistically significant (P = 0.06; the effect was stronger than the effect estimated on individual animals). For the mean diarrhea frequency, the effect of the treatment significantly reduced this parameter from 1.84 in the placebo group to 1.22 in the treated group (P = 0.035).

Performance data

In all trials, average body weight, weight gain, feed conversion, and cumulative feed intake did not differ significantly between the treatment groups and the control (placebo) group. Results are presented in Table S5 (available online from: www.canadianveterinarians.net).

Table 3. Presence of hemolytic *E. coli* in piglets with diarrhea treated with cell-free spent media (CFSM) in the first, second, and third trials.

Trial	Group	Pigs sampled	Positive hemolytic *E. coli*	Positive F4 *E. coli*
1[a]	A	23	5 (21.7%)	—
	B	23	9 (39.1%)	—
	C	17	3 (17.6%)	—
2[a]	A	23	0 (0%)	—
	B	18	4 (22%)	—
	C	8	4 (50%)	—
3[b]	A	17	17 (100%)	5 (29%)
	B	19	18 (95%)	6 (32%)
	C	20	20 (100%)	5 (20%)

[a] Hemolytic *E. coli* was assessed by plating at the University of Guelph (Ontario). Animals were sampled on the first day of diarrhea only.
[b] Swabs were taken daily from animals with diarrhea. Analysis was performed by Gallant Custom Laboratories (Cambridge, Ontario). The animals scored positive if at least 1 swab was positive for hemolytic *E. coli.*

Hemolytic *E. coli*

Analysis of fecal swabs was done to establish the presence of hemolytic *E. coli* and, in the third trial, F4+ ETEC. Hemolytic *E. coli* was identified in multiple samples, but not in all animals with diarrhea (Table 3). In the first 2 trials, positive animals ranged from 0 to 50%; however, the sampling was undertaken only once, at the appearance of diarrhea. Therefore, the results may be biased by false negatives for some of the swabs. The analysis for the third trial was done on multiple days to mitigate this bias. In that trial, hemolytic *E. coli* was detected in nearly all animals, whereas the F4+ ETEC was identified in 20 to 32% of animals in the groups.

faeG fimbriae gene expression analysis

Quantitative RT-PCR results showed that, when *E. coli* 21259 was treated with CFSM at 50 mg/mL, *faeG* expression was significantly reduced (4.3-fold reduction; $P < 0.0001$) relative to the untreated control. In cultures grown in media supplemented with 5 mg/mL CFSM, the treatment did not cause differential gene expression of *faeG* relative to the control (Figure 4).

Discussion

Weaning is stressful for piglets as it represents a sudden change in ambient conditions, social environment, and feed regimen. During that transition, gut dysbiosis may occur and create an opportunity for pathogens, particularly hemolytic *E. coli,* to grow and colonize the animal's gastrointestinal (GI) tract, causing post-weaning diarrhea and sometimes resulting in high mortality rates. To prevent and treat post-weaning diarrhea, producers use antimicrobials; however, this practice has been banned in several countries, and new alternatives to treatment are needed. In the present study, CFSM from *Lactococcus lactis* at different doses was administrated to piglets in drinking water for 14 d post-weaning, in 3 trials under natural post-weaning diarrhea challenge conditions, to evaluate its effects on diarrhea-related parameters compared to placebo treatment.

The results demonstrated that CFSM, administered for 14 d post-weaning and at a 24 mg/kg body weight test dose (2X),

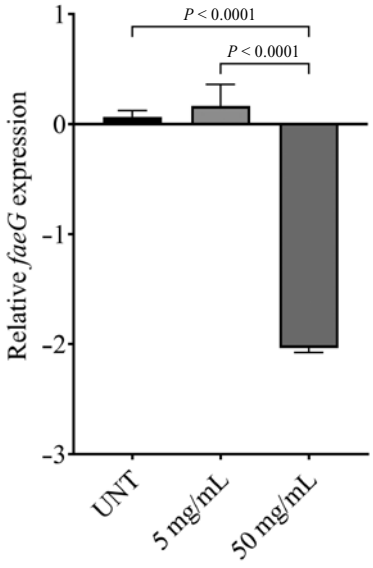


Figure 4. An RT-qPCR analysis for the expression of *faeG* in wild-type *E. coli* 21259 treated with cell-free spent media (CFSM) at 0 mg/mL (UNT), 5 mg/mL, and 50 mg/mL. Data are the mean and standard deviation of 3 biological replicates and 2 technical replicates. One-way analysis of variance (ANOVA) with Tukey multiple comparisons test was used to evaluate statistical significance. Error bars represent the standard deviation from the mean.

reduced diarrhea-related parameters compared to a placebo in post-weaning piglets facing a natural post-weaning diarrhea challenge. This treatment significantly reduced the frequency of diarrhea observed during the treatment period in the first 2 trials using the individual animal as the unit. The same result was demonstrated by combining data from all 3 trials and doing the statistical analysis per pen, looking specifically at the 2X treatment, which was equivalent in the 3 trials. One similar study evaluated the effect of the supernatant of a bioactive material from *Lactobacillus acidophilus* fermentation, at different test doses, on a challenge with F4+ *E. coli* (13). In that study, administering the bioactive molecules at 0.5 mL of concentrate per kg of body weight reduced the odds of a pig being sick by 2.142 times compared to the control group.

In the present study, diarrhea frequency observed in the third trial showed no significant differences between treatment and placebo groups. The low frequency and fecal score observed in this trial indicate that the challenge needed to be more severe and detecting differences was particularly difficult.

The mode of action of the CFSM from *L. lactis* on post-weaning diarrhea is hypothesized to be by inhibiting the quorum sensing (QS) signals of pathogens in the gut. The QS signals are essential for expressing virulence genes and pathogenesis in bacterial diseases. For example, in necrotic enteritis in poultry, the expression of the NetB toxin is controlled by QS signals through the Agr-like pathway (16). In post-weaning diarrhea, *E. coli* is recognized as a pathogen for disease progression through its adhesion to the lining and the expression of toxins, such as heat-stable and heat-labile enterotoxins (3). Furthermore, FaeG was shown to be necessary for post-weaning diarrhea pathogenesis for its adherent properties (2,14). In the present *in vitro* experiment, the *faeG* virulence gene was repressed in a representative F4+ ETEC strain of *E. coli* after treatment at 50 mg/mL CFSM. These results were also obtained when CFSM was tested against another strain of F4-expressing *E. coli* (data not shown), suggesting a conserved mode of action against *E. coli*. This result may support the hypothesis that CFSM reduces the expression of *faeG* in the GI tract, interfering with the adhesion of ETEC *E. coli* on porcine enterocytes and its capacity to cause diarrhea.

There is evidence that, in ETEC, the expression of the major fimbriae required for colonization is influenced by QS molecules. Previous work demonstrated that bacterial autoinducing molecules, in conjunction with host-derived signals such as norepinephrine and epinephrine, were needed to induce the expression of the *faeG* gene in F4+ ETEC (14). In that study, the authors suggested that a combination of AI-3 and host endocrine signals are necessary for the bacteria to detect when they have reached the correct location within the GI tract to begin colonization. A similar model was suggested by Hernandez *et al,* in 2020, upon the identification of the chemical structure for AI-3 and the proposed biosynthetic pathway, which allows enterohemorrhagic *E. coli* (EHEC) to induce expression of the locus of enterocyte effacement operons required for pathogenesis in response to nutrient status within the intestinal lumen (17,18).

In recent years, several investigations suggested that *E. coli* is also responsive to acyl-homoserine lactones QS molecules (AI-1) derived from Gram-negative bacteria in the GI environment, the detection of which can modulate the expression of flagella and Type-I fimbriae in F18ab ETEC (19). The fimbriae required for colonization and pathogenesis of this pathogen are regulated in response to multiple environmental factors, including nutrient availability, host-derived metabolites, and QS molecules, which may elicit their effects directly and indirectly (20–22).

In conclusion, this study determined that the CFSM resulting from *L. lactis* fermentation, administrated in drinking water during the post-weaning period of piglets under natural challenge conditions, reduced the frequency and prevalence of diarrhea. In addition, *in vitro* results demonstrated that treatment with the CFSM material in the cultured media, compared to non-treated culture media, had an inhibitory effect on expression of the *faeG* virulence gene necessary for the adhesion and pathogenicity of the enterotoxic *E. coli* 21259 strain. CVJ

References

1. Holman DB, Gzyl KE, Mou KT, Allen HK. Weaning age and its effect on the development of the swine gut microbiome and resistome. mSystems 2021;6:e00682–21.
2. Xia P, Zou Y, Wang Y, *et al.* Receptor for the F4 fimbriae of enterotoxigenic *Escherichia coli* (ETEC). Appl Microbiol Biotechnol 2015;99: 4953–4959.
3. Dubreuil JD. Enterotoxigenic *Escherichia coli* targeting intestinal epithelial tight junctions: An effective way to alter the barrier integrity. Microb Pathog 2017;113:129–134.
4. Hartadi E, Effendi M, Plumeriastuti H, Sofiana E, Wibisono F, Hidayatullah AR. A review of enterotoxigenic *Escherichia coli* infection in piglets: Public health importance. System Rev Pharm 2020;11: 687–698.
5. Zhou M, Guo Z, Yang Y, *et al.* Flagellin and F4 fimbriae have opposite effects on biofilm formation and quorum sensing in F4ac+ enterotoxigenic *Escherichia coli.* Vet Microbiol 2014;168:148–153.
6. Ruan X, Zhang W. Oral immunization of a live attenuated *Escherichia coli* strain expressing a holotoxin-structured adhesin-toxoid fusion

(1FaeG-FedF-LTA$_2$:5LTB) protected young pigs against enterotoxigenic *E. coli* (ETEC) infection. Vaccine 2013;31:1458–1463.
7. Zhang H, Xu Y, Zhang Z, You J, Yang Y, Li X. Protective immunity of a multivalent vaccine candidate against piglet diarrhea caused by enterotoxigenic *Escherichia coli* (ETEC) in a pig model. Vaccine 2018;36:723–728.
8. Luppi A. Swine enteric colibacillosis: Diagnosis, therapy and antimicrobial resistance. Porcine Health Manag 2017;3:16.
9. Bonetti A, Tugnoli B, Piva A, Grilli E. Towards zero zinc oxide: Feeding strategies to manage post-weaning diarrhea in piglets. Animals 2021; 11:642.
10. Zhang JS, Corredig M, Morales-Rayas R, Hassan A, Griffiths MW, LaPointe G. Effect of fermented milk from *Lactococcus lactis* ssp. cremoris strain JFR1 on *Salmonella* invasion of intestinal epithelial cells. J Dairy Sci 2019;102:6802–6819.
11. Zeinhom M, Tellez AM, Delcenserie V, El-Kholy AM, El-Shinawy SH, Griffiths MW. Yogurt containing bioactive molecules produced by *Lactobacillus* acidophilus La-5 exerts a protective effect against enterohemorrhagic *Escherichia coli* in mice. J Food Prot 2012;75:1796–1805.
12. Cella MA, Coulson T, MacEachern S, *et al.* Probiotic disruption of quorum sensing reduces virulence and increases cefoxitin sensitivity in methicillin-resistant *Staphylococcus aureus.* Sci Rep 2023;13:4373.
13. Nordeste R, Tessema A, Sharma S, *et al.* Molecules produced by probiotics prevent enteric colibacillosis in pigs. BMC Vet Res 2017;13:335.
14. Sturbelle RT, Avila LF, Roos TB, *et al.* The role of quorum sensing in *Escherichia coli* (ETEC) virulence factors. Vet Microbiol 2015;180: 245–252.
15. Livak KJ, Schmittgen TD. Analysis of relative gene expression data using real-time quantitative PCR and the 2(–delta delta CT) method. Methods 2001;25:402–408.
16. Yu Q, Lepp D, Mehdizadeh Gohari I, *et al.* The Agr-like quorum sensing system is required for pathogenesis of necrotic enteritis caused by *Clostridium perfringens* in poultry. Infect Immun 2017;85:e00975–16.
17. Hernandez DE, Sintim HO. Quorum sensing autoinducer-3 finally yields to structural elucidation. ACS Cent Sci 2020;6:93–96.
18. Kim CS, Gatsios A, Cuesta S, *et al.* Characterization of autoinducer-3 structure and biosynthesis in *E. coli.* ACS Cent Sci 2020;6:197–206.
19. Yang Y, Yao F, Zhou M, *et al.* F18ab *Escherichia coli* flagella expression is regulated by acyl-homoserine lactone and contributes to bacterial virulence. Vet Microbiol 2013;165:378–383.
20. Edwards RA, Schifferli DM. Differential regulation of fasA and fasH expression of *Escherichia coli* 987P fimbriae by environmental cues. Mol Microbiol 1997;25:797–809.
21. Huisman TT, de Graaf FK. Negative control of fae (K88) expression by the 'global' regulator Lrp is modulated by the 'local' regulator FaeA and affected by DNA methylation. Mol Microbiol 1995;16:943–953.
22. Gonyar LA, Kendall MM. Ethanolamine and choline promote expression of putative and characterized fimbriae in enterohemorrhagic *Escherichia coli* O157:H7. Infect Immun 2014;82:193–201.

Article

Small intestinal volvulus in 47 cows

Ueli Braun, Christian Gerspach, Claudia Volz, Monika Hilbe, Karl Nuss

Abstract

Objective

To describe the findings, treatment, and outcome of small intestinal volvulus (SIV) in 47 cows.

Animals and procedure

Retrospective analysis of medical records. Comparison of the findings for 18 surviving and 29 non-surviving cows.

Results

The most common abnormal vital signs were tachycardia (68.0%), tachypnea (59.6%), and decreased rectal temperature (51.1%). Signs of colic occurred in 66.0% of cows in the study. Rumen motility was reduced or absent in 93.6% of cows, and intestinal motility in 76.6%. Clinical signs on ballottement and/or percussion and simultaneous auscultation were positive on the right side in 78.7% of cows. Transrectal examination showed dilated small intestines in 48.9% of cows. The rectum contained little or no feces in 93.6% of cows. The principal laboratory abnormalities were hypocalcemia (74.1%), hypokalemia (73.8%), azotemia (62.8%), hypermagnesemia (61.6%), and hemoconcentration (60.0%). The principal ultrasonographic findings were dilated small intestines (87.1%) and reduced or absent small intestinal motility (85.2%). Forty-one of the 47 cows underwent right flank laparotomy and the SIV was reduced in 21 cows. When comparing the clinical and laboratory findings of 18 surviving and 29 non-surviving cows, the groups differed significantly with respect to severely abnormal general condition (16.7 *versus* 37.9%), rumen stasis (22.2 *versus* 79.3%), intestinal atony (16.7 *versus* 48.3%), serum urea concentration (6.5 *versus* 9.8 mmol/L), and serum magnesium concentration (0.98 *versus* 1.30 mmol/L). In summary, 38.3% of the cows were discharged and 61.7% were euthanized before, during, or after surgery.

Conclusion and clinical relevance

An acute course of disease, little or no feces in the rectum, and dilated small intestines were characteristic of SIV in this study population.

Résumé

Volvulus de l'intestin grêle chez 47 vaches

Objectif

Décrire les données, le traitement et les résultats du volvulus de l'intestin grêle (SIV) chez 47 vaches.

Animaux et procédure

Analyse rétrospective des dossiers médicaux. Comparaison des résultats pour 18 vaches survivantes et 29 vaches non survivantes.

Résultats

Les signes vitaux anormaux les plus courants étaient la tachycardie (68,0 %), la tachypnée (59,6 %) et la diminution de la température rectale (51,1 %). Des signes de coliques sont apparus chez 66,0 % des vaches étudiées. La motilité du rumen était réduite ou absente chez 93,6 % des vaches et la motilité intestinale chez 76,6 %. Les signes cliniques de ballottement et/ou percussion et auscultation simultanée étaient positifs du côté droit chez 78,7 % des vaches. L'examen transrectal a montré une dilatation de l'intestin grêle chez 48,9 % des vaches. Le rectum contenait peu ou pas de matières fécales chez 93,6 % des vaches. Les principales anomalies des analyses de laboratoire étaient l'hypocalcémie (74,1 %), l'hypokaliémie (73,8 %), l'azotémie (62,8 %), l'hypermagnésémie (61,6 %)

Department of Farm Animals (Braun, Gerspach, Volz, Nuss) and Institute of Veterinary Pathology (Hilbe), Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 260, CH-8057 Zurich, Switzerland.

Address all correspondence to Dr. Ueli Braun; email: ubraun@vetclinics.uzh.ch

et l'hémoconcentration (60,0 %). Les principaux résultats échographiques étaient une dilatation de l'intestin grêle (87,1 %) et une motilité intestinale réduite ou absente (85,2 %). Quarante et une des 47 vaches ont subi une laparotomie du flanc droit et le SIV a été corrigé chez 21 vaches. En comparant les résultats cliniques et biologiques de 18 vaches survivantes et de 29 vaches non survivantes, les groupes différaient significativement en ce qui concerne l'état général sévèrement anormal (16,7 contre 37,9 %), la stase du rumen (22,2 contre 79,3 %), l'atonie intestinale (16,7 contre 48,3 %), la concentration sérique d'urée (6,5 contre 9,8 mmol/L) et la concentration sérique de magnésium (0,98 contre 1,30 mmol/L). En résumé, 38,3 % des vaches ont reçu leur congé et 61,7 % ont été euthanasiées avant, pendant ou après l'intervention chirurgicale.

Conclusion et pertinence clinique

Une évolution aiguë de la maladie, peu ou pas de selles dans le rectum et un intestin grêle dilaté étaient caractéristiques du SIV dans cette population étudiée.

(Traduit par Dr Serge Messier)

Can Vet J 2024;65:267–277

Introduction

Twisting of the small intestine can occur either as small intestinal volvulus (SIV) or mesenteric torsion (1–5). Volvulus of the sigmoid flexure of the duodenum is another intestinal disorder but was not considered in the present study (6,7). Small intestinal volvulus describes simple or multiple rotation(s) of a small intestinal segment around its mesenteric axis (1,4,5,8,9). The cecum and spiral colon may also be involved in the torsion (1). Mesenteric torsion is the most serious form of small intestinal rotation and involves twisting of the entire small intestinal tract and the spiral colon, including the relevant mesenteries around the mesenteric root. Small intestinal volvulus preferentially affects the caudal jejunum and the ileum because the associated mesentery is longer and thus, the intestinal section is more mobile compared with the cranial part of the jejunum (1). Furthermore, the caudal part of the jejunum is often located outside of the omental bursa, which favors twisting of this portion (10). Small intestinal volvulus has been described in textbooks (8,9,11,12) and various publications (4,5,13). In an older report, volvulus of the distal jejunum was diagnosed in 4 cows (10). Of 35 cattle with a tentative diagnosis of SIV, only 7 were definitively diagnosed with this disorder (1). Of 100 cattle suspected of having intestinal obstruction, only 4 had SIV (13); and of 27 cows with mechanical ileus, only 3 had SIV (14). To date, the most comprehensive study of SIV in cattle described 51 cases (3).

Early clinical signs of SIV are characterized by sudden colic (8,10). Dilated small intestines were palpated transrectally in 4 of 4 (10) and in 17 of 24 cows with SIV (1). In some of the cows, a taut band running dorsoventrally (1) or taut mesenteric tissue running from the left upper quadrant to the right (3) could be palpated. Congested intestinal loops were only evident in long-standing cases upon rectal examination (3). After the first 12 h, signs of colic begin to diminish with a concurrent deterioration in general condition (8). The rectum typically contains mainly thick mucus. The general condition continues to deteriorate; without treatment, affected cattle die 2 to 3 d later (8). Analogous to other forms of mechanical ileus, dilated small intestines with a diameter $>$ 4 cm and reduced or absent intestinal motility are characteristic ultrasonographic findings for SIV (15). A tentative diagnosis of SIV is based on the history and clinical, transrectal, and ultrasonographic findings (14). In addition to the acuteness of the condition, a specific diagnosis of SIV is supported by dilated small intestines and tight bands palpated transrectally (3). The differential diagnosis should include other causes of ileus, such as mesenteric torsion and intestinal strangulation. A final diagnosis is often not possible without laparotomy 16) or postmortem examination. The only treatment option that offers a possibility of success is expeditious laparotomy and reduction of the volvulus (3,5). Severely compromised intestinal segments should be resected (4). Although SIV is discussed in most textbooks, only 1 study evaluated a large number of cattle with this condition (3). However, only 8 cattle were older than 6 mo and ultrasonography was not used. As the gastrointestinal tract differs fundamentally between adult cattle and calves, the goal of this study was to describe and analyze the clinical, laboratory, and ultrasonographic findings; treatment; and outcomes of 47 adult cattle with SIV.

Materials and methods

We analyzed the medical records of 47 cattle with SIV referred to the Department of Farm Animals, University of Zurich (Zurich, Switzerland), between January 1, 1986 and December 31, 2019. The present work is based on a dissertation (17).

Cattle and history

There were 41 cows and 6 heifers, all henceforth referred to as cows. These ranged in age from 1 to 13 y (median: 4.2 y). Numbers and breeds included 29 Brown Swiss, 13 Swiss Fleckvieh, 4 Holstein, and 1 crossbred cow. Fifteen cows were pregnant, 17 were open, and 15 did not have pregnancy status recorded in the medical history. The duration of pregnancy ranged from 4 to 38 wk (median: 12 wk). The last calving date was known in 20 cows and was between 1 and 25 wk (median: 10 wk) before admission. The duration of illness before admission ranged from 4 to 96 h (median: 12 h). Of 43 cows, 31 had anorexia and 12 had reduced feed intake. Signs of colic had occurred in 33 cows before admission.

Clinical examination

Each cow underwent a standard clinical examination (18–21). The general condition was evaluated by determining the demeanor, behavior, posture including recumbency, appetite, signs of abdominal pain, appearance of the hair coat and muzzle, skin elasticity, position of the eyes in the sockets, and skin surface temperature. General condition was classified as normal or mildly, moderately, or severely abnormal. Cows with a normal general condition were bright and alert and had normal behavior, posture, and appetite. The general condition was considered mildly abnormal when a mild decrease in alertness or mild signs of colic (defined below) were present. A moderate decrease in alertness and sometimes occasional grunting, or bruxism and marked signs of colic were observed in cattle with a moderately abnormal general condition. Cattle with a severely abnormal general condition showed marked apathy and were sometimes recumbent and unable to rise. The rumen was assessed for the degree of fill and the number and intensity of contractions. Tests for the presence of a foreign body included the pole test, back grip, and percussion of the abdominal wall over the region of the reticulum using a rubber hammer. Each test was carried out 4 times, and the reaction of the animal was observed each time. A test was considered positive when it elicited a short grunt at least 3 out of 4 times. Ballottement and simultaneous auscultation (BSA) and percussion and simultaneous auscultation (PSA) of the abdomen on both sides were also carried out. A BSA result was considered positive when splashing sounds were heard with a stethoscope while the abdominal wall was manually ballotted to produce a swinging motion. A PSA result was considered positive when a ringing sound or ping was heard on percussion of the abdominal wall with the handle of a hammer. Rectal examination was done in all cows. Feces were assessed for color, consistency, amount, fibre particle length, and any abnormal contents.

Each cow was observed for signs of pain (21,22). The number and severity of signs of colic/abdominal pain were determined. Signs of mild colic included mild restlessness, shifting of weight in the hind limbs, looking at the flank, lifting the tail, lifting of individual limbs, and tail swishing. Signs of moderate colic were moderate restlessness, brief periods of recumbency, kicking with the hind limbs, arching of the back, and marked tail swishing. Signs of severe colic were marked restlessness, frequent lying down and rising, sweating, grunting, and violent kicking at the abdomen. The cattle were divided into the colic, indolence (dullness), and intoxication phases. The colic phase was the initial phase accompanied by the described signs of pain. The indolence phase followed the colic phase and was characterized by apathy and a markedly abnormal general condition. In the last phase, intoxication, cattle had tachycardia, congested scleral blood vessels, pale mucous membranes, cool skin surface temperature, sunken eyes, and a dry muzzle.

Laboratory analyses

The collection and examination of blood, urine, and rumen fluid were done as described (20).

Ultrasonographic examination of the abdomen

In 31 cows, the abdomen was scanned from the right side as described (15).

Diagnosis

A tentative clinical diagnosis of ileus was made in cows with a history of colic or when signs of colic were recorded at the initial examination and the rectum contained little or no feces. A diagnosis of ileus was made when dilated small intestines and possibly tight bands were also palpated transrectally. A tentative diagnosis of ileus attributable to SIV was made in cows with grave transrectal findings that included congested, tubular small intestines and taut mesentery filling the abdominal cavity. An ultrasonographic diagnosis of ileus was made when dilated small intestines with a diameter $\geq$ 4.0 cm and no or subjectively decreased intestinal motility were observed. Involvement of the large intestine in SIV was suspected when gas- or fluid-filled sections of the large intestines were seen (23). The gold standard for diagnosis was based on laparotomy findings in cattle that underwent surgery and/or postmortem findings in cattle that were euthanized.

Laparotomy

A right-flank laparotomy was carried out in every cow. Before 2001, distal paravertebral anesthesia of the last thoracic and first 2 lumbar spinal nerves was done using lidocaine as described (24,25). Proximal paravertebral anesthesia of the same nerves was carried out starting in 2001. A vertical incision through all layers of the abdominal wall was made in the centre of the paralumbar fossa, starting 7 to 10 cm below the transverse processes and extending about 25 cm distally. After routine abdominal exploration, the small intestine was carefully examined to identify the site and extent of SIV. In cows with complete volvulus, reduction was attempted intra-abdominally, whereas in cows with segmental volvulus, reduction was attempted after the small intestine had been exteriorized on a Mayo table. After the surgical procedure, an antibiotic, most commonly amoxicillin, was infused into the abdomen in 1 L of isotonic saline solution or polyvinylpyrrolidone. The peritoneum, fascia, and transverse abdominal muscle and the internal and external oblique muscle layers were closed separately using a simple continuous suture pattern (Polysorb 2 USP atraumatic needle; Covidien-Medtronic, Minneapolis, Minnesota, USA). A continuous subcuticular suture (Polysorb 2.0 USP cutting needle; Covidien-Medtronic) and a modified mattress suture pattern was used to close the subcutaneous tissues, and metal clips (Appose, ULC 35W clips, 6.9 mm $\times$ 3.8 mm; Covidien-Medtronic) were used to close the skin.

Postoperative treatment

Cows that were discharged after a successful surgery were fasted for at least 24 h after surgery before feeding was gradually resumed. They received fluid therapy, antibiotics, analgesics, prokinetic drugs, and electrolyte replacement.

Euthanasia/slaughter

Cattle were euthanized using pentobarbital, or in earlier study years were sent to the slaughter facility of the veterinary hospital,

during or after the initial examination when they were in the intoxication phase or when the owner did not consent to surgery (21). Cattle were euthanized intraoperatively when catastrophic lesions (*e.g.,* ruptured intestines, fibrinous peritonitis, hemorrhagic infarction) were seen or complications (*e.g.,* becoming recumbent on the right side during surgery with exteriorization and subsequent contamination of the intestines) occurred, or after surgery when the clinical condition deteriorated.

Postmortem examination

All cows that died or were euthanized underwent postmortem examination. For slaughtered cows, only the internal organs were inspected.

Statistics

The software SPSS Statistics 26.0 (IBM Corp, New York, New York, USA) was used for analysis. Frequencies were determined for all variables, and the Shapiro-Wilk test was used to test the data for normality. Means ± SD were calculated for normally distributed data and medians (with ranges) were calculated for non-normal data. In addition, the 95% CIs were calculated for the means and medians, respectively. Differences in non-normal data between surviving (from admission to hospital discharge) and non-surviving cows were analyzed using the Mann-Whitney U test, and differences in nominal data were analyzed using the X^2 test. A value of $P < 0.05$ was considered statistically significant.

Results

General condition, abdominal contour, and signs of pain

The general condition was mildly abnormal in 23.4% (11/47) of the cows, moderately abnormal in 46.8% (22/47), and severely abnormal in 29.8% (14/47). One cow was recumbent upon initial examination and 3 others became recumbent during the examination. Twelve (25.5%) cows had uni- or bilateral abdominal distension.

Twelve of the 47 cows (25.5%) had nonspecific signs of pain, which included piloerection (5/47), bruxism (3/47), muscle fasciculations (2/47), and spontaneous grunting (2/47). Thirty-one cows (66.0%) were in the colic phase but the clinical signs were described in detail in only 24. These included restlessness (13/47), lordosis (12/47), treading (9/47), lying down and rising (6/47), kicking (6/47), and sweating (4/47). Of the cows with SIV, 23.4% (11/47) had 1 sign of visceral pain, 14.9% (7/47) had 2, 6.4% (3/47) had 3, and 6.4% (3/47) had 4 to 5 signs. These were assessed as mild (15/47), moderate (8/47), or severe (8/47). Fifteen (31.9%) cows were in the indolence phase (dullness phase) and 1 was in the intoxication phase. In addition, 53.2% (25/47) of cows had a tense abdominal wall (21/47) and/or an arched back (4/47).

Heart and respiratory rates and rectal temperatures (vital signs)

The most common vital sign abnormalities on initial examination were tachycardia (68.0%, 35/47), tachypnea (59.6%, 28/47), and lower-than-normal rectal temperature (51.1%, 24/47) (Table 1).

Digestive tract findings

The most common abnormal findings were minimal or no fecal material in the rectum (93.6%, 44/47), reduced or absent rumen motility (93.6%, 44/47), positive BSA and/or PSA on the right side (78.7%, 37/47), reduced or absent intestinal motility (76.6%, 36/47), and dilated small intestines palpated transrectally (48.9%, 23/47) (Figure 1; Table 1). At least 1 foreign body test was positive in 24.4% (10/41) of the cows, and 8.5% (4/47) of the cows had rumen tympany. A dilated rumen was diagnosed transrectally in 27.7% (13/47) of the cows. The feces were dark or black in 19.1% (9/47) of the cows, and the consistency ranged from liquid to pulpy (normal finding) to thick pulpy. Abnormal fecal contents included mucus, blood, and fibrin.

Other abnormal clinical findings

Other abnormal clinical findings included reduced skin elasticity (tenting of pinched skin lasted > 2 s) (67.4%, 31/46), reduced skin surface temperature (59.6%, 28/47), delayed capillary refill time (55.3%, 26/47), sunken eyes (51.1%, 24/47), moderately-to-severely hyperemic scleral vessels (45.7%, 21/46), a dry and cool muzzle (27.7%, 13/47), pale oral mucous membranes (19.1%, 9/47), and foul or ammonia-like breath (14.9%, 7/47).

Urinalysis

In 41 tested urine samples, pH ranged from 5.0 to 9.0 (median: 8.0); this was lower than normal (5.0 to 6.9) in 26.8% (11/41) and higher than normal (8.1 to 9.0) in 19.5% (8/41) of the cows. In 37 urine samples, specific gravity ranged from 1.003 to 1.058 (mean ± SD: 1.028 ± 14) and was decreased (< 1.020) in 27.0% (10/37) and increased (> 1.040) in 13.5% (5/37). Examination of 41 samples using Combur 9 test strips yielded hemoglobinuria/hematuria in 29.3% (n = 12), glucosuria in 26.8% (n = 11), ketonuria in 9.8% (n = 4) and proteinuria in 7.3% (n = 3) of the cows.

Laboratory findings

The principal abnormalities were hypocalcemia (74.1%, 20/27), hypokalemia (73.8%, 31/42), azotemia (62.8%, 27/43), hypermagnesemia (61.6%, 16/26), hemoconcentration (60.0%, 27/45), base excess (55.9%, 19/34), increased activity of aspartate aminotransferase (53.5%, 23/43), and acidosis (based on blood pH; 52.9%, 18/34) (Figure 2; Table 2).

Ultrasonographic findings

The principal ultrasonographic findings were dilated small intestines (87.1%, 27/31) with a diameter ranging from 4.0 to 10.0 cm, reduced or absent small intestinal motility (85.2%, 23/27), and free fluid in the abdomen (48.4%, 15/31). Subjectively, empty small intestines were seen in 7 cows and 1 cow had a dilated spiral colon. The actual site of the volvulus could not be visualized in any of the cows.

Comorbidities

Comorbidities unrelated to SIV were diagnosed in 34.0% (16/47) of the cows and included respiratory problems, ketonuria, gastrointestinal nematodes, dicrocoeliosis, and mastitis.

Table 1. Clinical findings in cows with intestinal volvulus.

Variable	Finding	Number of cattle	%
Heart rate	Normal (60 to 80 bpm)	13	27.7
(*n* = 47, median = 96 bpm,	Decreased (54 bpm)	2	4.3
95% CI = 88 to 104 bpm)	Mildly increased (81 to 100 bpm)	17	36.1
	Moderately increased (101 to 120 bpm)	9	19.1
	Severely increased (121 to 160 bpm)	6	12.8
Rectal temperature	Normal (38.5 to 39.0°C)	16	34.0
(*n* = 47, median = 38.4°C,	Decreased (35.6 to 38.4°C)	24	51.1
95% CI = 38.0 to 38.6°C)	Increased (39.1 to 40.0°C)	7	14.9
Respiratory rate	Normal (15 to 25 breaths/min)	16	34.0
(*n* = 47, median = 28 breaths/min,	Decreased (8 to 14 breaths/min)	3	6.4
95% CI = 24 to 32 breaths/min)	Increased (26 to 80 breaths/min)	28	59.6
Rumen motility	Normal	3	6.4
(*n* = 47)	Decreased	17	36.2
	Absent	27	57.4
Foreign body tests	All negative	31	75.6
(*n* = 41)	At least one test positive[a]	10	24.4
BSA and PSA on the left side	Both tests negative (normal)	44	93.7
(*n* = 47)	Only BSA positive	1	2.1
	Only PSA positive	1	2.1
	Both tests positive	1	2.1
BSA and PSA on the right side	Both tests negative (normal)	10	21.3
(*n* = 47)	Only BSA positive	21	44.7
	Both tests positive	16	34.0
Intestinal motility	Normal	11	23.4
(*n* = 47)	Decreased	19	40.4
	Absent	17	36.2
Transrectal findings[b]	Normal findings	18	38.3
(*n* = 47)	Rumen dilated	13	27.7
	Dilated loops of small intestines	23	48.9
	Colon and/or cecum dilated	3	6.4
	Findings inconclusive	3	6.4
Feces, amount	Normal	3	6.4
(*n* = 47)	Fecal output reduced	31	65.9
	Rectum empty	13	27.7
Feces, degree of comminution	Normal (well-digested)	26	55.3
(*n* = 47)	Moderately digested	5	10.6
	Poorly digested	3	6.4
	Rectum empty	13	27.7
Feces, consistency	Normal	16	34.1
(*n* = 47)	Thick, pulpy	9	19.1
	Thin, pulpy	4	8.5
	Pasty	4	8.5
	Liquid	1	2.1
	Rectum empty	13	27.7
Feces, color and abnormal contents	Normal (olive)	21	44.7
in the rectum	Dark	9	19.1
(*n* = 47)	Mucus	9	19.1
	Blood	7	14.9
	Fibrin	1	2.1
	Several abnormal contents	5	10.6

BSA — Ballottement and simultaneous auscultation; PSA — Percussion and simultaneous auscultation.
[a] Positive: At least 3 of 4 attempts elicited a grunt.
[b] The total number of findings was 60 (127.7%) because 13 cattle had > 1 abnormal transrectal finding.

Diagnoses

Based on the clinical findings, a tentative diagnosis of ileus was made in 21.3% (10/47), a diagnosis of ileus was made in 55.3% (26/47), and a diagnosis of ileus attributable to SIV was made in 2.1% (1/47) of the cows. Based on the ultrasonographic examination of 32 cows, a diagnosis of ileus was made in 90.6% (29/32). Among those 29 cows, a diagnosis of ileus was also made clinically in 25 cows, whereas in the remaining 4, no clinical diagnosis was made.

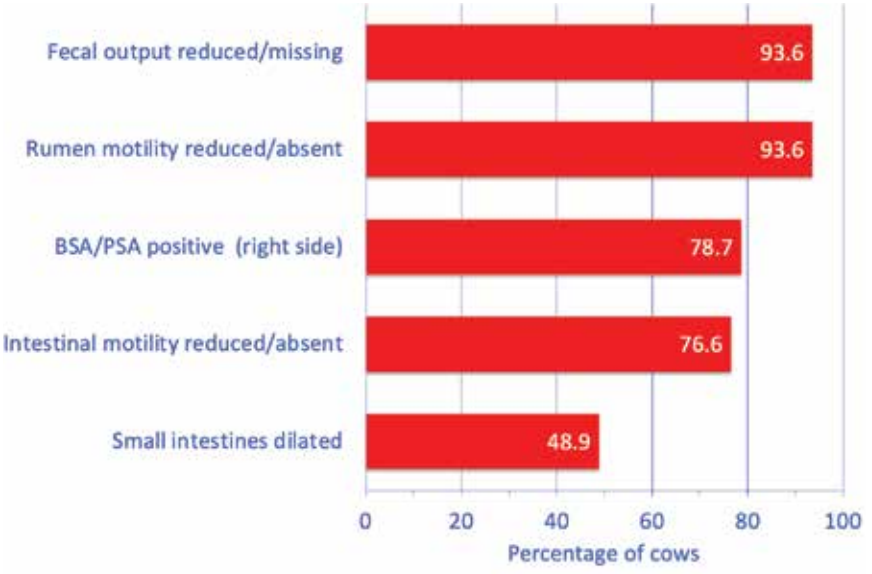


Figure 1. The most common digestive tract abnormalities in 47 cows with small intestinal volvulus.

BSA – Ballottement and simultaneous auscultation; PSA – Percussion and simultaneous auscultation.

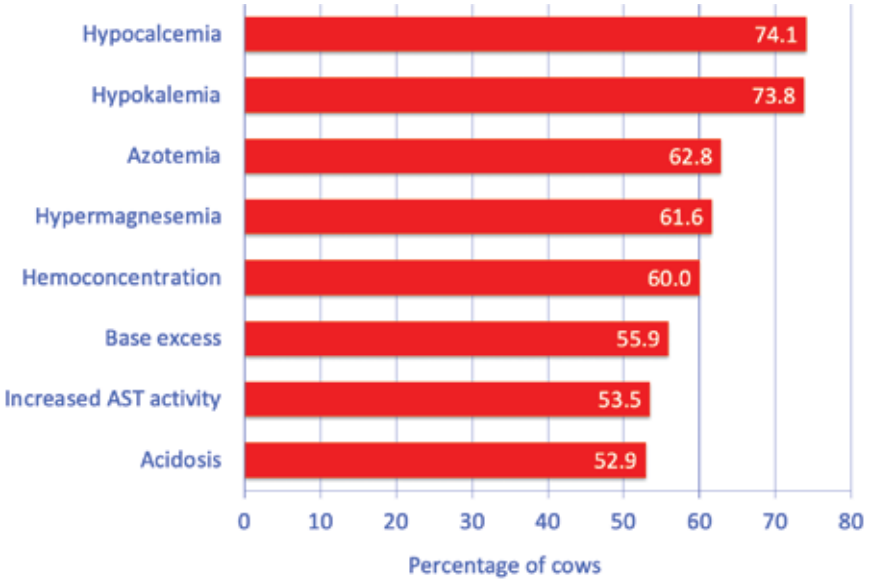


Figure 2. The most common abnormal blood variables in 47 cows with small intestinal volvulus.

Treatments and outcomes

Six cows died or were euthanized during or shortly after the initial examination (Figure 3), and 41 cows underwent right-flank laparotomy. Of those, 20 were euthanized intraoperatively; in the remaining 21, the surgery was completed. Of these latter, 3 died or were euthanized postoperatively and 18 were discharged. Thus, 61.7% (29/47) of the cows died spontaneously or were euthanized and 38.3% (18/47) were discharged.

Surgical findings and complications

All cows that underwent surgery had a right-flank laparotomy; 34 cows were standing, 3 were sedated and recumbent, and 1 was under general anesthesia during surgery. Three other cows were standing at the start of surgery but became recumbent. All cows had SIV that was segmental in 9 cows and complete in 38 (these numbers include the 6 cows that did not undergo surgery, in which the diagnosis was confirmed during postmortem examination). In addition to the pathological changes seen in the small intestine in 97.6% (40/41) of cows, 2 cows also had lesions in the cecum identified as fibrin deposits on, and edema of, the cecal wall. The changes, which were not associated with the examination, were mild to moderate in 18/41 and severe in 13/41. Eleven of 41 cows had increased amounts of abdominal fluid. Seven cows had fibrin or fibrinous adhesions in the abdomen, 6 had tears in the mesentery or greater omentum, and 2 had a ruptured bowel. Of the 44.7% (21/47) of cows in which

Table 2. Laboratory findings in cows with intestinal volvulus.

Variable (mean ± SD, median, 95% CI)	Finding	Number of cattle	%
Hematocrit (*n* = 45) (mean ± SD = 37.1 ± 6.7%, 95% CI = 35.1 to 39.1%)	Decreased (17 to 29%) Increased (36 to 52%)	4 27	8.9 60.0
WBC count (*n* = 42) (median = 9850/μL, 95% CI = 8500 to 11 700/μL)	Decreased (3600 to 4999/μL) Increased (10 001 to 29 300/μL)	3 20	7.1 47.6
Total protein (*n* = 44) (mean ± SD = 76.1 ± 12.4 g/L, 95% CI = 72.3 to 79.8 g/L)	Decreased (48 to 59 g/L) Increased (81 to 100 g/L)	4 15	9.1 34.1
Fibrinogen (*n* = 42) (median = 4.5 g/L, 95% CI = 4.0 to 6.0 g/L)	Decreased (1 to 3.9 g/L) Increased (7.1 to 12 g/L)	10 8	23.8 19.0
Urea (*n* = 43) (median = 7.1 mmol/L, 95% CI = 6.5 to 9.8 mmol/L)	Increased (6.6 to 27.3 mmol/L)	27	62.8
Bilirubin (*n* = 43) (median = 4.0 μmol/L, 95% CI = 3.6 to 5.2 μmol/L)	Increased (6.6 to 36.2 μmol/L)	11	25.6
Calcium (*n* = 27) (median = 2.03 mmol/L, 95% CI = 1.73 to 2.17 mmol/L)	Decreased (1.24 to 2.29 mmol/L) Increased (2.61 to 4.34 mmol/L)	20 1	74.1 3.7
Magnesium (*n* = 26) (median = 1.16 mmol/L, 95% CI = 0.91 to 1.40 mmol/L)	Decreased (0.73 to 0.79 mmol/L) Increased (1.01 to 1.82 mmol/L)	1 16	3.8 61.5
Inorganic phosphate (*n* = 27) (median = 1.60 mmol/L, 95% CI = 1.16 to 2.42 mmol/L)	Decreased (0.39 to 1.29 mmol/L) Increased (2.41 to 4.41 mmol/L)	9 6	33.3 22.2
Chloride (*n* = 43) (median = 97 mmol/L, 95% CI = 93 to 100 mmol/L)	Decreased (66 to 95 mmol/L) Increased (106 to 125 mmol/L)	16 9	37.2 20.9
Potassium (*n* = 42) (median = 3.30 mmol/L, 95% CI = 3.10 to 3.90 mmol/L)	Decreased (2.5 to 3.9 mmol/L) Increased (5.1 to 6.1 mmol/L)	31 2	73.8 4.8
AST (*n* = 43) (median = 104 U/L, 95% CI = 89 to 114 U/L)	Increased (104 to 5810 U/L)	23	53.5
γ-GT (*n* = 43) (median = 21.0 U/L, 95% CI = 17.0 to 24.0 U/L)	Increased (31 to 262 U/L)	5	11.6
pH (*n* = 34) (median = 7.40, 95% CI = 7.36 to 7.43)	Decreased (7.17 to 7.40) Increased (7.41 to 7.50)	18 4	52.9 11.8
pCO_2 (*n* = 34) (median = 45.0 mmHg, 95% CI = 42.9 to 49.6 mmHg)	Decreased (33.5 to 34.9 mmHg) Increased (45.1 to 64.3 mmHg)	2 17	5.9 50.0
Bicarbonate (*n* = 34) (mean ± SD = 26.6 ± 6.6 mmol/L, 95% CI = 24.3 to 28.9 mmol/L)	Decreased (14.5 to 19.9 mmol/L) Increased (30.1 to 43.1 mmol/L)	5 8	14.7 23.5
Base excess (*n* = 34) (mean ± SD = 2.5 ± 6.9 mmol/L, 95% CI = 0.8 to 4.9 mmol/L)	Decreased (−11.5 to −2.1 mmol/L) Increased (2.1 to 18.0 mmol/L)	9 19	26.5 55.9
Rumen chloride (*n* = 37) (median = 20.0 mmol/L, 95% CI = 17.0 to 24.0 mmol/L)	Increased (31 to 63 mmol/L)	9	24.3

the surgery was completed, a segmental SIV was reduced in 9 and a complete SIV was reduced in 12. Two cows underwent additional intestinal resection, and in 5 others the cecum was evacuated. The remaining 42.6% (20/47) were euthanized during surgery because of severe intestinal lesions or because reduction of the volvulus was not possible. Intraoperative complications occurred in 7 cows; these manifested as recumbency with subsequent intestinal contamination in 2 cows, recumbency without contamination in 5 cows, spontaneous death in 1 cow, and bowel rupture in 1 other cow.

Postoperative treatments

All cows (18/18) that were discharged received 10 L of a solution containing 50 g glucose and 9 g sodium chloride/L, daily for 1 to 7 d (median: 3 d), administered as a slow IV drip *via* an indwelling jugular vein catheter. Antibiotic treatment was administered for 4 or 5 d and included penicillin G procaine (12 000 IU/kg) given IM (15/18), amoxicillin (7 mg/kg) given IM (1/8), and danofloxacin (1.2 mg/kg) given IV (1/18; a cow with a respiratory problem). With one exception, all cows (17/18) received flunixin meglumine (1 mg/kg), ketoprofen (3 mg/kg), or metamizole (35 mg/kg) administered IV for 2 to 3 d. Prokinetic drugs were used for 1 to 7 d (median: 3 d) in 14 cows. Five cows received neostigmine (Konstigmin; Vetoquinol, Bern, Switzerland), 40 to 45 mg, administered *via* a continuous drip infusion; and 9 received IM metoclopramide (30 mg), usually 7 to 9 times at 8 h intervals (metoclopramide was only used in the first few study years). Five cows with hypocalcemia (calcium < 2.0 mmol/L) received 500 mL of 40% calcium borogluconate administered IV. In 7 cows,

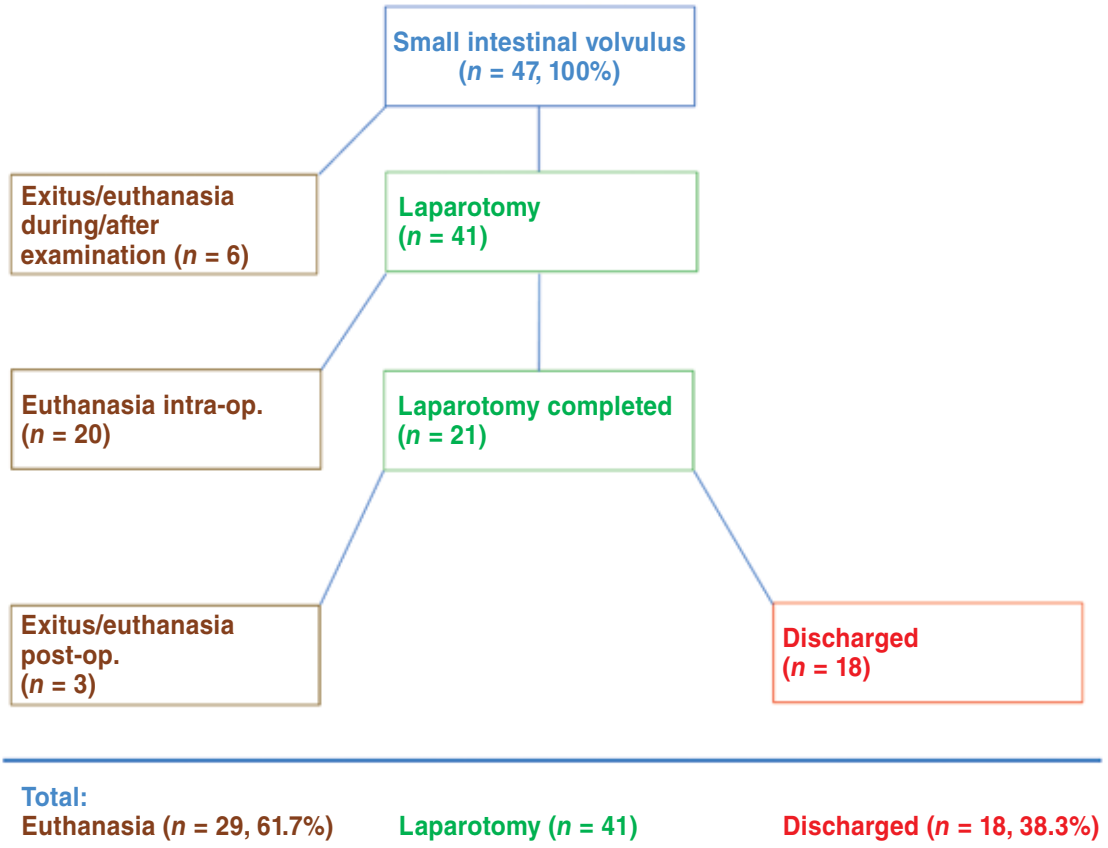


Figure 3. Treatment flowchart for 47 cows with small intestinal volvulus.
op. – Operation.

hypokalemia (potassium < 4.0 mmol/L) was treated with daily oral doses of 60 to 100 g of potassium chloride until normokalemia occurred.

Short-term outcomes of 21 cows in which the surgery was completed

Three cows died or were euthanized within 3 d of surgery because of progressive deterioration. With 1 exception, the general condition of the surviving cows improved and returned to normal within 1 to 10 d (median: 3.0 d) of surgery. The appetite returned to normal in all remaining 18 cows within 2 to 10 d (median: 3.0 d) and fecal output became normal within 1 to 7 d (median: 3.0 d). In the first 7 d after surgery, the median rectal temperature ranged from 38.5 to 38.9°C. The median heart rate, which was elevated at 96 bpm on admission, returned to the normal range, from 72 to 76 bpm, in 1 to 7 d following surgery. Thirteen cows were discharged and in good health within 5 d after surgery, and the remaining 5 cows within 6 to 14 d after surgery.

Comparison of 18 surviving and 29 non-surviving cows

The median duration of illness on admission was 12 h in both groups. Furthermore, the median heart rate (88 *versus* 100 bpm), rectal temperature (38.5 *versus* 38.4°C), and respiratory rate (28 *versus* 28 breaths per min) did not differ significantly between the groups. In contrast, the groups differed significantly with respect to the following variables assessed on admission: severely abnormal general condition (16.7 *versus* 37.9%, $P < 0.05$), rumen stasis (22.2 *versus* 79.3%, $P < 0.01$), and intestinal atony on auscultation (16.7 *versus* 48.3%, $P < 0.05$) (Figure 4). Of the laboratory variables, concentrations of urea (6.5 *versus* 9.8 mmol/L, $P < 0.01$) and magnesium (0.98 *versus* 1.30 mmol/L, $P < 0.05$) differed significantly between surviving and non-surviving cows.

Long-term outcomes of the 18 discharged cows

The long-term outcome was determined 2 y after discharge *via* a telephone interview. Eleven (61.1%) cows had remained productive in their respective herds, 4 had been slaughtered for economic reasons, and the outcome was not known for the remaining 3 cows.

Postmortem findings

The principal findings for the 29 cows that died or were euthanized were SIV and hemorrhagic infarction of the involved intestines (Figure 5). Blood clots in the intestinal lumen were seen in 4 cows, bleeding intestinal ulcers were seen in 1, and an intussusception in the twisted area of intestines was seen in 1 other. Five other cows had acute fibrinous peritonitis and 2 had ruptured intestines.

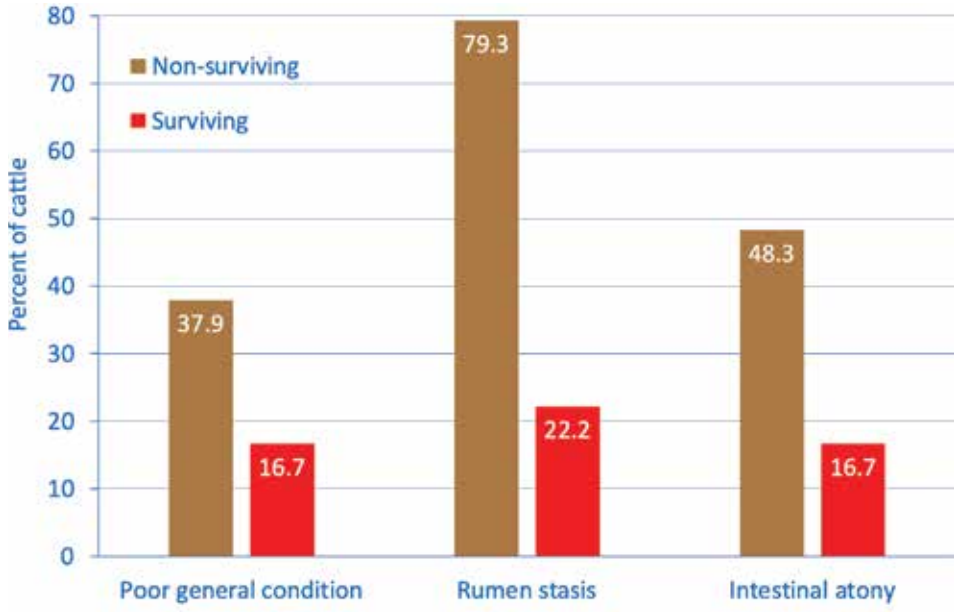


Figure 4. Differences in poor general condition ($P < 0.05$), rumen stasis ($P < 0.01$), and intestinal atony ($P < 0.05$) in cows with small intestinal volvulus that survived ($n = 29$) and those that did not survive ($n = 18$).

Figure 5. Photograph showing segmental small intestinal volvulus in a 5-year-old Brown Swiss cow. The cow was normal when put on pasture in the morning but had severe colic a few hours later. The cow was referred to our clinic immediately and operated on, but could not be saved. The proximal 2/3 of the jejunum were twisted and severely dilated and the intestinal wall had a dark red to purplish-blue discoloration.

Discussion

Compared with SIV, intestinal changes are less severe in cattle with intussusception (19) and more severe in those with mesenteric torsion (21). This is reflected by the spectrum of clinical findings, which in cattle with SIV often lie between those of intussusception (19) and mesenteric torsion (21). A good example to illustrate this is colic. When combined with reduced or absent fecal output, colic is a primary sign of mechanical ileus in cattle (26). In the present study, 66.0% (31/47) of the cows had signs of colic, compared with 46.8% (59/126) of cattle with intussusception (19). The frequency of colic in cattle with mesenteric torsion was 65.6% (40/61) (21), similar to that in cows with SIV. The colic phase lasts only about 12 h (22), which likely explains why 34.0% (16/47) of cows with SIV did not have signs of colic. It can be assumed that, at the time of admission, the cows without colic had already progressed to the indolence or even the intoxication phase. It is likely that these cows had colic before admission, because 70.2% (33/47) had a history of colic and similar observations have been reported by others (3,26). Of 51 cattle with SIV, 64.7% (33/51) had a history of colic; but at the time of admission, only 39.2% (20/51) had signs of colic. Therefore, it is important to remember that, although colic is a cardinal sign of SIV, its absence does not rule out the condition.

Tachycardia occurred in 68% (32/47) of cows with SIV. The frequency of tachycardia in cows with SIV was higher than that in cattle with intussusception (38.1%, 48/126) (19) and lower than that in cattle with mesenteric torsion (80.3%, 49/61) (21). Mesenteric torsion and SIV have more severe hemodynamic effects and a more rapid onset of toxemia than intussusception and strangulation (12). Of all clinical signs, rumen atony had the highest predictive value for survival; 79.3% (23/29) of the non-surviving cows had no rumen motility, compared with only 22.2% (4/18) of cows that survived. Thus, rumen atony in cows with SIV is a prognostic sign of poor outcome. Likewise, intestinal atony is a cardinal sign of ileus but was seen in only 36.2% (17/47) of cows with SIV. Tests by BSA or PSA were frequently positive on the right side. However, positive BSA and/or PSA also occurs with other conditions, including right abomasal displacement, abomasal torsion, cecal dilatation, and severe diarrhea. This finding is always serious and pointed to a disorder on the right side of the abdomen in our study population. Dilated small intestine is typical of small intestinal ileus (26) and could be palpated transrectally in 48.9% (23/47) of cows with SIV. Thus, the likelihood of transrectal findings without dilated small intestines in cows with SIV is relatively high, at more than 50%. Dilated large intestines could be palpated in only

6.4% (3/47) of cows with SIV, compared with 44.1% (26/59) of cows with mesenteric torsion (21), 13.6% (3/22) of cows with ileal impaction (27), and no cows with intussusception (19). Dilated small intestines could be palpated transrectally in 4 of 4 cows with SIV (10), whereas in 8 adult cattle with SIV, dilated intestinal loops could only be palpated after the disorder had progressed (3).

In addition to tachycardia and hypothermia, 51.1 to 66.0% of cows with SIV had sunken eyes, prolonged capillary refill time, reduced skin surface temperature, and reduced skin elasticity. This was similar to findings in cows with internal herniation (28), intussusception (19), and mesenteric torsion (21), and reflected shock-associated changes. Of 12 cows with ileal impaction, 10 of which had only mild changes in general condition, < 50% had vital signs typical of shock (27). In summary, comparing clinical signs of cows with different forms of ileus shows that the frequency and severity of clinical signs of cows with SIV fall between those of cows with intussusception and mesenteric torsion. The most serious clinical signs are almost always seen in cows with mesenteric torsion because of the grave tissue changes associated with this condition.

The principal laboratory changes in cows with SIV were hypocalcemia (74.1%, 20/27), hypokalemia (73.8%, 31/42), azotemia (62.8%, 27/43), hypermagnesemia (61.5%, 16/26), and hemoconcentration (60.0%, 27/45); the latter 2 results also reflect shock. By comparison, hemoconcentration was seen in 61.1% (77/126) and 71.7% (43/60) and azotemia was seen in 62.1% (77/124) and 52.5% (31/59) of cows with intussusception and mesenteric torsion, respectively (19,21). The cause of hypermagnesemia is thought to be reduced glomerular filtration because of dehydration (29); this is supported by the observation that the surviving and non-surviving cows differed significantly with respect to median magnesium (0.98 *versus* 1.30 mmol/L) and urea (6.5 *versus* 9.8 mmol/L) concentrations. Hypochloremic metabolic alkalosis was a rare finding because SIV is an acute disease and the ileus was primarily located in the jejunum (hypochloremia, 37.2%, 16/43; increased blood pH, 11.8%, 4/34; increased rumen chloride concentration, 24.3%, 9/37) in the present study. It is therefore possible that the time from the occurrence of the volvulus to clinical examination was too short for the electrolyte and blood-gas changes to become manifest, which has been suggested by other authors (16,30). Another possibility for the frequent occurrence of acidosis in the present study (52.9%, 18/34) is the secondary development of metabolic acidosis caused by an increase in L-lactate in addition to the underlying alkalosis. The increase in L-lactate results from ischemia of the intestinal wall and subsequent necrosis (1,26,31).

Almost 25% of the cows underwent surgery in lateral or sternal recumbency; some intentionally from the start of surgery and others because they became recumbent during the procedure. The risk of unintentional recumbency and possible contamination during surgery in cows with suspected SIV should be considered carefully when planning the surgery. It may be prudent to conduct the surgery of compromised and fractious cows under sedation and in sternal or lateral recumbency.

Concerning outcome, the percentage of cows discharged was 38.3% (18/47) of those with SIV, which was higher than that of cows with mesenteric torsion (23%, 14/61) (21) and lower than that of cows with intussusception (44.4%, 56/126) (19), internal herniation (55.6%, 10/18) (28), and ileal impaction (100%, 22/22) (27). In previous reports, 100% (4/4) (10) and 27.5% (14/51) of cattle with SIV (3) were discharged. Early diagnosis and immediate surgical treatment were considered crucial for a successful outcome. The success rate was 66.7% (10/15) when the duration of illness was up to 12 h, but was only 15.8% (3/19) in cattle that had been ill for 13 to 48 h. Cattle that had been ill for longer than 2 d did not survive (3).

In conclusion, intestinal ileus must be ruled out in cattle with acute onset of severe illness accompanied by reduced or absent fecal output, even in the absence of colic. However, identifying the type of ileus is difficult based on clinical findings. Laboratory examinations are critical for determining the degree of dehydration and assessing electrolyte and acid-base imbalances to optimize supportive treatment. Ultrasonography aids in the diagnosis of ileus, but the actual volvulus in this study could not be visualized. Immediate surgical treatment is essential for a favorable outcome.

Acknowledgments

The authors thank the technicians of the medical laboratory for the hematological and biochemical analyses, the veterinary students for monitoring the cows during the night, and the agricultural assistants for their help with the clinical examinations. Thanks also to the many veterinarians who examined and treated the patients and assisted in the surgeries. CVJ

References

1. Anderson DE, Constable PD, St. Jean G, Hull BL. Small-intestinal volvulus in cattle: 35 cases (1967–1992). J Am Vet Med Assoc 1993;203:1178–1183.
2. Smith DF. Surgery of the bovine small intestine. Vet Clin North Am Food Anim Pract 1990;6:449–460.
3. Rademacher G, Lorenz I. Diagnose, therapie und prognose des volvulus intestini beim rind [article in German]. Tierärztl Umschau 1998;53:93–105.
4. Anderson DE, Ewoldt JMI. Intestinal surgery of adult cattle. Vet Clin North Am Food Anim Pract 2005;21:133–154.
5. Desrochers A, Anderson DE. Intestinal surgery. Vet Clin North Am Food Anim Pract 2016;32:645–671.
6. Vogel SR, Nichols S, Buczinski S, *et al.* Duodenal obstruction caused by duodenal sigmoid flexure volvulus in dairy cattle: 29 cases (2006–2010). J Am Vet Med Assoc 2012;241:621–625.
7. Russell S. Duodenal sigmoid flexure volvulus and gall bladder displacements in dairy cows. Vet Rec 2013;173:121–122.
8. Dirksen G, Doll K. Dünndarmverschlingung. In: Dirksen G, Gründer HD, Stöber M, eds. Innere Medizin und Chirurgie des Rindes. Berlin, Germany: Parey Buchverlag, 2002:525–527.
9. Radcliffe RM. Small-intestine surgery in cattle. In: Fubini SL, Ducharme NG, eds. Farm Animal Surgery. St. Louis, Missouri: Elsevier, 2017:309–317.
10. Fubini SL, Smith DF, Tithof PK, Perdrizet JA, Rebhun WC. Volvulus of the distal part of the jejunoileum in four cows. Vet Surg 1986;15:150–152.
11. Constable PD, Hinchcliff KW, Done SH, Grünberg W. Diseases of the intestines of ruminants. Veterinary Medicine. A Textbook of the Diseases of Cattle, Horses, Sheep, Pigs, and Goats. St. Louis, Missouri: Elsevier, 2017:523–530.
12. Francoz D, Guard CL. Volvulus of the large and small intestine around the mesenteric root. In: Smith BP, Van Metre DC, Pusterla N, eds. Large Animal Internal Medicine. St. Louis, Missouri: Elsevier, 2020:896.

13. Pearson H, Pinsent PJN. Intestinal obstruction in cattle. Vet Rec 1977; 101:162–166.
14. Steiner S, Krametter-Frötscher R, Baumgartner W. Mechanischer ileus beim erwachsenen rind, eine retrospektive studie [article in German]. Wien Tierärztl Mschr 2008;96:166–176.
15. Braun U. Ultrasonography of the gastrointestinal tract in cattle. Vet Clin North Am Food Anim Pract 2009;25:567–590.
16. Anderson DE. Intestinal volvulus of cattle. In: Anderson DE, Rings DM, eds. Current Veterinary Therapy. Food Animal Practice. St. Louis, Missouri: Saunders Elsevier, 2009:120–121.
17. Volz C. Klinische, labordiagnostische und sonographische Befunde sowie Therapie und Verlauf bei 168 Rindern mit Volvulus jejunalis, Torsio mesenterialis und Colonscheibentorsion [Dr. med. vet. dissertation]. Zurich, Switzerland: University of Zurich, 2021.
18. Rosenberger G. Clinical Examination of Cattle. Berlin, Hamburg, Germany: Paul Parey, 1979.
19. Braun U, Gerspach C, Volz C, Boesiger M, Hilbe M, Nuss K. A retrospective review of small intestinal intussusception in 126 cattle in Switzerland. Vet Rec Open 2023;10:e58.
20. Braun U, Nuss K, Reif S, Hilbe M, Gerspach C. Left and right displaced abomasum and abomasal volvulus: Comparison of clinical, laboratory and ultrasonographic findings in 1982 dairy cows. Acta Vet Scand 2022; 64:40.
21. Braun U, Gerspach C, Volz C, Hilbe M, Nuss K. Dilated small and large intestines combined with a severely abnormal demeanor are characteristic of mesenteric torsion in cattle. J Am Vet Med Assoc 2023;261: 1531–1538.
22. Gründer HD. Kolik beim rind [article in German]. Prakt Tierarzt 1984; 66:84–86.
23. Braun U, Amrein E, Koller U, Lischer C. Ultrasonographic findings in cows with dilatation, torsion and retroflexion of the caecum. Vet Rec 2002;150:75–79.
24. Nuss K, Schwarz A, Ringer S. Lokalanästhesien beim wiederkäuer [article in German]. Tierärztl Prax 2017;45(G):159–173.
25. D'Anselme O, Hartnack A, Andrade JSS, Alfaro Rojas C, Ringer SK, de Carvalho Papa P. Description of an ultrasound-guided erector spinae plane block and comparison to a blind proximal paravertebral nerve block in cows: A cadaveric study. Animals 2022;12:2191.
26. Dirksen G. Ileus beim Rind. In: Dirksen G, Gründer HD, Stöber M, eds. Innere Medizin und Chirurgie des Rindes. Berlin, Germany: Parey Buchverlag, 2002:514–517.
27. Nuss K, Lejeune B, Lischer C, Braun U. Ileal impaction in 22 cows. Vet J 2006;171:456–461.
28. Ruf-Ritz J, Braun U, Hilbe M, Muggli E, Trösch L, Nuss K. Internal herniation of the small and large intestines in 18 cattle. Vet J 2013;197: 374–377.
29. Grünberg W, Constable P, Schröder U, Staufenbiel R, Morin D, Rohn M. Phosphorus homeostasis in dairy cows with abomasal displacement or abomasal volvulus. J Vet Intern Med 2005;19:894–898.
30. Doll K. Hämatologische und klinisch-chemische untersuchungsbefunde bei kälbern und jungrindern mit Ileus [article in German]. Tierärztl Prax 1991;19:44–47.
31. Fubini SL, Yeager AE, Divers TJ. Noninfectious diseases of the gastrointestinal tract. In: Peek SF, Divers TJ, eds. Rebhun's Diseases of Dairy Cattle. St. Louis, Missouri: Elsevier, 2018:168–248.

Review Article Compte rendu

Basic triage in dogs and cats: Part II

Laura Ilie, Elizabeth Thomovsky

Abstract

Background

Emergency cases can be presented at any time of the day or night. All small animal practitioners need to have the skills to triage and stabilize common emergency cases, even if cases are ultimately referred to another facility.

Objective and procedure

The second part of this 3-part review article series discusses animals that collapse at home as well as dogs and cats with bleeding. A stepwise approach to categorize and stabilize these cases is outlined, along with helpful tips to optimize the referral experience, if indicated.

Results

Having a robust and methodical approach to animals that collapse is important for many emergency cases, as the causes and treatment methods vary. Bleeding can lead to acute death if left untreated and knowing the steps to stop bleeding is important for patient stabilization.

Conclusion and clinical relevance

Do not refer emergent cases before completing basic stabilization. Many emergency cases do not require emergent referral and can be worked up by the primary veterinarian or sent to a referral clinic on an appointment basis after appropriate stabilization steps have occurred.

Résumé

Triage de base chez les chiens et les chats : Partie II

Contexte

Les cas d'urgence peuvent être présentés à toute heure du jour ou de la nuit. Tous les praticiens des petits animaux doivent avoir les compétences nécessaires pour trier et stabiliser les cas d'urgence courants, même si les cas sont finalement transférés vers un autre établissement.

Objectif et procédure

Le deuxième de cette série de trois articles traite des animaux qui s'effondrent à la maison ainsi que des chiens et des chats qui saignent. Une approche par étapes pour catégoriser et stabiliser ces cas est décrite, ainsi que des conseils utiles pour optimiser l'expérience de référence, si elle est indiquée.

Résultats

Avoir une approche robuste et méthodique face aux animaux qui s'effondrent est important dans de nombreux cas d'urgence, car les causes et les méthodes de traitement varient. Les saignements peuvent entraîner une mort aiguë s'ils ne sont pas traités et connaître les étapes à suivre pour arrêter le saignement est important pour la stabilisation du patient.

Conclusion et pertinence clinique

Ne référez pas les cas urgents avant d'avoir terminé la stabilisation de base. De nombreux cas d'urgence ne nécessitent pas de référence urgente et peuvent être traités par le vétérinaire initial ou envoyés à une clinique de référence sur rendez-vous après que les mesures de stabilisation appropriées ont été prises.

(Traduit par Dr Serge Messier)

Can Vet J 2024;65:278–288

Emergency and Critical Care, VCA Arboretum View Animal Hospital, 2551 Warrenville Road, Downers Grove, Illinois 60515, USA (Ilie); Veterinary Clinical Sciences, Purdue University, 625 Harrison Street, West Lafayette, Indiana 47907, USA (Thomovsky).

Address all correspondence to Dr. Elizabeth Thomovsky; email: ethomovs@purdue.edu

Introduction

Primary care veterinarians in private general and emergency practice often carry out basic triage and stabilize animals from the "red" or "orange" groups [see Figure 1 in Part I of this review (1)] before referring them for definitive diagnostics and management. This article continues our outline of the most frequently encountered emergency situations [see Figure 2 in Part I of this review (1)] leading to referral in both dogs and cats and provides guidelines for how to stabilize animals before transport.

Section 1: Collapse

Acute collapse is defined as sudden loss of postural tone. The dog or cat may be able to sit but not stand (hind limb collapse) or be completely recumbent and unable to stand or sit (complete collapse). During a collapsing episode, the animal is fully awake and aware of its surroundings.

Collapsing should be differentiated from syncope (fainting). The latter is characterized by a transient period of loss of postural tone along with loss of consciousness. Syncopal episodes are short and the animal regains consciousness and postural tone afterwards. Most syncopal events are linked to arrhythmias [see Part III of this review (2)].

Immediate triage and care are required for a collapsed patient. These conditions are in 2 main categories: shock (cardiogenic, distributive, or hypovolemic) and non-shock.

Step #1: Is this animal having trouble breathing (*e.g.,* left-sided congestive heart failure or respiratory disease)? Does this animal have severe or end-stage heart disease?

If the animal is presented collapsed with signs of respiratory distress and auscultable crackles in the lung fields (*i.e.,* "loud auscultation"), severe heart disease might be suspected. Stabilize as detailed in the respiratory distress section [see Figure 3 in Section 1 in Part I of this review (1)].

Step #2: Is this animal cardiovascularly stable?

If the animal is not cardiovascularly stable, as manifested by clinical signs such as weak pulses, pale gums, hypotension, or sinus bradycardia/tachycardia:

- Evaluate ECG and measure blood pressure.
- Obtain a rapid point-of-care ultrasound (if available) of the thorax and the abdomen, looking for free fluid in the pleural space, abdomen, or pericardium.
  - Is there internal or external bleeding? (If yes, see Section 2.)
- Obtain baseline bloodwork, including at least glucose, lactate, packed cell volume/total protein (PCV/TP), sodium, and potassium (and ideally, a full CBC, chemistry, and electrolyte panel).
- Perform basic stabilization to end points as detailed in Box 1 and Box 2.

Box 1. How to perform basic stabilization of a hypotensive or hypovolemic dog or cat.

- Administer crystalloid fluids to treat shock and improve end points (see **Box 2**). Give 1/4 to 1/3 of the calculated shock dose (dog shock volume: 90 mL/kg; cat shock volume: 45 to 60 mL/kg) IV.
  - Bolus the fluids as quickly as possible in dogs. For example, in a 10-kilogram dog, give an initial bolus of 300 mL ($1/3 \times 90$ mL/kg) over ideally < 10 min.
  - In cats, administer calculated bolus over 10 to 15 min (slower if cat becomes nauseous).
  - Do not use a fluid pump in medium-to-large dogs; use a pressure bag or squeeze the fluid bag. A fluid pump can be used in most cats or in small dogs to give the fluids within the appropriate timeframe. Fluid pumps cannot give more than 250 mL within 15 min.
- Administer crystalloid fluids to end points (see **Box 2**).
- Do not worry about whether the fluids will worsen anemia; it is most important to deliver oxygen to tissues by increasing vascular volume and improving perfusion with crystalloids.
- Synthetic colloids may be considered [*e.g.,* VetStarch (Zoetis)].
  - Dogs: Administer IV in bolus volumes of 5 mL/kg given as quickly as possible (up to a total of 20 mL/kg).
  - Cats: Administer synthetic colloids in bolus volumes of 3 mL/kg over 10 to 15 min (up to a total of 10 mL/kg).
  - Give colloids with crystalloids to resuscitate to end points (**Box 2**). Colloids primarily lengthen the duration that crystalloids remain in the bloodstream rather than expand vascular volume.
  - Both human and canine studies have suggested that using synthetic colloids can lead to development of acute kidney injury and cause coagulopathies and platelet dysfunction (1–3).
- Is this animal possibly septic? (See Step #7 below for more information.)
  - If yes, beware of administering large volumes of fluids that can leak from the vasculature, cause edema, increase myocardial depression, and cause vasodilatory shock.
  - Administer broad-spectrum antibiotics as soon as sepsis is suspected.
- Transfusion of packed red blood cells or whole blood is rarely used for resuscitation. Their use is reserved for scenarios where the measured PCV/TP is < 15 to 20%[a] and:
  - total shock bolus amount of crystalloids has been given within the course of 1 h and the dog or cat is still hypotensive and/or tachycardic;
  - hypotension persists despite crystalloid and/or colloid administration;
  - blood pressure has normalized (typically, systolic blood pressure > 90 to 100 mmHg or mean blood pressure > 80 mmHg) and animal remains weak or is tachycardic.

[a] In cases of acute traumatic blood loss, significantly higher PCV values may result in weakness, tachycardia, tachypnea, and weakness, still indicating a need for transfusion.

References

1. Boyd CJ, Claus MA, Raisis AL, *et al.* Evaluation of biomarkers of kidney injury following 4% succinylated gelatin and 6% hydroxyethyl starch 130/0.4 administration in a canine hemorrhagic shock model. J Vet Emerg Crit Care 2019;29:132–142.
2. Gauthier V, Holowaychuk MK, Kerr CL, Bersenas AME, Wood RD. Effect of synthetic colloid administration on coagulation in healthy dogs and dogs with systemic inflammation. J Vet Intern Med 2015;29: 276–285.
3. Hayes G, Benedicenti L, Mathews K. Retrospective cohort study on the incidence of acute kidney injury and death following hydroxyethyl starch (HES 10% 250/0.5/5: 1) administration in dogs (2007–2010). J Vet Emerg Crit Care 2016;26:35–40.

Step #3: Could this dog have pericardial effusion?

If a dog is presented with sinus tachycardia, poor femoral pulse quality, and muffled heart sounds, especially if it is a large-breed dog (*e.g.,* Labrador or golden retriever), it may have pericardial effusion. Ideally, use point-of-care ultrasound to detect presence and quantity of pericardial effusion and presence/absence of cardiac tamponade (*i.e.,* collapsed right atrium). If ultrasound is

Box 2. End point resuscitation goals for animals.

Give fluids to restore vital signs (respiratory rate, mucous membranes, and capillary refill time) and pulse quality. Ideally, heart rate will also improve to closer to normal (10 to 15% decrease from baseline). Septic animals (see Step #7) often remain tachycardic despite appropriate resuscitation. Other resuscitation goals include:

- blood glucose > 80 mg/dL,
- restoration of blood pressure (systolic: > 90 mmHg and/or 10 to 15% increase from baseline),
- normalization of elevated blood lactate levels,
- improvement of lactate (at least trending towards normal).

not available, use thoracic radiographs to detect a large, globoid heart (may be absent with limited pericardial effusion or acute pericardial bleeding). On an ECG, P-QRS complexes alternate height depending on heart movement (closer or farther from ECG leads; electrical alternans).

Background

During cardiac tamponade, fluid in the pericardial sac increases intrapericardial pressure, leading to diastolic collapse of the right atrium and/or ventricle. Blood cannot fill the right side of the heart and less blood is available to pump (decreased cardiac output), leading to cardiogenic shock which manifests as hypotension, pale gums, collapse, tachycardia, cold extremities, weak pulses, and muffled heart sounds. Ascites may also be present, as well as pulsus paradoxis (palpated pulse is stronger during expiration and weaker during inspiration). Immediate pericardiocentesis is needed to relieve pressure on the right side of the heart.

Pericardial effusion ± only mild tamponade manifests as collapse, lethargy, increased respiratory rate and effort, anorexia, and vomiting (3). Physical examination usually reveals a prolonged capillary refill time (CRT), pale gums, muffled heart sounds, weak pulses, possible arrhythmias, and tachycardia.

Causes for pericardial effusion include cardiac neoplasia (*e.g.,* hemangiosarcoma, chemodectoma, lymphoma, mesothelioma), idiopathy, secondary to a left atrial tear or secondary to coagulopathy, systemic inflammatory disease (4), or infectious diseases (5). Idiopathic or neoplastic causes are the most likely to produce volumes of fluid leading to tamponade. Depending on etiology, animals with pericardial effusion have a poor to guarded long-term prognosis.

Emergency stabilization

If the animal is collapsed or hemodynamically unstable, perform pericardiocentesis (Box 3) to reduce the risk of dying during transport to a referral clinic.

Practice tips

1. DO NOT perform pericardiocentesis if patient is stable (normal blood pressure, ambulatory, normal ECG or very mild arrhythmia) and can be transferred to a referral center within 20 to 30 min. Ideal echocardiographic visualization for disease such as a heart-based mass occurs with some pericardial effusion present.

Box 3. How to perform pericardiocentesis.

- Place peripheral IV catheter and connect patient to an ECG.
- Place animal in sternal or left-sided recumbency.
- Ideally, use an ultrasound probe to identify the best site for pericardiocentesis (*i.e.,* where there is obvious fluid). Without ultrasound, perform pericardiocentesis at heart location: right 4th to 6th intercostal space at costochondral junction.
- Shave and clean skin.
- Give butorphanol, 0.2 mg/kg, IV, for sedation, ± lidocaine locally at site of needle insertion.
- Using a sterile technique, insert a large, long, fenestrated catheter [*e.g.,* 14- to 18-gauge (depending on animal), at least 7 to 10 cm]. May need stab incision through skin.
- Once catheter enters the pericardial space, sanguineous or serosanguineous fluid will appear in catheter hub. Advance the catheter slightly (~1 cm) while holding the stylet. Remove stylet, connect catheter to extension set with 3-way stopcock, and drain fluid.
- Before removing large volumes of fluid, place a small amount in a red-top tube to ensure the fluid does not clot (characteristic of pericardial effusion). Clotting is suggestive that needle has entered the heart; remove catheter and try again.
- If an arrhythmia occurs when the needle is in pericardial sac, catheter may be touching the myocardium and need to be repositioned.
- If the arrhythmia is severe (usually a ventricular arrhythmia), give 2 mg/kg bolus of lidocaine slowly, IV, and start CRI if arrhythmia persists.
- Start IV crystalloids once pericardial fluid has been removed and there is no tamponade.
- Monitor ECG and blood pressure to ensure they have improved.

2. Do not give diuretics or other medications, as they may cause hypovolemia and worsen clinical signs. Diuretics are only indicated with clear signs of pulmonary edema and left-sided congestive heart failure.
3. Obtain an echocardiogram with a cardiologist to further investigate the underlying cause and provide prognostic information.

Step #4: Is this cat suffering from an aortic thromboembolism?

If there is concern that a cat is in acute pain and dragging 1 or more limbs with decreased pulses in that limb, the top differential diagnosis is an aortic thromboembolism [see Part III of this review (2)].

Step #5: Does this animal have a severe tachy- or bradyarrhythmia?

If a dog or cat is collapsed due to a severe cardiac arrhythmia with heart rate > 180 bpm (dog) or > 240 bpm (cat) or < 60 bpm (dog or cat), stabilize as detailed for arrhythmia [see Part III of this review (2)].

Step #6: Is there internal or external bleeding?

If the animal has collapsed due to severe bleeding, stabilize as detailed in Section 2 and Figure 1.

Step #7: Is this animal septic?

Sepsis is a clinical syndrome of systemic inflammatory response to a source of infection (bacterial, viral, fungal, or protozoal). Untreated, this can lead to septic shock, multi-organ failure,

Table 1. Common sources of infection in septic dogs and cats.

Type	Source
Gram-positive bacteria	Skin Injured soft tissue Intravenous catheters Respiratory system (pneumonia/pyothorax)
Gram-negative bacteria	Urogenital system (pyometra/pyelonephritis) Gastrointestinal system (most common in dogs and cats) Trauma Osteomyelitis Bite wounds Endocarditis

and possibly death. Early detection and rapid and aggressive treatment are critical.

Background

Sources for infection in septic animals are numerous (Table 1). In both dogs and cats, the most common source is leakage from the gastrointestinal tract due to obstruction, dehiscence of a previous surgical site or biopsy, or gastrointestinal neoplasia (6).

Depending on the stage of the condition (acute *versus* late), clinical signs of sepsis in dogs and cats include fever or hypothermia, tachycardia, bounding or poor pulse quality, injected or pale mucous membranes, rapid or slow CRT, hypotension (systolic blood pressure < 80 mmHg), and hypoglycemia (blood glucose < 60 mg/dL). Some animals have vomiting, diarrhea, weakness, lethargy, or anorexia.

Emergency stabilization

The initial resuscitative goal is to restore hemodynamic stability with crystalloids. To avoid fluid overload, "Give them as much [fluid] as they need and not a drop more" (7). The first 6 h after diagnosis of sepsis are critical; perform basic stabilization (Box 1) to end points (Box 2).

Practice tips

1. Many septic animals have abdominal effusion (*i.e.,* septic peritonitis), which gives a clue to underlying disease. Abdominocentesis (± ultrasound) will provide a fluid sample; compare glucose and lactate concentrations to those in peripheral blood.
   - If abdominal fluid glucose concentration is ≤ 20 mg/dL than peripheral blood, there is a very high chance of septic peritonitis (8).
   - If abdominal fluid lactate concentration is ≥ 2 mmol/L than peripheral blood, there is a high chance of septic peritonitis (8).
2. In-house fluid cytology identifying intracellular bacteria confirms sepsis.
3. After fluid therapy is initiated, obtain a quick ultrasound or repeat abdominal tap, especially if no obvious fluid is detected initially; fluid administration may produce more fluid.
4. When in doubt, treat an animal as if it has sepsis: carry out cautious fluid resuscitation, treat hypoglycemia, and start broad-spectrum antimicrobials.

Table 2. Clinical signs of anaphylaxis in dogs and cats.

System affected	Clinical signs
Cardiovascular	Sinus tachycardia Sinus bradycardia (cats) Collapse Pale mucous membranes and prolonged CRT Hypotension Hypothermia Arrhythmia
Respiratory	Dyspnea Tachypnea Bronchospasm Stridor (dog) Open-mouth breathing (cat)
Digestive	Vomiting Diarrhea (± hemorrhagic) Nausea Hypersalivation
Cutaneous	Pruritus Erythema/hyperemia Urticaria Facial edema
Neurologic	Weakness Seizures Incoordination Depression/stupor
Ocular	Blepharospasm Conjunctival hyperemia Chemosis

CRT — Capillary refill time.

Step #8: Is this animal in anaphylactic shock?

Anaphylaxis is a systemic, immediate hypersensitivity reaction caused by IgE-mediated release of mediators from mast cells and basophils. Anaphylaxis develops a few minutes after contact with the allergen and affects multiple organs. In dogs, "shock organs" are gastrointestinal and liver. In cats, anaphylaxis primarily affects pulmonary and gastrointestinal systems. In both species, cardiovascular, respiratory, neurologic, and cutaneous systems can be affected (Table 2). Signs of hepatic involvement manifest as increases in serum alanine aminotransferase, gallbladder edema, and sometimes fulminant liver failure (including elevated clotting times), most of which become apparent chronically.

Background

Clinical signs of anaphylaxis vary and depend on reaction severity, interval after reaction, and patient comorbidities. Multiple organ systems are affected but not all clinical signs will be present (Table 2) (9). Causes of anaphylaxis include ophthalmic antibiotics (cats) (10), vaccines, envenomation, insect bites, antibiotics, blood products, NSAIDs (dogs), opioids, contrast substances, and food (9).

Emergency stabilization

Provide immediate medical attention to a dog or cat with anaphylaxis as its condition can rapidly deteriorate.

- If respiratory distress is present, provide oxygen immediately. Severe upper airway edema may require intubation [see Section 1 in Part I of this review (1)].
- Place peripheral IV catheter as soon as possible.

- If hypotension is noted, see Box 1.
- If the animal is not yet hypotensive, start crystalloids at 120 mL/kg per day.
- Epinephrine, IV or IM, 0.01 mg/kg. Can repeat every 5 to 15 min (maximum: 0.5 mg/dog).
- Diphenhydramine, 2 mg/kg, IM + ranitidine, 0.5 to 2.5 mg/kg diluted, slowly IV (10 min).
- If bronchospasm is suspected, albuterol (1 or 2 puffs) may be given by metered-dose inhaler every 15 min, up to 3 doses. Alternatively, administer aminophylline, 5 to 10 mg/kg, IV, if albuterol is not available and the dog or cat is in respiratory distress due to bronchospasm.

Practice tips

1. Steroids are *contraindicated in acute anaphylactic shock.* The dog or cat may receive a low dose of steroids once it is hemodynamically stable.
   - Steroids may increase gastrointestinal tract damage if the animal is not hemodynamically stable.
   - Steroids are largely used for anti-inflammatory effects with urticaria, facial edema, and pruritus. Their response is too slow (several hours) to be beneficial in acute anaphylaxis (9,11).
2. Many dogs with anaphylaxis have abdominal effusion consistent with blood (similar hematocrit to peripheral blood, low TP). It is VITAL not to confuse anaphylaxis with hemoabdomen and take the dog to surgery. Anaphylaxis-induced hemoabdomen commonly resolves on its own but in some cases may require red blood cell and/or plasma therapy if there is a coagulopathy induced by anaphylaxis (12,13). Consider a prothrombin time/activated partial thromboplastin time test to evaluate the coagulation system.
3. Point-of-care ultrasound may reveal hepatic congestion and gallbladder wall edema in dogs, which may help to suggest anaphylaxis (14).
4. Animals with anaphylaxis will have increased alanine aminotransferase (14), likely secondary to liver hypoxia.
5. Inform the owner that the dog may require a few days in the hospital for full recovery, as rebound reactions can occur 24 to 48 h after the first anaphylaxis episode.

Step #9: Is this dog (rarely cat) suffering from heat stroke?

Heat stroke is caused by exposure to a high environmental temperature or strenuous exercise. A core body temperature > 41.0°C is consistent with heat stroke (15). The severity of clinical signs is determined by duration and maximal temperature.

Severe hyperthermia causes a systemic inflammatory response potentially progressing to multi-organ failure, including circulatory collapse, encephalopathy, acute respiratory distress syndrome, acute liver and renal failure, coagulopathy, rhabdomyolysis, intestinal ischemia, and eventually death.

Background

Heat stroke is most frequent during summer when the weather is hot and humid. However, abrupt transition from cool to warm (*e.g.,* in the spring) can also lead to heat stroke. Working dogs and brachycephalic breeds are predisposed but heat stroke can occur in any dog confined in a hot or humid environment without proper ventilation and water. Upper airway disease (*e.g.,* laryngeal paralysis) or obesity impairs panting and predisposes to heat stroke.

Box 4. How to cool a hyperthermic dog (or cat).

- Put cool water on the body and neck and use a fan to improve convective heat loss.
- Provide IV fluid therapy with room-temperature crystalloid fluids, with rate based on needs (more if the animal is in shock) and presence/absence of pulmonary edema or respiratory distress.
- Apply ice packs to jugular veins and head only (peripheral vasoconstriction will slow cooling).
- Stop cooling measures when rectal temperature reaches 39.4°C (to avoid rebound hypothermia).
- If hyperthermia is severe and persistent, consider a cold-water retention enema (10 to 20 mL/kg of cold water in rectum *via* long red rubber catheter). This invalidates rectal temperature.

Clinical signs include, but are not limited to, a wide range of body temperatures (depending on stage of disease progression and attempted cooling measures), panting, tachycardia with weak pulses, hyperemic gums, a wide range of neurologic signs (from normal mentation to prostration and coma, ataxia, or seizures), hemorrhagic diarrhea, and petechia (16).

The history may provide information about heat stroke cause and duration. Prognosis varies based on severity of clinical signs, duration of heat, previous medical conditions, and secondary complications. Poor prognostic indicators are persistent neurologic deficits, hypoglycemia (17), severe or refractory hypotension, arrhythmias, disseminated intravascular coagulation, and acute renal injury (18). In a retrospective study, mortality was 50% (18).

Emergency stabilization

If the animal is hyperthermic, provide cooling measures immediately (Box 4). It is difficult to assess respiration or mentation until the animal has been cooled.

Many dogs with heat stroke are presented with respiratory difficulties. Since many hyperthermic dogs are brachycephalic or have underlying upper airway disease, ensure the airway is patent and the dog is able to ventilate. Dogs with heat stroke may be presented with another lung pathology that reduces oxygenation (*e.g.,* pulmonary edema, pulmonary bleeding, or a pulmonary inflammatory response due to heat-induced tissue and endothelial injury).

Provide oxygen while still allowing panting. Avoid placing the animal in an oxygen cage with poor ventilation or temperature control or using a tight oxygen mask; use a loose mask or flow-by oxygen. If respiratory distress continues despite oxygen therapy, treat as described for respiratory distress in Section 1 in Part I of this review (1).

Dogs with heat stroke are also in shock and can have arrhythmias. If the animal is cardiovascularly unstable (*i.e.,* low blood pressure, poor peripheral pulses, obtunded, tachy- or brady-arrhythmia), address any arrhythmias [see Part III of this

review (2)] and stabilize as described in Box 1 to end points (Box 2). Administer antibiotics to prevent sepsis (Table 1).

Ideally, do baseline bloodwork including CBC, chemistry with electrolytes, and coagulation profile. At a minimum, monitor blood glucose, lactate, and PCV/TP hourly until the animal is stable. Ideally if a patient is referred, its blood glucose should be > 90 mg/dL, lactate should be trending down towards normal, and PCV/TP should be > 20%.

Practice tips

1. Avoid alcohol on paws or ice water baths, as vasoconstriction traps hot blood centrally.
2. Avoid steroids or NSAIDs (gastrointestinal tract is already damaged).

Step #10: Is this dog or cat suffering from metabolic derangements (hypo-/hyperglycemia, electrolyte abnormalities, anemia/polycythemia, toxin ingestion)?

Background

Most metabolic diseases cannot be addressed immediately and require further diagnostics. Some metabolic derangements (hypoglycemia, hyperkalemia, severe anemia) lead to collapse and can be fatal if not addressed immediately.

In an emergency room, 28% of dogs and 16% of cats with hyperkalemia (potassium > 6 mEq/L) had muscle weakness (19), which can contribute to unwillingness to stand. Hyperkalemia will cause bradycardia and other cardiac arrhythmias, including atrial standstill and asystole (death), if untreated. Potassium concentration > 8.0 mg/dL causes the most profound cardiac changes, with arrhythmias and bradycardia occurring at lower concentrations. Hyperkalemia occurs most commonly in dogs and cats with urethral obstruction or anuric/oliguric renal failure, and in dogs with hypoadrenocorticism.

Obtain a full chemistry panel, point-of-care analyzer panel, or, at a minimum, blood glucose and PCV/TP in collapse cases.

Emergency stabilization

Hypoglycemia. Correct hypoglycemia immediately when identified (Box 5).

Hyperkalemia. If a cat or dog is exhibiting changes to heart rate or rhythm or potassium concentration is > 7.5 mEq/L, correct potassium immediately to prevent death.

- 10% calcium gluconate, 0.5 to 1.5 ml/kg, IV over 15 min; this does not change potassium concentration but rapidly and transiently (30 to 60 min) corrects arrhythmias.
- Regular insulin, 0.25 to 0.5 U/kg, IV; then 4 mL of 50% dextrose/unit of insulin (diluted), IV. Insulin reduces potassium concentration (may take 20 to 30 min; lasts several hours).
- Treat underlying cause of hyperkalemia.

Anemia. DO NOT refer an animal without correcting hypotension (Box 1). Tachycardia occurs secondary to anemia, so crystalloid or colloid fluids will likely not fully correct tachycardia. Blood pressure should improve as fluid volume improves peripheral perfusion. Administer bolus fluids as needed to obtain systolic blood pressures ≥ 70 to 80 mmHg before sending an anemic animal to a referral clinic.

Box 5 How to correct hypoglycemia.

- Correct hypoglycemia immediately. If a peripheral venous catheter is present, give a bolus of 50% dextrose diluted at least 1:1 with saline to reduce osmolality and lessen chance of phlebitis and red blood cell hemolysis. If an intraosseous catheter is used, dilute the 50% dextrose 1:4 or 1:5 before administration.
- Doses vary widely, but a common starting dosage is 0.5 to 1.0 mL/kg of 50% dextrose, IV or IO (diluted at least 1:1 with saline) (1,2). It is extremely important to check blood glucose at 5 to 10 min after giving the dextrose bolus, to ensure the blood sugar has normalized. *Do not assume that a single dose of dextrose has corrected the hypoglycemia.*
- If the dog or cat remains hypoglycemic, do not hesitate to re-dose the dextrose (same or increased amount) and check again. Consider placing the animal on a CRI of crystalloid fluids with 2.5 to 5% dextrose to maintain normoglycemia. If the animal is hyperglycemic after the bolus, do not be concerned; endogenous insulin release normalizes the blood glucose. Transient iatrogenic hyperglycemia is not dangerous.
- If a catheter is not present, give sugar orally. Apply 50% dextrose, corn syrup, honey, or maple syrup to mucous membranes in the mouth. This may be less successful than IV treatment; oral glucose induces a greater insulin response than IV glucose administration *via* induction of gut incretins such as glucagon-like protein (GLP-1; *e.g.,* the incretin effect) (1–3). Recheck blood glucose 5 to 10 min after oral dextrose administration to determine if hypoglycemia has been corrected.

References

1. Olutunbi I, Heading K. Hypoglycemia in dogs: Causes, management, and diagnosis. Can Vet J 2018;59:642–649.
2. Morgan RK, Cortes Y, Murphy L. Pathophysiology and aetiology of hypoglycaemic crises. J Small Anim Pract 2018;59:659–669.
3. Reusch CE, Padrutt I. New incretin hormonal therapies in humans relevant to diabetic cats. Vet Clin Small Anim 2013;43:417–433.

Practice tips

1. If a dog or cat had clinical hypoglycemia at presentation and duration of travel to a referral institution is > 30 to 60 min, consider preparing the owner to give oral or IV dextrose *en route.*
2. When assessing PCV/TP to detect anemia, evaluate serum for icterus. This can suggest differential diagnoses (*e.g.,* anemia with icterus implies immune-mediated hemolytic anemia). If the animal is hyperglycemic, test serum for ketones (place serum on a urine dipstick ketone pad) to diagnose diabetic ketoacidosis. This information is important for prognostication and suggesting approximate costs of treatment before referral.

Step #11: Did this animal ingest a toxin?

Background

There are numerous sources of toxin ingestion (*e.g.,* prescribed and illicit drugs, household plants, insecticides, and herbicides). Following is a succinct, general approach to stabilization after ingestion of any toxin; for further information on a specific toxin, the reader is referred to other sources.

Clinical signs of toxicity vary based on age, underlying medical conditions, toxin type, toxin amount, and interval since ingestion. Obtain a thorough but rapid history including

name of drug and active substance, identity of item ingested, or name/picture of plant or mushroom ingested. If a drug was ingested, ascertain if it is extended-release, long-acting or sustained-release. Finally, determine if the animal exhibited clinical signs at home and if the owner administered medications or attempted to induce emesis.

Emergency stabilization

- Ensure the animal is stable (cardiovascular and respiratory).
- Induce emesis ONLY in asymptomatic patients with recent ingestion (< 4 to 6 h) or unknown time of ingestion.
  - — Dogs:
    - Apomorphine, 0.03 mg/kg, IV (compounded) or in conjunctival sac (tablet).
    - Ropinirole ophthalmic solution (dopamine agonist) approved for topical use.
  - — Cats:
    - Xylazine, 0.4 to 0.7 mg/kg, IM (20,21); dexmedetomidine 7 to 10 μg/kg, IM (22); or hydromorphone, 0.1 mg/kg, SC (23).
    - It is difficult to induce emesis in cats.
  - — If the animal is comatose or hyperthermic, has tremors or abnormal mentation, or otherwise is not a safe candidate for induction of emesis, consider gastric lavage.
- Administer activated charcoal with or without a cathartic.
  - — Use if ingested toxin binds to charcoal. Can give 1 to 3 g/kg, PO, once (24).
  - — Avoid activated charcoal with metals, caustic substances, or very small molecules (*e.g.,* xylitol, alcohol, iron, or zinc) (24).
  - — Avoid activated charcoal in dogs with megaesophagus, history of arytenoid lateralization surgery, or if predisposed to aspiration pneumonia.
- Administer appropriate antidote (if known).
  - — Consider 20% IV lipid administration for lipid soluble toxins that will be "trapped" in the "lipid sink" created by the lipid infusion. Examples include ivermectin, moxidectin, lidocaine and other local anesthetics, calcium channel blockers, pyrethrins, bromethalin, and cannabis (24).
  - — Administer lipids as 1.5 ml/kg bolus, followed by 0.25 mL/kg per minute for 30 to 60 min.
  - — If clinical signs persist, continue giving bolus doses of 1.5 mL/kg, q4h to q6h for 24 h. If clinical signs do not improve after 24 h, discontinue administration. Monitor serum for lipidemia every 4 to 6 h and discontinue administration if lipemia is noted.
  - — The use of intralipids is off label in animals. Reported side effects include pancreatitis, lipemia, corneal cholesterol deposits (in cats; resolved within 2 wk), fat-overload syndrome, coagulopathy, and hypersensitivity reactions.

Practice tip

Call either of these centers for a detailed veterinary toxicology consultation (fee per call):

- ASPCA Animal Poison Control: 888-426-4435.
- Pet Poison Helpline: 855-213-6680.

Step #12: Was the dog or cat electrocuted?

Background

Electrocution is very rare and usually is caused by chewing on an electrical cord. Depending on current intensity and type (alternating current causes more damage than direct current) (25), the severity of clinical signs will vary.

Electrocution may cause muscle spasms, loss of consciousness, arrhythmias, respiratory distress, or cardiorespiratory arrest. The most frequent clinical sign is respiratory distress due to either upper airway edema or noncardiogenic pulmonary edema [see Section 1 in Part I of this review (1)]. Dogs and cats can also have superficial- to full-thickness burns on the tongue, lips, or roof of the mouth.

Emergency stabilization

- Stabilize respiratory distress [see Section 1 in Part I of this review (1)].
- Provide pain medication (ideally, full mu-agonist opioid; *e.g.,* methadone, 0.2 mg/kg, IV).
- Due to concerns for worsening noncardiogenic pulmonary edema, give small volume of IV fluids or hypertonic saline (3 mL/kg of 7.2% NaCl diluted 1:4 with sterile water, slowly over 10 min) rather than larger boluses of crystalloid fluids.
- Treat any cardiac arrhythmias [see Part III of this review (2)].
- Treat seizures [see Section 2 in Part I of this review (1)].

Practice tips

1. Check electrolytes in electrocution cases; hyperkalemia occurs due to tissue necrosis or persistent muscular convulsions during electrical shock.
2. Urinalysis may indicate myoglobinuria or hemoglobinuria secondary to muscle necrosis. Do not worry if you cannot obtain a urine sample immediately.
3. Animals may require prolonged hospitalization, feeding tube, or reconstructive surgery.
4. Some dogs develop cataracts months after electrocution.

Step #13: Did this animal collapse due to orthopedic or neurologic disease (*e.g.,* fractures, spinal cord disease)?

Evaluate as detailed in Part III of this review (2).

Preparing to refer a dog or cat that is presented collapsed

- The time to refer the animal is *after* stabilization of vital signs. Treat respiratory distress and normalize heart rate, blood pressure, mucous membrane color, and other vital signs.
- Treat hypoglycemia.
- Perform pericardiocentesis, if required, to relieve cardiac tamponade.
- Cool a dog with heatstroke or electrocution to 39.4 to 40.0°C.
- In a septic animal or dog with heatstroke, give the first dose of antibiotics.
- In an animal with anaphylactic shock, give at least 1 dose of epinephrine.

- Decontaminate dogs and cats with toxin exposure by inducing emesis (or gastric lavage) ± activated charcoal.
- Treat any pain.
- Inform the owner that the animal may decompensate during transfer, especially in cases of pericardial effusion, sepsis, aortic thromboembolism, or anaphylaxis.
- Ensure the animal has a patent IV catheter, if possible.
- Advise referral institution of times and doses of all drugs administered.
- Call ahead to the referral institution to alert them and discuss the case.

Section 2: Acute bleeding in the dog or cat

Anemia is commonly a reason for referral, but chronically anemic animals rarely require immediate cessation of bleeding. Acute bleeding identified during triage is addressed immediately (Figure 1).

Background: Reasons for acute bleeding

There are 2 major reasons for bleeding: physical damage to a blood vessel or coagulopathy.

Non-coagulopathic hemorrhage. Most cases of a damaged vessel causing hemorrhage are due to trauma (blunt force or secondary to neoplastic cells eroding a nearby blood vessel) or occur post-surgery. Theoretically, bleeding will stop when a clot can form.

Coagulopathic hemorrhage. Dogs with coagulopathies bleed due to an inability to form a clot and may not stop bleeding until the coagulopathy is addressed. Coagulopathies are rare in cats but behave similarly to those in dogs.

Coagulation involves interactions among the vascular endothelium, platelets, and coagulation factors. The coagulation system has 2 parts: primary (platelet-based) and secondary (coagulation factor-based) hemostasis.

Primary hemostasis. Platelets provide a surface for a clot to form and have granules containing factors and proteins that aid in coagulation. They are covered in surface glycoproteins that mediate adhesion to the endothelium and bind to other platelets, mediating signaling between platelets and other cells.

Platelet plug formation is divided into 3 phases: adhesion, activation, and aggregation. Damaged endothelium can attract and adhere to platelets. These platelets become activated, changing shape, altering surface charge, and releasing granule contents to promote platelet aggregation and create a platelet plug. These processes occur in tandem and concurrent with the secondary coagulation cascade (Figure 2). Inadequate platelets (thrombocytopenia) or dysfunctional platelets (thrombocytopathy) lead to primary coagulopathies.

Secondary hemostasis. The secondary coagulation cascade is mediated by hepatic-sourced clotting factors, is activated by the same tissue endothelial damage that causes platelet adhesion, and occurs on the surface of platelets (Figure 2). The initial phase (initiation phase) produces a limited amount of thrombin (factor II), whereas the subsequent amplification and propagation phases culminate in large amounts of thrombin and fibrin. Bleeding occurs with deficiencies in ≥ 1 coagulation factor(s).

Step #1: Stop the bleeding

Emergency stabilization

External hemorrhage might be arterial or venous and commonly occurs from the nose, mouth, or peripheral wounds. Internal hemorrhage [abdomen, thorax, gastrointestinal tract, or around fractures (fracture hematoma)] is more difficult to identify on physical examination. When you have identified external hemorrhage or are faced with a weak or collapsed animal (Section 1) in which you suspect internal hemorrhage or have ultrasonographically identified free fluid (abdomen, thorax, or pericardium), take immediate steps to stop bleeding.

Option 1: Apply pressure wrap and/or tourniquet

The most common way to control bleeding is to apply pressure using a hand, gauze, or hemostatic dressing (26). Ideally, a circumferential wrap, including inner layers of rolled gauze and conforming gauze with an outer layer of self-adherent bandage material, is applied and pulled tightly (27). Ensure the wrap does not impede breathing if placed around the head, neck, or thorax. If possible, elevate the bleeding area 15 cm above the heart (27).

A pressure wrap can be applied around the abdomen or around fractures, using material similar to that for wrapping an extremity (28). Abdominal pressure wraps should extend from the hind limbs to above the diaphragm. Usually, folded towels are placed between the hind limbs, in the inguinal region bilaterally, and on the ventral abdomen to equalize pressure and facilitate wrapping (28). Increased intra-abdominal pressure may slow bleeding from organs or veins but may not suppress arterial bleeding. Wraps surrounding a fracture should extend from the joint above to the joint below the fracture and are placed as a tighter modified Robert Jones bandage or splint.

A tourniquet can be used judiciously for distal extremity or tail wounds, but due to concerns about direct or ischemic tissue damage (28), use this only if pressure wraps are not practical or ineffective and bleeding is life-threatening. Tourniquets should be > 5 cm wide and applied proximal to the bleeding, tightly enough to eliminate a distal palpable pulse. More than 1 tourniquet can be used if bleeding and/or a pulse continue (27,28). Avoid tourniquets over joints, as they cannot be tightened sufficiently and will cause long-term damage.

If there is any strikethrough of the bandage material, DO NOT remove the existing material (this disturbs the clot) but add additional dressing and self-adherent bandage material (28).

Option #2: Other methods of achieving hemostasis

When bleeding is not amenable to a wrap, application of pressure, or a tourniquet (*e.g.,* oral or nasal bleeding), other options must be employed.

Sedation. Sedation is helpful in hemostasis as it can i) allow safe access to places such as the mouth to facilitate application of pressure or hemostatic agents, and ii) reduce peripheral blood pressure. Common drugs include dexmedetomidine (dog: 2 to 10 μg/kg, IV or IM; cat: 5 to 10 μg/kg, IV or IM) or acepromazine (dog or cat: 0.05 to 0.2 mg/kg, IV or IM). Dexmedetomidine has peripheral vasoconstrictive effects, rapid

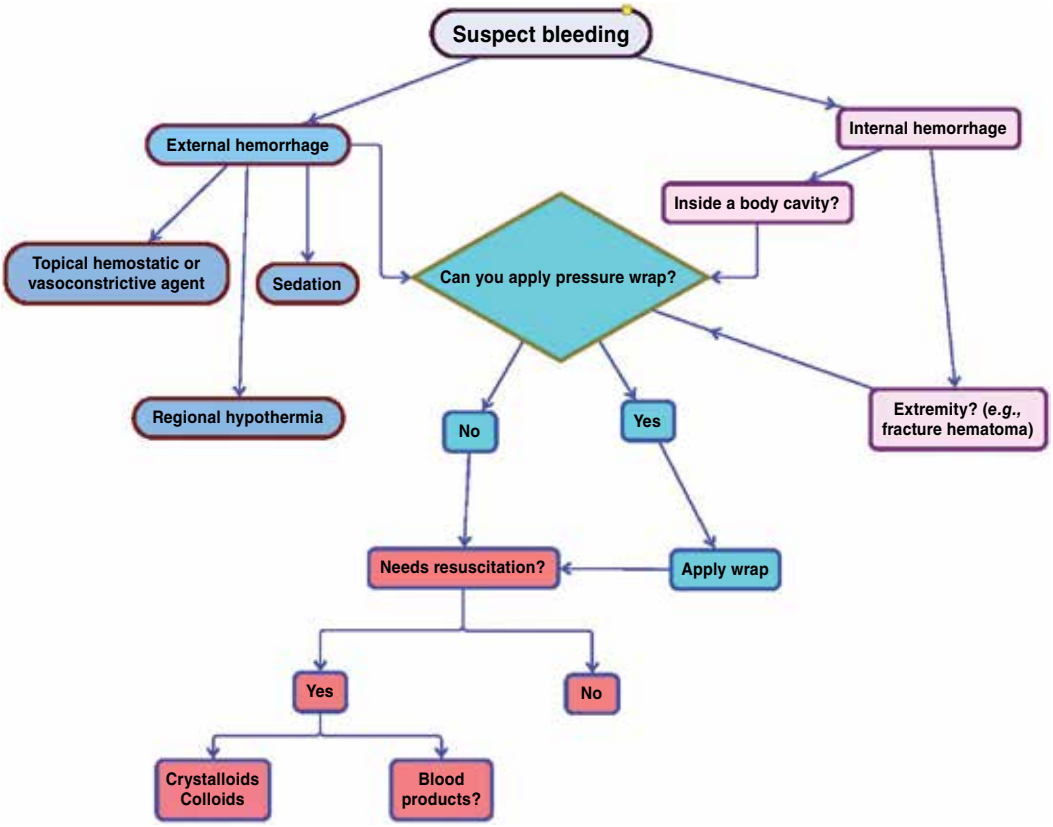


Figure 1. Flowchart illustrating the approach to a bleeding patient.

onset, and is reversible. Acepromazine has peripheral vasodilatory effects but a slower onset. An opioid is often combined with either drug for analgesia and sedation. General anesthesia (gas or injectable) can be used to vasodilate and slow blood flow plus facilitate application of pressure or other interventions.

Hemostatic agents are used for external hemorrhage; their most common components are chitin/chitosan, zeolite, and kaolin. Chitin/chitosan exists in arthropod skeletons and is produced by algae (29). It causes vasoconstriction to hold platelets and clotting factors locally and promote clot formation (29); it also has antibacterial activity (29). Zeolite agents [*e.g.,* QuikClot (Teleflex)] contain minerals that absorb blood and fluid and promote clot formation (29). Kaolin-based agents activate factor XII and thus intrinsic and common pathways of coagulation (Figure 2). These were shown to be efficacious in human clinical (30) and *in vitro* (31) studies.

Hemostatic agents can be used in granular form or impregnated in gauze and applied to extremity wounds before pressure bandages (30). For a bleeding nose or mouth or other region not amenable to pressure, continued bleeding, saliva, or the tongue can remove granules; however, impregnated gauze packed into or held on the site may be effective (sedation is likely necessary).

Other. Bleeding may be controlled by epinephrine or phenylephrine on gauze applied topically to surfaces such as the nose (sedation is likely necessary). Chilling (ice or cold water) can cause vasoconstriction and slow bleeding.

In adolescent humans with cancer-related bleeding who were receiving conventional therapy, topical Yunnan Baiyao improved hemostasis (32). No veterinary studies have explored topical use of Yunnan Baiyao, but anecdotally, the author (LI) feels that topically applied powder from Yunnan Baiyao oral capsules induced hemostasis. Oral use of Yunnan Baiyao in dogs is controversial, with 1 study (in healthy, non-bleeding dogs) suggesting changes in thromboelastographic variables consistent with improved hemostasis (33), another reporting no change in thromboelastographic variables (34), and a 3rd reporting no change in clinical bleeding in dogs with pericardial effusion (35). Healthy cats given oral Yunnan Baiyao had no changes in thromboelastographic variables (36). The appropriate dose and interval for slowing or stopping bleeding with oral Yunnan Baiyao in cats and dogs are unknown.

Step #2: Resuscitate the dog or cat

If substantial blood loss has occurred or bleeding is internal and cannot be immediately stopped, treatment is needed. Hypovolemia (causing hypotension and shock) is a more emergent issue than anemia. Feline shock is identified by hypotension, hypothermia, and bradycardia (in contrast to tachycardia in dogs). See Box 1 for treatment and stabilization of hypovolemia and hypotension. In some cases where ongoing hemorrhage is occurring while awaiting definitive repair (such as with a bleeding splenic mass), permissive hypotension is allowed. Thus, resuscitation goals are to keep the systolic blood pressure high enough to deliver oxygen, but not in the normal range. No consensus exists as to the exact blood pressure goals, but an example might be systolic blood pressures between 60 to 90 mmHg

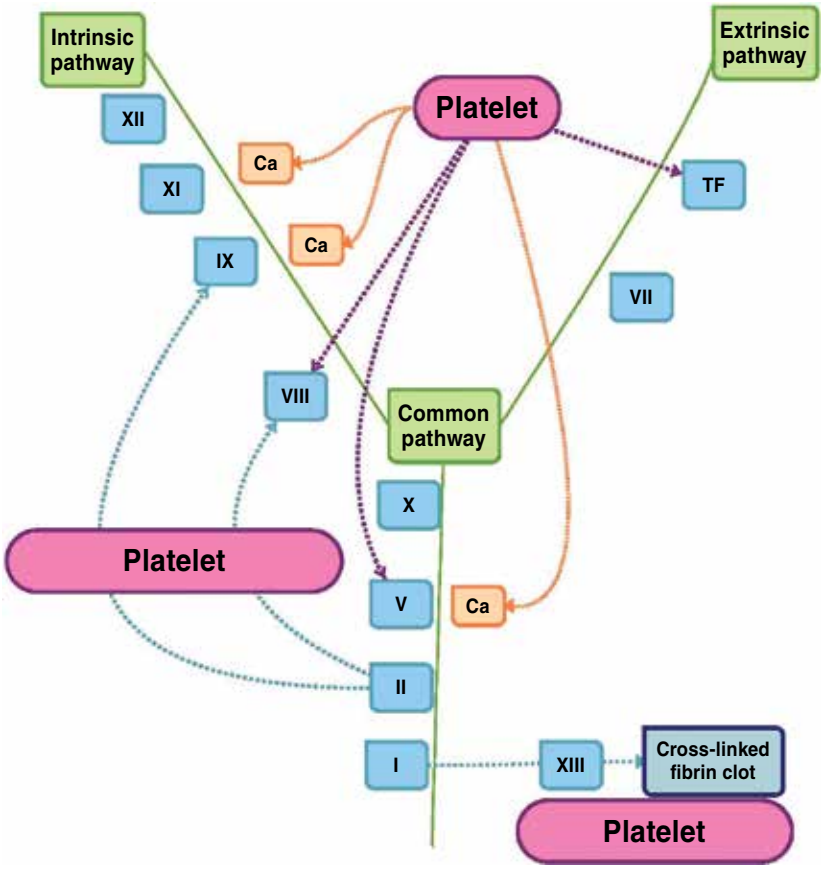


Figure 2. The secondary coagulation cascade.

rather than in the normal range (*i.e.,* > 120 mmHg) until the bleeding has been stopped (37).

Practice tips

1. Differentiation of primary *versus* secondary coagulation disorders is not important during triage. Stopping bleeding (if possible) and resuscitation (if needed) are the most important first steps.
2. Continue monitoring after treatment. Animals may go back into shock [tachycardia (or bradycardia in cats), hypotension, declining mentation], implying continued bleeding. Repeat resuscitation with fluids, colloids, and/or blood products while reexamining for a source of active hemorrhage. This occurs mostly with internal hemorrhage (*e.g.,* splenic masses or coagulopathies) for which control of bleeding is difficult.
3. Definitive treatment for internal hemorrhage requires transfusion to provide platelets and/or clotting factors (coagulopathy), or surgery (*e.g.,* splenectomy).
4. A CBC, blood smear evaluation, and prothrombin time/activated partial thromboplastin time test are the first steps to differentiate primary *versus* secondary coagulation disorders.

Preparing to refer a cat or dog that is bleeding

- External hemorrhage: Refer animal after controlling active external hemorrhage with a wrap and/or tourniquet, plus resuscitation as required.
- Internal hemorrhage: Refer animal after initial resuscitation to improve hypotension. Stopping internal hemorrhage is difficult without a specific diagnosis.
- Communicate to referral institution times and doses of all fluids, blood products, and drugs administered.
- Call ahead, especially if you expect bleeding to occur during transportation.

Refer to Part III of this review [Basic triage in dogs and cats: Part III (2)] for information on the approach to arrhythmias and stabilization of animals that are emergently unable to stand or walk. CVJ

References

1. Thomovsky E, Ilie L. Basic triage in dogs and cats: Part I. Can Vet J 2024;65:162–172.
2. Ilie L, Thomovsky E. Basic triage in dogs and cats: Part III. Can Vet J 2024:In press.
3. Fahey R, Rozanski E, Paul A, Rush JE. Prevalence of vomiting in dogs with pericardial effusion. J Vet Emerg Crit Care 2017;27:250–252.
4. Covey KH, Connolly DJ. Pericardial effusion associated with systemic inflammatory disease in seven dogs (January 2006–January 2012). J Vet Cardiol 2018;20:123–128.
5. Sebastián-Marcos P, Santarelli G, Gómez S, Palacio MJF. Canine leishmaniasis associated with pericardial effusion in a 4-year-old dog. J Vet Cardiol 2019;23:32–37.
6. Mittleman BE, Otto CM. Sepsis and septic shock. In: Silverstein DC, Hopper K, eds. Small Animal Critical Care Medicine. St. Louis, Missouri: Elsevier, 2015:472–479.
7. EMCrit RACC [Internet]. Weingart S. EMCrit 111 — Fluids in Sepsis, a New Paradigm — Paul Marik [posted November 9, 2013]. Available from: https://emcrit.org/emcrit/fluids-severe-sepsis Last accessed June 17, 2020.

8. Bonczynski JJ, Ludwig LL, Barton LJ, *et al.* Comparison of peritoneal fluid and peripheral blood pH, bicarbonate, glucose, and lactate concentration as a diagnostic tool for septic peritonitis in dogs and cats. Vet Surg 2003;32:161–166.
9. Shmuel DL, Cortes Y. Anaphylaxis in dogs and cats. J Vet Emerg Crit Care 2013;23:377–394.
10. Hume-Smith KM, Growth AD, Rishniw M, Walter-Grimm LA, Plunkett SJ, Maggs DJ. Anaphylactic events observed within 4 h of ocular application of an antibiotic-containing ophthalmic preparation: 61 cats (1993–2010). J Feline Med Surg 2011;13:744–751.
11. Aharon MA, Prittie JE, Buriko K. A review of associated controversies surrounding glucocorticoid use in veterinary medicine and critical care. J Vet Emerg Crit Care 2017;27:267–277.
12. Hnatusko AL, Gicking JC, Lisciandro GR. Anaphylaxis-related hemoperitoneum in 11 dogs. J Vet Emerg Crit Care 2021;31:80–85.
13. Summers AM, Culler C, Cooper E. Spontaneous abdominal effusion in dogs with presumed anaphylaxis. J Vet Emerg Crit Care 2021;31: 483–489.
14. Quantz JE, Miles MS, Reed AL, White GA. Elevation of alanine transaminase and gallbladder wall abnormalities as biomarkers of anaphylaxis in canine hypersensitivity patients. J Vet Emerg Crit Care 2009;19: 536–544.
15. Flournoy SW, Wohl JS, Macintire DK. Heatstroke in dogs: Pathophysiology and predisposing factors. Compend Contin Educ Pract Vet 2003;25:410–418.
16. Johnson SJ, McMichael M, White G. Heatstroke in small animal medicine: A clinical practice review. J Vet Emerg Crit Care 2006;16: 112–119.
17. Drobatz KJ, Macintire DK. Heat-induced illness in dogs: 42 cases (1976–1993). J Am Vet Med Assoc 1996;209:1894–1899.
18. Bruchim Y, Klement E, Saragusty J, *et al.* Heat stroke in dogs: A retrospective study of 54 cases (1999–2004) and analysis of risk factors for death. J Vet Intern Med 2006;20:38–46.
19. Hoehne SN, Hopper K, Epstein SE. Retrospective evaluation of the severity of and prognosis associated with potassium abnormalities in dogs and cats presenting to an emergency room (January 2014–August 2015): 2441 cases. J Vet Emerg Crit Care 2019;29:653–661.
20. Willey JL, Julius TM, Claypool SPA, Clare MC. Evaluation and comparison of xylazine hydrochloride and dexmedetomidine hydrochloride for the induction of emesis in cats: 47 cases (2007–2013). J Am Vet Med Assoc 2016;248:923–928.
21. Thies M, Bracker K, Sinnott V. Retrospective evaluation of the effectiveness of xylazine for inducing emesis in cats: 48 cats (2011–2015). J Vet Emerg Crit Care 2017;27:658–661.
22. Thawley VK, Drobatz JK Assessment of dexmedetomidine and other agents for emesis induction in cats: 43 cases (2009–2014). J Am Vet Med Assoc 2015;247:1415–1418.
23. Nystrom MR, Odunayo A, Okafor CC. Assessment of hydromorphone and dexmedetomidine for emesis induction in cats. J Vet Emerg Crit Care 2019;29:360–365.
24. Lee JA. Approach to drug overdose. In: Silverstein DC, Hopper K, eds. Small Animal Critical Care Medicine. St. Louis, Missouri: Elsevier, 2015:385–389.
25. Mann FA. Electrical and lightning injuries. In: Silverstein DC, Hopper K, eds. Small Animal Critical Care Medicine. St. Louis, Missouri: Elsevier, 2015:799–802.
26. Hanel RM, Palmer L, Baker J, *et al.* Best practice recommendations for pre-hospital care of dogs and cats. J Vet Emerg Crit Care 2016; 26:166–233.
27. Plunkett SJ. Emergency Procedures for the Small Animal Veterinarian. 2nd ed. Philadelphia, Pennsylvania: Elsevier, 2000:101–132.
28. Palmer L. Clinical update concepts of prehospital traumatic hemorrhage control in the operational K9. J Spec Oper Med 2018;18:123–130.
29. Achneck HE, Sileshi B, Jamiolkowski RM, Albala DM, Shapiro ML, Lawson JH. A comprehensive review of topical hemostatic agents: Efficacy and recommendations for use. Ann Surg 2010;251:217–228.
30. Chávez-Delgado ME, Kishi-Sutto CV, Albores de la-Riva XN, Rosales-Cortes M, Gamboa-Sánchez P. Topical usage of kaolin-impregnated gauze as a hemostatic in tonsillectomy. Surg Res 2014; 192:678–685.
31. Cripps MW, Cornelius CC, Nakonezny PA, Vazquez N, Wey JC, Gales PE. *In vitro* effects of a kaolin-coated hemostatic dressing on anticoagulated blood. J Trauma Acute Care Surg 2018;85:485–490.
32. Ladas EJ, Karlik JB, Rooney D, *et al.* Topical Yunnan Baiyao administration as an adjunctive therapy for bleeding complications in adolescents with advanced cancer. Support Care Cancer 2012;20:3379–3383.
33. Tansey C, Wiebe ML, Hybki GC, *et al.* A prospective evaluation of oral Yunnan Baiyao therapy on thromboelastographic parameters in apparently healthy dogs. J Vet Emerg Crit Care 2018:221–225.
34. Frederick J, Boysen S, Wagg C, Chalhoub S. The effects of oral administration of Yunan Baiyao on blood coagulation in beagle dogs as measured by kaolin-activated thromboelastography and buccal mucosal bleeding times. Can J Vet Res 2017;81:41–45.
35. Murphy LA, Panek CM, Bianco D, *et al.* Use of Yunnan Baiyao and epsilon aminocaproic acid in dogs with right atrial masses and pericardial effusion. J Vet Emerg Crit Care 2017;27:121–126.
36. Patlogar JE, Tansey C, Wiebe M, *et al.* A prospective evaluation of oral Yunnan Baiyao therapy on thromboelastographic parameters in apparently healthy cats. J Vet Emerg Crit Care 2019;29:611–615.
37. Hall K, Drobatz K. Volume resuscitation in the acutely hemorrhaging patient: Historic use to current applications. Front Vet Sci 2021;8:638104.

Commentary Commentaire

Is Canada ready for a new veterinary college?

Baljit Singh

Canada currently has 5 veterinary colleges: 1 in Quebec to serve the francophone population and 4 to serve the English-speaking population. Canada's first veterinary college, the Ontario Veterinary College, was established in 1862. The Western College of Veterinary Medicine (WCVM) opened nearly 100 y later, in the mid-1960s, at the University of Saskatchewan. The Atlantic Veterinary College was started at the University of Prince Edward Island in 1985, to serve the Atlantic provinces; and the University of Calgary Faculty of Veterinary Medicine (UCVM) took shape in 2006, to serve the needs of Albertans.

Given that it has been nearly 2 decades since the opening of the UCVM and there is a historical pattern of opening a veterinary college every 20 y, Canada is not only due to open a new veterinary college but is in dire need of one.

There is an ongoing and serious shortage of veterinarians across Canada and the United States. Twenty years ago, it was believed that the opening of veterinary colleges in St. Kitts and Grenada and their subsequent accreditation by the Council on Education of the American Veterinary Medical Association (AVMA) would lead to an abundance of veterinary graduates, bordering on an oversupply and potentially saturating the market. That dire prediction has not been realized. Today, the opposite problem exists, and we now need to increase the capacity to train more veterinarians.

The United States has continued to open veterinary colleges to address this problem, with the latest established by Rowan University in New Jersey and the Arkansas State University. Canada has not taken any steps in this direction.

One of the strategies in Canada has been to rely on immigration to meet the demand for veterinarians. However, in contrast to their United States counterparts and likely because of their deep-seated cultural biases, Canadian veterinary colleges have largely failed to support immigrant veterinarians who are graduates of colleges not accredited by the AVMA/CVMA Council on Education. Despite CVMA's National Examining Board creating a mechanism for graduates of nonaccredited veterinary colleges to gain credentials by completing 1 y of clinical training, none of the Canadian veterinary colleges has taken any steps to support this initiative; and considering that colleges such as the Ontario Veterinary College even refuse to conduct the Clinical Proficiency Examination for these graduates, let us not hold our breath that they will have a change of heart any time soon.

We can meet the demand for veterinarians by increasing capacity in Canadian veterinary colleges. Canadian colleges continue to ask provincial governments to increase funding to create more permanent student seats at existing veterinary colleges. Recently, the Government of Saskatchewan added approximately 5 or 6 additional seats to the WCVM's incoming veterinary classes. This decision was based on the advocacy of both the Saskatchewan Veterinary Medical Association and the WCVM. Similarly, following coordinated advocacy by the UCVM and the Alberta Veterinary Medical Association, the Government of Alberta is adding 50 additional seats at the UCVM, bringing the class size to 100 starting in 2025. Only time will tell if these additional veterinarians graduating 5 to 6 y from now will alleviate the shortage that has persisted for years.

A new college would create a steady supply of veterinarians. Besides adding several permanent seats funded through a provincial government, the college could potentially also make a real difference to the shortage of veterinarians in Canada by concurrently serving, through federal funding, as a Canadian centre for credentialing hundreds of Canadian citizens and permanent residents who are graduates of veterinary colleges not accredited by the AVMA/CVMA Council on Education. Therefore, the college could have a unique dual partnership in both provincial and federal funding.

The new college could have an innovative focus on Canada's North. This unique area of Canada has become increasingly populated and has increased its economic activity in various industries, including mining and trade. Further, the college could have a genuine One Health/Planetary Health focus, integrating human, animal, and ecosystem health to create academic programming where students from human, animal, and environmental health backgrounds come together to learn ways of addressing issues of climate change in northern communities.

One could argue that we should simply add more students to one or more of the existing veterinary colleges in Canada. That can be done, but it will not address the limitations of the current physical infrastructure and the number of academic veterinary

Dr. Singh is a former Dean of the University of Calgary Faculty of Veterinary Medicine and is currently the Vice President of Research and a Professor at the University of Saskatchewan.

Address all correspondence to Dr. Baljit Singh; email: baljit.singh@usask.ca

medical teachers and researchers, as would be done through the creation of a new veterinary college.

The creation of new laboratories, potentially 70 to 100 new academic positions, and expanded graduate training opportunities in One Health are all valid reasons to consider putting our efforts, time, and funding toward a new veterinary college.

If we are going to sustain a growing economy, population, and demands, there needs to be a new veterinary college in Canada. The question now is which province will take the initiative and establish the next exceptional veterinary college for Canada.

Acknowledgment

I thank Ms. Leslie-Ann Schlosser for editing the article.

New Products
Nouveaux produits

Dechra introduces an innovative alpha-2 agonist/antagonist Zenalpha® (Medetomidine and Vatinoxan hydrochlorides injection) for minimizing the stress surrounding sedation and maximizes procedural efficiency.

Dechra Veterinary Products is proud to announce the launch of Zenalpha, a novel alpha-2 agonist/antagonist combination that helps minimize negative cardiovascular effects in dogs.

Zenalpha adds vatinoxan to medetomidine to stabilize critical physiological parameters and provide sedation and analgesia for short procedures with no reversal needed in most cases.

Zenalpha's quicker onset (5–15 minutes), faster recovery (approximately 45 minutes) and fewer cardiovascular effects during clinical examinations lead to increased efficiency for exams and clinic workflows.

Zenalpha is an exciting addition to Dechra's complete anesthetic and analgesic range, giving veterinarians more options and flexibility to effectively care for their patients.

Ask your Dechra representative for more information.

Contact: Dechra Veterinary Products, 1 Holiday Avenue East Tower, Suite 345, Pointe-Claire, Quebec H9R 5N3; Customer Service: 1-855-332-9334; email: technical.ca@dechra.com to enquire about this new product.

Answers to Quiz Corner
Corrigé du test éclair

1. D) This is a cranial cruciate ligament (CrCL) rupture. Concurrent medial meniscal injury is very common with CrCL rupture.

A CrCL rupture is more common in larger-breed dogs, but those of any size may be affected. Rupture most commonly occurs due to CrCL degeneration. The exact cause is unknown but it is likely multifactorial.

There are multiple surgical techniques that can stabilize the stifle. Most cases (80 to 90%) improve regardless of technique used. Surgeons should inspect the menisci during any procedure given the likelihood of concurrent injury.

With medical management alone, only 60% of dogs return to normal activities. Also, clinicians should inform owners that dogs in 40 to 50% of cases will go on to injure the contralateral CrCL.

References

1. Fossum TW. Small Animal Surgery. 5th ed. Philadelphia, Pennsylvania: Elsevier, 2019:1227–1243.
2. Cohn L, Côté É. Clinical Veterinary Advisor: Dogs and Cats. 4th ed. St. Louis, Missouri: Elsevier, 2020:219–221.

2. B) Open heifers could begin demonstrating estrus behavior starting 18 d from the originally observed heat, so you should start watching then.

The bovine estrous cycle lasts for 18 to 21 d. Ovulation occurs roughly 8 to 16 h after the end of behavioral estrus. Often, breeders follow the "a.m./p.m. rule," inseminating animals in the afternoon that were seen in heat that morning. This ensures semen is in the reproductive tract at the time of ovulation.

If you begin watching for behavioral heat signs 21 d from the first service, you are likely to be late and miss the next standing heat in nonpregnant cows.

Timed artificial insemination programs remove the variability in individual animal cycles and the necessity to observe standing heat.

1. D) Il s'agit d'une rupture du ligament croisé crânial (RLCC). Une lésion concomitante du ménisque médial est très fréquente dans les cas de RLCC.

Bien qu'elle soit plus courante chez les chiens de grande race, la RLCC peut affecter les chiens de toutes tailles. La rupture est le plus souvent due à la dégénérescence du ligament. La cause exacte est inconnue, mais elle est probablement multifactorielle.

Il existe de nombreuses techniques chirurgicales permettant de stabiliser le genou. Dans la plupart des cas (80-90 %), une amélioration est constatée peu importe la technique utilisée. Les chirurgiens devraient vérifier les ménisques durant l'intervention, étant donné la probabilité d'une lésion concomitante.

Avec une prise en charge médicale, seulement 60 % des chiens reprennent leurs activités normales. Les cliniciens devraient également informer les propriétaires qu'une rupture du ligament croisé crânial controlatéral survient ultérieurement dans 40 à 50 % des cas.

Références

1. Fossum TW. Small Animal Surgery. 5th ed. Philadelphia, Pennsylvania: Elsevier, 2019:1227–1243.
2. Cohn L, Côté É. Clinical Veterinary Advisor: Dogs and Cats. 4th ed. St. Louis, Missouri: Elsevier, 2020:219–221.

2. B) Les génisses non gestantes peuvent commencer à démontrer des signes d'œstrus à partir de 18 jours après les chaleurs précédentes, c'est donc à ce moment qu'il faudrait commencer à les surveiller.

Le cycle œstral des bovins dure de 18 à 21 jours. L'ovulation se produit environ 8 à 16 heures après la fin des comportements évoquant l'œstrus. Souvent, les éleveurs suivent la règle « AM/PM », c'est-à-dire qu'ils inséminent l'après-midi les vaches qu'ils ont vues en chaleur le matin même. Cette méthode permet de s'assurer que la semence est présente dans l'appareil reproducteur au moment de l'ovulation.

Si vous commencez à surveiller les signes comportementaux associés aux chaleurs 21 jours après la saillie, c'est peut-être trop tard et vous risquez de manquer les prochaines chaleurs des génisses toujours non gestantes.

Reference

1. Peek SF, Divers TJ. Rebhun's Diseases of Dairy Cattle. 3rd ed. St. Louis, Missouri: Elsevier, 2018:495–500.

Les programmes d'insémination à moments fixes éliminent la variabilité des cycles individuels des animaux et la nécessité d'observer les signes de chaleurs et de réceptivité à la monte.

Référence

1. Peek SF, Divers TJ. Rebhun's Diseases of Dairy Cattle. 3rd ed. St. Louis, Missouri: Elsevier, 2018:495–500.

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

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

Index of Advertisers

Index des annonceurs

The participation of advertisers in the *The CVJ* is an indication of their commitment to the advancement of veterinary medicine in Canada. We encourage our readers to give their products and services appropriate consideration. — Ed.

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

Veterinary Practice Management
Gestion d'une pratique vétérinaire

Provincial associate compensation

Rémunération des vétérinaires salariés selon les provinces

Maisey Kent, Darren Osborne

Introduction

One of the hottest management topics in veterinary medicine for 2023 was associate wages. Demand for veterinary services, fueled by the pandemic puppy/kitten boom, was at an all time high and practices across the country were looking to get some much-needed extra help by bringing on more veterinarians. As the demand for associate veterinarians heated up, salaries started to climb. Nationally, the average increase in associate earnings was 9% in 2023; almost 3 times the 3.1% rate of inflation posted by Statistics Canada.

Introduction

L'un des sujets brûlants de 2023 en matière de gestion en médecine vétérinaire était la rémunération des vétérinaires salariés. La demande pour les services vétérinaires, alimentée par le boom d'adoption de chiots et de chatons durant la pandémie, avait atteint un sommet sans précédent et les pratiques partout au pays cherchaient à obtenir l'aide supplémentaire dont elles avaient tant besoin en recrutant plus de vétérinaires. Comme la demande pour les médecins vétérinaires s'est accrue, les salaires ont suivi à la hausse. À l'échelle nationale, l'augmentation moyenne des salaires des vétérinaires salariés a été de 9 % en 2023, soit près de trois fois le taux d'inflation de 3,1 % affiché par Statistique Canada.

Maisey Kent is the Economic Analyst reporting to the Director of Economic Research for the Ontario Veterinary Medical Association. She completed an MBA with an emphasis in Information Systems Management from Delta State University and has worked as a healthcare and supply chain consultant prior to this role.

Darren Osborne has been the Director of Economic Research for the Ontario Veterinary Medical Association for over 20 years. He completed an MA (Economics) from York University and has worked as an economic analyst in veterinary medicine, dentistry, human medicine, and the transport industry.

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

Address all correspondence to the CVMA (admin@cvma-acmv.org).

Maisey Kent est analyste économique pour l'Ontario Veterinary Medical Association où elle relève du directeur de la recherche économique. Elle est titulaire d'une maîtrise en administration des affaires avec spécialisation en gestion des systèmes d'information de la Delta State University et a travaillé comme consultante dans le domaine des soins de santé et de la chaîne d'approvisionnement avant d'occuper son poste actuel.

Darren Osborne est directeur de la recherche économique pour l'Ontario Veterinary Medical Association depuis plus de 20 ans. Il a obtenu une maîtrise en économie de l'Université York et a travaillé comme analyste économique en médecine vétérinaire, en médecine dentaire, en médecine humaine et dans l'industrie des transports.

Le présent article est rédigé dans le cadre du Programme de gestion des affaires de l'ACMV, qui est cocommandité par IDEXX Laboratories, Petsecure assurance maladie pour animaux, Merck Santé animale et la Banque Scotia.

Veuillez adresser toute correspondance à l'ACMV (admin@cvma-acmv.org).

Average compensation by province

Comparing associate compensation across the provinces looks like a suspension bridge, with the highest salaries in Newfoundland and Labrador, followed by British Columbia with Ontario closely behind for second and third place. After accounting for annual hours worked and the cost of living in each of the provinces, Newfoundland and Labrador move to an even higher first place position but the rest of the provinces settle into different places.

Rémunération moyenne par province

Si on illustrait sur un graphique la rémunération des vétérinaires salariés dans les provinces d'un océan à l'autre, la courbe ressemblerait à un pont suspendu : les salaires les plus élevés ont été versés à Terre-Neuve-et-Labrador, et la Colombie-Britannique et l'Ontario suivent de près en deuxième et troisième positions. En tenant compte du nombre annuel d'heures travaillées et du coût de la vie dans chacune des provinces, Terre-Neuve-et-Labrador se hisse encore plus haut au premier rang, mais les autres provinces occupent des positions différentes.

Table 1/Tableau 1. Associate Statistics./Statistiques concernant les vétérinaires salariés.

	Canada	BC C.-B.	AB Alb.	SK Sask.	MB Man.	ON Ont.	QC Qc	NB N.-B.	NS N.-É.	PEI Î.-P.-É.	NL T.-N.-L.
Associate Compensation Salaire	119 530	130 000	115 000	110 000	106 000	127 000	104 000	110 000	115 000	95 000	180 000
Associate Hours Heures travaillées	1651	1656	1840	1762	1840	1656	1504	1615	1610	1824	1564
Cost of Living Index (Statistics Canada) Indice du coût de la vie (Statistique Canada)	100	108	112	98	95	105	87	83	89	85	87
COLFTE Associate Compensation Salaire ETP ajusté en fonction du coût de la vie	127 271	127 199	97 777	111 176	106 207	127 513	139 132	143 980	140 114	106 919	232 746
Associate Wage as percent of Gross Rémunération des vétérinaires salariés, en % du revenu brut	16%	19%	14%	14%	11%	16%	18%	18%	18%	18%	17%
Annual Increase 2022–2023 Augmentation de salaire 2022-2023	9%	12%	4%	13%	6%	10%	5%	10%	24%	16%	44%

Hours worked and cost of living

The difference in average hours worked can vary by as much as 336 hours or 10 weeks, from one province to another. Associate veterinarians in Quebec work the least number of hours at 1504 in comparison to their counterparts in Alberta and Manitoba who work 1840 hours and associates in Prince Edward Island who work only 16 hours less at 1824. To accurately compare wages across the provinces, the hours worked must be considered, so the average in each province was converted to a 1750 full-time equivalent. That meant provinces that had average annual hours higher than 1750 saw their compensation figures lowered and provinces that had fewer average annual hours had their figures increased to reflect what could have been earned if the average associate worked 1750 hours. Converting to a full-time equivalent wage increased the national figure 6% since the average associate worked 1651 hours — 6% lower than the full-time equivalent figure.

In additional to different hours worked, the cost of living differed across the country as well. In New Brunswick, the average family spends 25% less than the average family in Alberta — $100 000 earned in New Brunswick would be equivalent to $75 000 in Alberta. By adjusting for the cost of living in each province, economic differences between the provinces are neutralized and makes for a more accurate comparison of associate earnings.

Heures travaillées et coût de la vie

Les différences entre les provinces quant au nombre moyen d'heures travaillées étaient parfois importantes, atteignant jusqu'à 336 heures ou 10 semaines par année. Les vétérinaires salariés du Québec sont ceux qui ont travaillé le moins d'heures (1504), tandis que leurs homologues de l'Alberta et du Manitoba (1840 heures) ainsi que ceux de l'Île-du-Prince-Édouard (1824 heures) sont ceux qui ont travaillé le plus d'heures. Pour établir une comparaison juste des salaires entre les provinces, il faut tenir compte du nombre d'heures travaillées. Ainsi, le salaire moyen dans chaque province a été converti en un équivalent temps plein (ETP) de 1750 heures. Cela signifie que le salaire moyen a été ajusté à la hausse ou à la baisse dans les provinces où le nombre moyen d'heures travaillées était inférieur ou supérieur à 1750 heures, respectivement, afin de refléter le salaire qu'aurait gagné un médecin vétérinaire à temps plein ayant travaillé 1750 heures durant l'année. La conversion en équivalent temps plein fait augmenter la moyenne nationale de 6 %, car le vétérinaire salarié moyen a travaillé 1651 heures, soit 6 % de moins que les 1750 heures de l'équivalent temps plein.

Outre les différences d'heures travaillées, le coût de la vie diffère également d'une province à l'autre. Le ménage moyen dépense 25 % de moins au Nouveau-Brunswick qu'en Alberta – ainsi, un salaire de 100 000 $ au Nouveau-Brunswick équivaut à un salaire de 75 000 $ en Alberta. L'ajustement des

Associates in Atlantic Canada and Quebec worked fewer hours than the national average and reside in provinces with a relatively lower cost of living so their salary adjustment was significantly higher than other provinces. On the other side of the country, a higher cost of living and longer hours worked brought the comparative salaries down for British Columbia and Alberta. The middle of the country stayed much the same since the hours worked and cost of living were close to the national average or in the case of Manitoba, the lower cost of living cancelled out more annual hours, so the difference was only $207.

After accounting for the cost of living and annual hours worked, Eastern Canada had the highest earning associates in 2023. Newfoundland and Labrador had the highest adjusted salaries, but comparing Newfoundland and Labrador associate salaries to the rest of Canada is like playing fantasy hockey with Wayne Gretzky on your team. It's so much higher than every other province, its not even a fair comparison. Outside of Newfoundland and Labrador, the greatest transformation was with New Brunswick and Quebec. In both provinces, fewer annual hours and a lower cost of living moved them from third and fourth from the bottom in annual associate earnings to second and third from the top.

Most competitive market to hire

To select the most competitive market for hiring associate veterinarians in the country, the change in salaries from year-to-year was used to measure competition between practices. This assumes the laws of supply and demand were at work in the market for associate veterinarians. In provinces where there were more jobs and less associates, the increase in salaries from one year to another would have been higher to attract and retain talent. Not surprising, the most competitive market in 2023 was also Newfoundland and Labrador with a 44% increase in salaries over the previous year. This was followed by Nova Scotia at 24% and Prince Edward Island at 16%. Quebec, Manitoba, and Alberta were least competitive provinces with growth in salaries less than 10%.

Hardest to pay

From an employer's perspective, paying higher salaries is easier if revenues are higher. Looking at associate incomes as a percentage of gross revenues (associate full-time equivalent income to full-time equivalent practice revenue) shows which provinces have it easier or harder than others. Nationally, associate wages equated to 16% of total revenue for the average practice. That meant that for every $100 of revenue, $16 was spent on associate salaries. Although one might expect Newfoundland and Labrador, with its extraordinarily high salaries to be the highest province in associate earnings to practice revenue, their higher-than-average revenue offset their higher associate salaries and brought them to last place in Eastern Canada and middle of the pack for the nation. The province with the highest associate salary to gross revenue was British Columbia where revenues did not keep up with associate wages and the average associate salary was 19% of total gross revenue. That suggests practices in British Columbia pay more in associate wages for every dollar of revenue than the rest of Canada. The province with the lowest associate wage to practice revenue ratio was Manitoba at 11%.

données en fonction du coût de la vie dans chaque province neutralise les différences économiques entre les provinces et permet une comparaison plus juste du salaire des vétérinaires salariés.

Les vétérinaires salariés des provinces de l'Atlantique et du Québec ont travaillé moins d'heures que la moyenne nationale et habitent dans des provinces où le coût de la vie est relativement moins élevé, de sorte que leur ajustement salarial a été plus important que dans les autres provinces. À l'autre bout du pays, un coût de la vie plus élevé et un plus grand nombre d'heures travaillées ont fait baisser les salaires utilisés pour la comparaison en Colombie-Britannique et en Alberta. Dans le milieu du pays, le salaire ajusté est resté pratiquement inchangé puisque les heures travaillées et le coût de la vie étaient proches de la moyenne nationale ou, dans le cas du Manitoba, le coût de la vie plus bas a annulé l'effet du nombre d'heures travaillées plus élevé, de sorte que la différence n'était que de 207 $.

Les données ajustées en fonction du coût de la vie et du nombre annuel d'heures travaillées révèlent que ce sont les vétérinaires salariés de l'est du Canada qui avaient les meilleurs salaires en 2023. C'est à Terre-Neuve-et-Labrador que les salaires ajustés étaient les plus élevés, mais comparer les salaires à Terre-Neuve-et-Labrador à ceux du reste du Canada, c'est comme faire partie d'une ligue de hockey virtuelle en ayant Wayne Gretzky dans son équipe. Les salaires y sont tellement plus élevés que dans toutes les autres provinces que la comparaison devient injuste. Si on exclut Terre-Neuve-et-Labrador, c'est au Nouveau-Brunswick et au Québec que le changement a été le plus important. Dans ces deux provinces, le nombre moindre d'heures travaillées par année et le coût de la vie plus faible ont fait en sorte qu'elles sont passées des troisième et quatrième rangs du bas du classement pour la rémunération des vétérinaires salariés aux deuxième et troisième rangs du haut de ce classement.

Marché le plus compétitif pour l'embauche

Pour connaître le marché le plus compétitif du pays en matière de recrutement de vétérinaires salariés, l'évolution des salaires par rapport à l'année précédente a été utilisée pour mesurer la concurrence entre les pratiques. Cela suppose que les lois de l'offre et de la demande sont à l'œuvre dans le marché des vétérinaires salariés. Ainsi, dans les provinces où il y avait plus d'emplois et moins de vétérinaires, l'augmentation des salaires par rapport à l'année précédente aurait été plus importante pour attirer et retenir les candidats. Sans surprise, le marché le plus compétitif en 2023 était celui de Terre-Neuve-et-Labrador, avec une augmentation de 44 % des salaires par rapport à l'année précédente. Cette province était suivie de la Nouvelle-Écosse (24 %) et de l'Île-du-Prince-Édouard (16 %). Le Québec, le Manitoba et l'Alberta étaient les provinces les moins compétitives, avec une croissance des salaires inférieure à 10 %.

Marché où il est plus difficile de payer les vétérinaires salariés

Pour les employeurs, il est plus facile de payer des salaires plus élevés si les revenus sont plus importants. L'analyse de la rémunération des vétérinaires salariés en pourcentage du

Thanks to all the associate veterinarians who completed the Canadian Veterinary Medical Association (CVMA) Annual Survey of Compensation and Benefits for Associate Veterinarians. Within each province, associate salaries are affected by type of practice, seniority, area of the province, method of compensation, and assisting in management. For more information on what drives associate salaries, consult your CVMA provincial report on Compensation and Benefits for Associate Veterinarians on the CVMA website (www.canadianveterinarians.net, click on 'Veterinary Resources' and then *'Business Management'*). Information on practice revenues comes from the CVMA Annual Practice Owners Economic Survey. ■

revenu brut (revenu des vétérinaires salariés en équivalent temps plein par rapport au revenu de la pratique en équivalent temps plein) montre quelles provinces ont plus de facilité ou plus de difficulté que d'autres. À l'échelle nationale, la rémunération des vétérinaires employés représentait 16 % du revenu total de la pratique moyenne. Cela signifie que pour chaque tranche de 100 $ de revenus, 16 $ ont été dépensés pour payer les vétérinaires salariés. Bien que l'on puisse s'attendre à ce que Terre-Neuve-et-Labrador, avec ses salaires extraordinairement élevés, soit la province où le pourcentage du revenu consacré à la rémunération des vétérinaires salariés était le plus élevé, les revenus plus élevés que la moyenne dans cette province ont compensé les salaires plus élevés du personnel vétérinaire, et l'ont amenée au dernier rang dans l'est du Canada et au milieu du peloton à l'échelle nationale. La province où la rémunération des vétérinaires salariés était la plus élevée par rapport au revenu brut était la Colombie-Britannique, où les revenus n'ont pas suivi la hausse des salaires et où la rémunération moyenne des vétérinaires salariés représentait 19 % du revenu brut total. Cela signifie que les pratiques en Colombie-Britannique ont payé en salaires du personnel vétérinaire une plus forte proportion de chaque dollar de revenu que celles du reste du Canada. La province où le pourcentage du revenu consacré à la rémunération des vétérinaires salariés était le plus faible était le Manitoba, avec 11 %.

Merci à tous les vétérinaires qui ont répondu au sondage annuel de l'Association canadienne des médecins vétérinaires (ACMV) sur la rémunération et les avantages sociaux des vétérinaires salariés. Partout au pays, les salaires des vétérinaires salariés sont influencés par le type de pratique, l'ancienneté, la région de la province, la méthode de rémunération et la participation à la gestion. Pour en savoir plus sur les facteurs qui déterminent les salaires des vétérinaires, consultez le rapport de l'ACMV sur la rémunération et les avantages sociaux des vétérinaires salariés de votre province sur le site Web de l'ACMV (allez au www.veterinairesaucanada.net et cliquez sur « Ressources pour les médecins vétérinaires » et ensuite sur « Gestion des affaires »). Les données sur les revenus des pratiques proviennent du sondage économique annuel de l'ACMV auprès des propriétaires de pratiques. ■

Veterinary Dermatology
Dermatologie vétérinaire

Pemphigus foliaceus in cats

Veronica Izydorczyk, Charlie Pye

Introduction

Pemphigus foliaceus (PF), the most common autoimmune dermatosis in cats (1), typically presents with pustular and crusting lesions (1–3). Implicated in the pathogenesis of PF are autoantibodies targeting antigens likely associated with desmosomes or other intercellular linker proteins (4–6) that maintain adhesive bonds between epidermal keratinocytes; impairment of these intercellular adhesions results in acantholysis (intercellular separation) (5–7). When acantholysis occurs in the upper epidermis, intracorneal and subcorneal pustules arise (5,7). Although the major target antigen causing feline PF has not been identified, recent detection of anti-keratinocyte autoantibodies in PF-affected cats at a higher rate than in healthy cats is a step toward identifying the major target antigen (4). The target antigen is suspected to differ from that reported in dogs (desmocolin-1) (4,8). Desmoglein-1, the major target antigen in human PF, is currently considered the most relevant potential major target antigen in feline PF (8).

Clinical presentation

In cats, as in dogs, PF most commonly affects middle-aged individuals (1,3,6,9). Unlike in dogs, for which there is a breed predisposition in Akitas and chows, there is no true breed predisposition in cats, although PF is more often reported in the domestic shorthair than in other breeds (1–3,9). Further, PF does not exhibit a sex predisposition in either species (1,2,6).

There are several potential triggers for PF in cats, including medications, vaccines, and concurrent disease (1). There are multiple reports of cats developing PF within a few weeks after vaccination, specifically for rabies (1,9). There have been numerous possible drug associations mentioned in the literature; however, in many instances, direct causation cannot be established, as the implicated drugs were not reintroduced to affected animals (6,9). Doxycycline was strongly suspected as the trigger in 1 cat, as accidental reintroduction caused a disease flare (1). Cimetidine, enilconazole/neomycin/triamcinolone/amoxicillin, and itraconazole/lime sulfur were also suspected triggers in

Dr. Izydorczyk is a dermatology intern and Dr. Pye is a Board-certified veterinary dermatologist at the Atlantic Veterinary College, University of Prince Edward Island.

Address all correspondence to Dr. Veronica Izydorczyk; email: vizydorczyk@upei.ca

The Veterinary Dermatology column is a collaboration of *The Canadian Veterinary Journal* and the Canadian Academy of Veterinary Dermatology (CAVD). The CAVD is a not-for-profit organization, with a mission to advance the science and practice of veterinary dermatology in Canada, in order to help animals suffering from skin and ear disease to live the lives they are meant to. The CAVD invites everyone with a professional interest in dermatology to join (www.cavd.ca). Annual membership fee is $50. Student membership fees are generously paid by Royal Canin Canada.

Figure 1. Cat with pemphigus foliaceus exhibiting crusting lesions affecting the periocular region, muzzle, and chin.
Photograph courtesy of Frédéric Sauvé, DVM, MSc, DiplACVD.

Figure 2. Paw of a cat with pemphigus foliaceus exhibiting crusting lesions affecting the claw fold, consistent with paronychia.
Photograph courtesy of Frédéric Sauvé, DVM, MSc, DiplACVD.

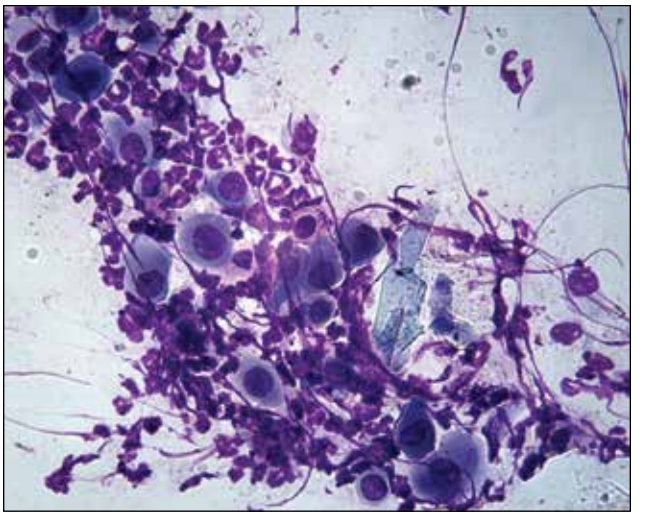


Figure 3. Cytological sample from a case of pemphigus foliaceus. Note the large, circular, acantholytic cells with darkly staining nuclei among the neutrophils.
Photomicrograph courtesy of Frédéric Sauvé, DVM, MSc, DiplACVD.

3 cats in which PF resolved spontaneously after withdrawal of the offending medication (1). Cefovecin, clindamycin/carprofen, and ipodate were implicated in the cases of 3 cats, all of which needed treatment beyond withdrawal of the offending medication. In the case of cats treated with cefovecin and clindamycin/carprofen, immunosuppressant therapies were eventually withdrawn (1). Other medications indicated as possible triggers for PF, albeit with less convincing evidence, include methimazole, ronidazole, penicillin G, vitamin B12, oxytocin, and radioactive iodine (1,9). Thymoma and leishmaniosis have been identified as disease processes with potential to trigger PF in cats (1).

Lesions associated with feline PF include pustules, crusts, erosions, ulcerations, and alopecia (3,7,9). Due to their transient nature, pustules are less common than crusts, which often span multiple hair follicles (2,6). Lesions most commonly affect the head/face (including nose, pinnae, and eyes), claw folds, and paw pads, and are typically bilaterally symmetrical (Figure 1) (1–3). Lesions can also affect the periareolar and perianal regions (1,3). Typically, lesions affect multiple locations (1,3). However, there are several reports of cats presenting only with crusting lesions and infection around the claw folds, known as paronychia (Figure 2) (1,10).

Pruritus affects ~65 to 80% of cats with PF (1,3,6,9). Systemic clinical signs are also common and include fever, lethargy, and anorexia (1,3,6,9). Systemic clinical signs appear to be more frequent in cats than in dogs, in which systemic signs most often occur in cases of severe and widespread disease (1,2). Lameness has also been reported in pets when lesions involve paws or claw folds (9).

Diagnosis

Diagnosis is based on clinical signs, microscopic confirmation through cytology and histopathology, and exclusion of other possible differential diagnoses (1,3).

Cytology is most beneficial when a smear is obtained from an intact pustule but cytology can be done using material from underneath crusts (3). Cytology findings include nondegenerate neutrophils, acantholytic cells, and microorganisms such as bacteria or yeast if secondary infection is present (2). Acantholytic cells typically appear as round, darkly staining cells with central nuclei (Figure 3) (2,6).

Biopsies are best taken from intact pustules; however, if those are not present, crusted lesions should be obtained (3). On histopathology, there are usually pustules located in the superficial epidermis (intracorneal or subcorneal) (3,6,7,11). Pustules are primarily composed of neutrophils and acantholytic cells, which can present as individual cells or rafts of multiple cells, although eosinophils can also be noted (2,3,11). Dermal inflammation is predominantly neutrophilic but mast cells and plasma cells can be seen with some frequency, although eosinophils are not commonly part of the dermal inflammation (3,9). The epidermis is

hyperplastic with the *stratum corneum* exhibiting orthokeratotic hyperkeratosis (3).

Differential diagnoses for superficial epidermal pustules in cats with acantholysis are limited but include pustular dermatophytosis and subcorneal pustular dermatitis caused by *Staphylococcus* spp., although the latter has not been well-described in cats (1,2). Although fungal cultures are often recommended in the literature as part of the diagnostic work, case reports suggest they are not routinely done (3,9). Bacterial cultures based on cytology results should also be considered, to guide antimicrobial therapy.

General blood work, including a complete blood (cell) count (CBC) and serum biochemistry panel, along with FIV/FeLV testing, are warranted before starting immunosuppressive treatments. Changes on blood work tend to be nonspecific (3). Leukocytosis and neutrophilia are the most common changes (3,7,9), whereas monocytosis, lymphopenia, eosinophilia, or anemia may also be present (3,9).

Treatment

Immunosuppression is the mainstay of PF treatment (7). Glucocorticoid monotherapy is the most common initial therapy for cats, with complete remission achieved in most animals (1,7,9). Prednisolone is the most commonly used glucocorticoid, but other options include triamcinolone and dexamethasone (1,7). In 1 case series (3), triamcinolone was more likely to induce remission and had less frequent adverse effects than prednisone. Unfortunately, it is not possible to compare the response to triamcinolone to that of prednisolone, which has greater bioavailability in cats, due to low case numbers in more recent case series (1,3,9). High-dose oral glucocorticoid pulse therapy, similar to that recommended for dogs, has been used in cats, but there is a perceived lack of benefit, as the interval to disease remission and the cumulative dose of glucocorticoid did not vary greatly from standard treatment protocols (1). Previously recommended doses for treatment were as high as 6.6 mg/kg per day, but lower doses (2 mg/kg per day) are equally effective at inducing remission (1,9,10). The most common adverse effects of glucocorticoids include polyuria, polydipsia, and polyphagia; the most serious adverse effects are diabetes mellitus, upper respiratory infections, urinary tract infections, and steroid hepatopathy (1,9). Injectable glucocorticoids should be used cautiously due to their anecdotally higher risk of causing severe adverse effects such as diabetes mellitus (9). Non-glucocorticoid options for treatment may need to be considered in animals not responding to glucocorticoids, in those with comorbidities that preclude the use of glucocorticoids, in those with severe adverse effects secondary to glucocorticoids, and in those in which glucocorticoids cannot be tapered to a dose considered safe for long-term use (7).

Other non-glucocorticoid treatments used as monotherapy or in combination with steroids with varying results include cyclosporine, chlorambucil, and gold salts. Cyclosporine (Atopica for Cats; Elanco, Mississauga, Ontario) is a calcineurin inhibitor labeled for management of feline allergic skin disease (12). Case series reported variable results for its use in the treatment of feline PF (1,9,12). As a monotherapy, it was efficacious for some, but not all, cases, with some case series suggesting a longer interval to disease remission (1,6,9,12). As an adjunct therapy, cyclosporine had efficacy comparable to that of chlorambucil in terms of interval to disease remission and overall disease response (12). The same case series reported it could also provide a glucocorticoid sparing effect, allowing systemic glucocorticoids to be reduced or eliminated (12). Although other case series reported on cyclosporine as an adjunct therapy, it is difficult to draw conclusions due to limited case numbers (1,9). Gastrointestinal clinical signs are the most common adverse effects of cyclosporine, but there are also rare reports of fulminant systemic disease (toxoplasmosis and mycobacterium) and neoplasia (12). Although there were isolated cases of neoplasia in cyclosporine-treated animals, increased prevalence of neoplasia was not reported in published clinical trials (13). Cats treated with cyclosporine should be tested for FIV/FeLV and have toxoplasma titers determined before initiation of treatment, to prevent treatment-induced development of clinical signs associated with these infectious diseases. Cats should also be kept indoors and not fed raw diets, and attempts should be made to taper cyclosporine to the lowest effective dose (12).

Chlorambucil is an alkylating agent often used as an adjunct treatment for its glucocorticoid-sparing effects or in cases of refractive disease (7). Although it can be used as a monotherapy for PF, it is difficult to draw conclusions about efficacy because of limited numbers of pets treated with chlorambucil monotherapy in recent case reports (1,9). Myelosuppression is a possible severe adverse effect and warrants routine blood work (7). Gold salts are mentioned in several case series as a possible treatment but are no longer commercially available (9).

Decisions regarding initial and maintenance treatment are usually based on multifactorial considerations of clinician preference, comorbidities, severity of disease, and response to treatment (9). Regardless of drug choice, the objective of initial therapy is to promptly achieve disease remission or resolution of the majority of lesions. Further, the objective of maintenance treatment is to determine the lowest effective dose that prevents relapse and decreases occurrence of adverse effects.

There are several alternative treatment options. Topical glucocorticoids can be used but should be reserved for localized disease (7). Prolonged use of potent topical steroids results in cutaneous atrophy or alopecia, and systemic absorption is possible (7). Topical steroids can be used with other therapies; *e.g.,* a recent case report outlines the successful management of PF with topical hydrocortisone acetate and oral pentoxifylline (14). Oclacitinib (Apoquel; Zoetis, Parsippany, New Jersey, USA) is another alternative therapy described in 2 case reports in which the animal's concurrent comorbidities precluded the use of glucocorticoids or immunosuppressive agents (15,16). In both reports, oclacitinib provided clinical improvement with subsequent dosage reductions within a generally short interval (15,16). Although no major adverse effects were reported and results appeared favorable, this use of oclacitinib was off label as safety studies have not yet been done in cats (15,16). More research into the use of oclacitinib for immune-mediated diseases is needed before it can become a treatment recommended by dermatologists.

Prognosis

Pemphigus foliaceus in cats generally has a good prognosis (1,6). One case series suggested that 90% of affected cats achieve disease control within 1 mo, with the interval to disease control varying only slightly depending on treatment protocol (1). This contrasts with dogs, in which reaching disease remission is less likely and often takes much longer (1). Most cats do, however, require long-term therapy and most often experience relapse with tapering or discontinuation of therapy (1,9). Relapse can also occur as part of the waxing and waning disease process (9). Thus, even with a good prognosis, client education regarding financial cost, time commitment, and emotional burden should be undertaken (9). Notably, in a quality-of-life survey for the owners of cats with PF, more than 60% of owners perceived that their cat was stressed by veterinary visits. The use of anxiolytics before appointments should be emphasized to improve both client and patient experience (9). However, euthanasia or death associated directly with PF or adverse effects of treatments appears less common in cats than in dogs (1).

References

1. Bizikova P, Burrows A. Feline pemphigus foliaceus: Original case series and a comprehensive literature review. BMC Vet Res 2019;15:22.
2. Olivry T. A review of autoimmune skin diseases in domestic animals: I — superficial pemphigus. Vet Dermatol 2006;17:291–305.
3. Preziosi DE, Goldschmidt MH, Greek JS, *et al.* Feline pemphigus foliaceus: A retrospective analysis of 57 cases. Vet Dermatol 2003;14: 313–321.
4. Levy BJ, Mamo LB, Bizikova P. Detection of circulating anti-keratinocyte autoantibodies in feline pemphigus foliaceus. Vet Dermatol 2020; 31:378–e100.
5. Olivry T, Linder K. Dermatoses affecting desmosomes in animals: A mechanistic review of acantholytic blistering skin diseases. Vet Dermatol 2009;20:313–326.
6. Miller WH, Griffin CE, Campbell KL. Muller and Kirk's Small Animal Dermatology. 7th ed. St. Louis, Missouri: Elsevier, 2012.
7. Rosenkrantz WS. Pemphigus: Current therapy. Vet Dermatol 2004;15: 90–98.
8. Bizikova P, Dean GA, Hashimoto T, Olivry T. Cloning and establishment of canine desmocollin-1 as a major autoantigen in canine pemphigus foliaceus. Vet Immunol Immunopathol 2012;149:197–207.
9. Jordan TJM, Affolter VK, Outerbridge CA, Goodale EC, White SD. Clinicopathological findings and clinical outcomes in 49 cases of feline pemphigus foliaceus examined in Northern California, USA (1987–2017). Vet Dermatol 2019;30:209–e65.
10. Simpson DL, Burton GG. Use of prednisolone as monotherapy in the treatment of feline pemphigus foliaceus: A retrospective study of 37 cats. Vet Dermatol 2013;24:598–601.
11. Olivry T, Linder KE. Dermatoses affecting desmosomes in animals: A mechanistic review of acantholytic blistering skin diseases. Vet Dermatol 2009;20:313–326.
12. Irwin KE, Beale KM, Fadok VA. Use of modified ciclosporin in the management of feline pemphigus foliaceus: A retrospective analysis. Vet Dermatol 2012;23:403–e76.
13. Nuttall T, Reece D, Roberts E. Life-long diseases need life-long treatment: Long-term safety of ciclosporin in canine atopic dermatitis. Vet Rec 2014;174:s3–s12.
14. Hobi S, Beatty JA, Sandy JR, Barrs VR. Successful management of feline pemphigus foliaceus with pentoxifylline and topical hydrocortisone aceponate. Vet Med Sci 2022;8:937–944.
15. Nosach NR, Blanco AD, Duarte MJ. Oclacitinib as a therapeutic proposal in feline pemphigus foliaceus. Jpn J Vet Dermatol 2023;29:71–76.
16. Carrasco I, Martínez M, Albinyana G. Beneficial effect of oclacitinib in a case of feline pemphigus foliaceus. Vet Dermatol 2021;32:299–301.

Diagnostic Ophthalmology
Ophtalmologie diagnostique

Shayna Levitt, Marina L. Leis, Lynne S. Sandmeyer

History and clinical signs

A 5-year-old spayed female shih tzu dog was examined by the ophthalmology service at the Western College of Veterinary Medicine (Saskatoon, Saskatchewan). This dog was originally presented to the emergency service for evaluation of a large orbital swelling that appeared at the site of her previous left-sided enucleation. The reason for enucleation was unknown as the dog was adopted from a shelter. The menace response and palpebral, oculocephalic, direct, and consensual pupillary light reflexes were normal in the right eye. The Schirmer tear test (Schirmer Tear Test Strips; Alcon Canada, Mississauga, Ontario) value was 22 mm/min in the right eye. The intraocular pressure was estimated with a rebound tonometer (Tonovet; Tiolat, Helsinki, Finland) and was 22 mmHg in the right eye. Fluorescein staining (Fluorets; Bausch & Lomb Canada, Markham, Ontario) of the cornea was negative. Retropulsion of the right eye was unremarkable. On direct examination of the left orbit, there was marked protrusion of thin, mildly alopecic skin over the orbital space that was moderately firm on palpation. Aspiration of this space with a 22G needle confirmed the orbital swelling was due to filling with air. Following application of 0.5% tropicamide (Mydriacyl; Alcon Canada), examination of the right eye using a transilluminator (Welch Allyn Finoff Transilluminator; Welch Allyn, Mississauga, Ontario) and handheld biomicroscope (Kowa SL-17 Portable Slit Lamp; Kowa, Tokyo, Japan) was unremarkable. Indirect ophthalmoscopic (Heine Omega 500; Heine Instruments Canada, Kitchener, Ontario) examination was completed and did not reveal abnormalities in the right eye. Photographs of this dog at presentation following shaving of the affected site are provided for your assessment (Figure 1).

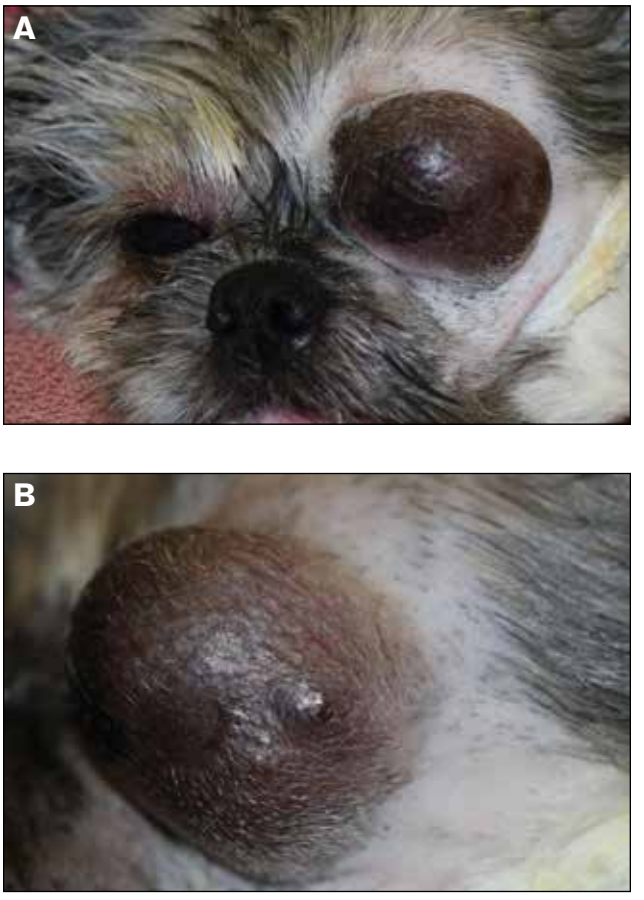


Figure 1. Clinical photographs of the face (A) and left orbit (B) of a 5-year-old shih tzu dog at presentation, following shaving of the lesion.

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

Discussion

The ophthalmic diagnosis was orbital emphysema (or pneumatosis) of the left eye. Differential diagnoses for an orbital swelling following enucleation include orbital cellulitis, orbital seroma or abscess, orbital neoplasia, or an orbital cyst. Enucleation is a routine surgery used to remove painful, blind eyes that are refractive to treatment for a variety of intraocular diseases (1,2). There is little information available about the prevalence of postoperative complications following enucleation; however, the prevalence of surgical site infections was reported to be 5%, according to 1 study (1). Other potential early postoperative complications of enucleation include hemorrhage and edema (1–4). In addition, intraoperative damage to the optic chiasm through excessive tension on the optic nerve may rarely lead to blindness in the contralateral eye, but is more commonly

Department of Small Animal Clinical Sciences, Western College of Veterinary Medicine, University of Saskatchewan, 52 Campus Drive, Saskatoon, Saskatchewan S7N 5B4.

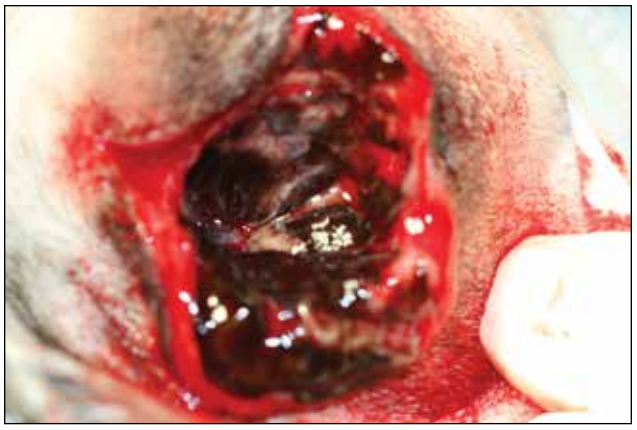


Figure 2. An intraoperative photograph of the pigmented, air-filled orbital cyst that originated from conjunctival remnants in a 5-year-old shih tzu dog.

reported in cats (2). Although some publications have suggested that a certain level of conjunctival remnants is acceptable (2,4), incomplete removal of adnexal tissues such as the nictitating membrane, conjunctiva, or meibomian glands has been reported to cause complications such as draining fistulas, mucous-filled cysts, or orbital emphysema (2–4). These complications tend to occur later, usually developing between 30 d to 1 y after enucleation (1–3).

Orbital emphysema is thought to occur due to retention of conjunctiva within the orbit, resulting in an accumulation of secretory material within this space and preventing obliteration and scarring of the lower nasolacrimal canaliculus that normally occurs when the conjunctival tissue is transected (2–4). The condition is more commonly encountered in brachycephalic breeds (2–4). The increased intranasal expiratory pressure in brachycephalic breeds, combined with the failure to remove adnexal tissues, is suspected to contribute to development of orbital emphysema (2–4). The increased intranasal expiratory pressure in these breeds, secondary to anatomic factors such as stenotic nares and an elongated soft palate, may cause air to build up in the orbit by creating a pressure differential necessary to force air through the nasolacrimal duct in a retrograde fashion, and may prevent the duct from fibrosing by continually forcing it open during healing (2). In a case report, a Japanese chin dog developed orbital emphysema of its previous enucleation site after experiencing respiratory distress (3). Alternatively, orbital emphysema may also occur *via* communication with the frontal or paranasal sinuses following a traumatic event (3).

Diagnosis of orbital emphysema includes confirmation of an air-filled space *via* fine-needle aspiration in addition to cranial imaging, such as computed tomography or radiographs, to investigate possible causes of air accumulation in the orbit, such as a paranasal sinus fracture (2,3). A Jones test (injecting fluorescein into the orbital cavity to assess drainage from the nose) can be done to evaluate the patency of the nasolacrimal duct; however, this may not be reliable, as pressure occlusion of the nasolacrimal punctum or canaliculus can create a reversing-valve effect (2,4). A Jones test was not done in this case.

In this case, a computed tomographic scan was obtained and revealed left-sided enucleation and left orbital emphysema with concurrent bilateral malformation of the nasolacrimal duct, likely associated with brachycephalic skull conformation. A small focus of gas was present adjacent to the apparently enlarged nasolacrimal duct, suggesting that increased pressure within in the nasal cavity led to gas entrapment in the orbit. No fractures were present.

The treatment for persistent orbital emphysema is surgical exploration with ligation of the patent nasolacrimal duct (2). Surgery was performed to explore the orbit of this dog and a large, pigmented, epithelial-enclosed cyst was identified (Figure 2). The epithelium was resected and the opening to the nasolacrimal canaliculus was ligated with a simple cruciate suture. Histopathology of the excised tissue confirmed an epithelial-lined cyst.

Postoperative therapy included ocular lubrication (Optixcare; Aventix, Burlington, Ontario) in the right eye, q6h for 1 wk; and oral meloxicam (Metacam; Boehringer Ingelheim, Duluth, Georgia, USA), q24h for 5 d, as needed for pain and inflammation. No complications or recurrence were noted.

Enucleation is a relatively common procedure with a subjectively low complication rate. However, it is important to completely remove all epithelial tissues at the time of surgery. This includes the eyelid margins, the bulbar and palpebral conjunctiva, and the nictitating membrane. When even small amounts of these tissues remain, adverse consequences such as failed incisional closure, cyst formation, and orbital emphysema may occur and require surgical correction.

References

1. Dacanay SJ, Barber RM, Diehl KA, Myrna KE. Incidence and risk factors for surgical site infection following enucleation in dogs. Front Vet Sci 2023;9:1086956.
2. Ward S, Neaderland MH. Complications from residual adnexal structures following enucleation in three dogs. J Am Vet Med Assoc 2011;239:1580–1583.
3. Gornik KR, Pirie CG, Alario AF. Orbital and subcutaneous emphysema following enucleation and respiratory distress in a Japanese chin. J Am Anim Hosp Assoc 2015;51:413–418.
4. Bedford PGC. Orbital emphysema as an unusual complication to enucleation. J Small Anim Pract 1979;20:551–555.

Canadian Veterinary Medical Association

Association canadienne des médecins vétérinaires

Stabilize your business insurance rates today.

The CVMA Insurance Program is the only program in Canada with the exclusive Protected Self insurance structure, designed to provide superior coverage at the best price.

Made for Canadian Vets

Western FINANCIAL GROUP
Canada's Insurance Broker

Get more info at westernfinancialgroup.ca/cvma

Business Directory Annuaire des entreprises

LEBA III™

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

Cleans Teeth with the Ease of a Spray

THE LEBA III DIFFERENCE

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

VETERINARY
WDDC
Vet. Purchasing
MidWest
DISTRIBUTORS

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

Used by veterinarians since 1994.

Email: tellus@lebalab.com Office tel: 1-519-542-4236

To contact us, call toll free:1-866-532-2522

LebaLab Inc.

Senvelgo

Our liquid oral feline diabetes solution is

Dropping Soon

Simplify the treatment of feline diabetes with Senvelgo™, a once-daily liquid oral solution.

- Administered with or without food*
- Low risk of hypoglycemic events†
- Less long-term monitoring required

* Refer to the Canadian Package Insert for details.
† Compared to typical insulin therapy.

Reference: Current Canadian Senvelgo™ Label.

Boehringer Ingelheim

Life forward