Letters to the Editor

Involving ACVAA diplomates to decrease anesthetic risk

I am writing on behalf of the Board of Directors of the American College of Veterinary Anesthesia and Analgesia (ACVAA). Our board members read with interest the *JAVMA* News story[1] in the February 1, 2016, issue discussing the ongoing debate surrounding the use of anesthesia-free dentistry in companion dogs and cats. The ACVAA has previously stated that it supports the American Animal Hospital Association's guidelines requiring that all dental cleanings in dogs and cats be performed with the animal under general anesthesia and endotracheally intubated.[2]

While not wanting to further discuss any viewpoints regarding anesthesia-free dentistry, we did want to address a comment attributed to Joshua Bazavilvazo, founder and chief executive officer of Pet Dental Services, that some pets "truly cannot go under anesthesia." We also wanted to support statements made by Dr. Curt Coffman of Arizona Veterinary Dental Specialists that owner education regarding anesthetic risk is important, and that "almost every pet can have anesthesia."

Importantly, the ACVAA Board of Directors would like to increase public and professional awareness of the accessibility of ACVAA diplomates for provision of high-quality general anesthesia by board-certified veterinary specialists. Particularly for those companion animals who are deemed a high anesthetic risk because of comorbidities, involvement of an ACVAA diplomate—either via direct management of the case or by consultation—can greatly optimize patient care and outcome. Today, diplomates of the ACVAA can be found in many referral practices throughout North America and around the world, and some travel to general practices to assist with individual case management.

In conclusion, the ACVAA Board of Directors wants to emphasize that involvement of an ACVAA diplomate in a companion animal's general anesthetic care can greatly decrease perceived anesthetic risk and can allay owner fears. A list of current ACVAA diplomates can be found at www.acvaa.org/Directory.

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1. Burns K. Below the surface of anesthesia-free dentistry. *J Am Vet Med Assoc* 2016;248:242–247.
2. ACVAA. Position statements: anesthesia-free dentistry. Available at: www.acvaa.org/docs/Anesthesia_Free_Dentistry.pdf. Accessed Feb 29, 2016.

Practicing caution with prescription of antimicrobials

Reading the recent "What Is Your Diagnosis?" article describing a dog with a penetrating oropharyngeal foreign body,[1] I was concerned that the duration of antimicrobial administration following foreign body removal (1 month of amoxicillin–clavulanic acid and 20 days of enrofloxacin) was excessive and not in keeping with the statement in the AVMA policy on judicious therapeutic use of antimicrobials[2] that "therapeutic exposure to antimicrobials should be minimized by treating only for as long as needed for the desired clinical response." I would hope that in the future, editors would highlight cases that are in compliance with the AVMA positions on antimicrobial sustainability.[2] Practitioners should be aware that excessive duration of antimicrobial use is a more important instigator of antimicrobial resistance than is failure to complete a short course of treatment. When prescribing antimicrobials, one should follow the principle of using "as much as needed and as little as possible."

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1. Baik NJ, Thompson MS. What Is Your Diagnosis? *J Am Vet Med Assoc* 2016;248:263–265.
2. AVMA. Judicious therapeutic use of antimicrobials. Available at: www.avma.org/KB/Policies/Pages/Judicious-Therapeutic-Use-of-Antimicrobials.aspx. Accessed Feb 22, 2016.

The authors respond:

We agree that judicious use of antimicrobials is of critical importance in veterinary medicine today. To our knowledge, however, there currently are no established guidelines in veterinary medicine for the appropriate duration of antimicrobial treatment for animals with wounds secondary to penetrating foreign bodies. For the case described in our report, antimicrobial culture and susceptibility testing was performed at the time of surgery to ensure that the

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organisms were susceptible to the antimicrobials that were administered and that both antimicrobials were necessary for treatment.

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Fond memories of veterinary mentors

Congratulations on the fine coverage of American Pharoah in the February 15 issue of *JAVMA*.[1] The photo of Dr. McGee petting American Pharoah with Dr. Edward Fallon in the background brings back fond memories of 1959 when these 2 veterinarians were still actively practicing.

I was a third-year veterinary student at Cornell University then, and I loved traveling to Lexington to ride with the local veterinarians. Riding with Drs. McGee and Fallon, in particular, was a special treat because they always took pains to educate me as we rode together.

On one occasion, Dr. McGee operated on a mare with a rectovaginal tear. Anesthesia and recovery were more challenging back then, but because of the guarded prognosis for success of this type of repair, Dr. McGee opted to perform the surgery with the mare under general anesthesia and positioned in dorsal recumbency to provide better access to the dorsal aspect of the vagina. Thankfully, everything went smoothly. This was a good example of why Dr. McGee was recognized for his expertise in equine reproduction.

Dr. Edward Fallon, a Cornell University graduate, was the one I spent the most time riding with, and there was no finer man I could have had the privilege of spending time with.

Looking at the photograph, one can see the love and compassion between man and horse, a relationship that is so necessary to success in racing and other horse sports. The photograph and article describe and illustrate this relationship beautifully.

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1. Larkin M. Crowning achievement. *J Am Vet Med Assoc* 2016;248:340–347.

Treatment of immune-mediated polyarthritis in dogs

We were pleased to see the recent study from Rhoades et al[1] comparing the efficacy of prednisolone and cyclosporine for the treatment of immune-mediated polyarthritis (IMPA) in dogs. This study provides valuable information for clinicians treating dogs with this frustrating condition.

Interestingly, of the 10 dogs treated with cyclosporine, only 8 had resolution of synovial fluid cytologic abnormalities on day 45 of treatment. Two dogs also developed what appeared to be opportunistic infections. Recent work in our laboratory suggests an explanation for this mixed bag of outcomes.

Cyclosporine works by inhibiting calcineurin, an enzyme essential for T-cell production of cytokines such as interleukin-2, and activated T-cell interleukin-2 expression is a measure of the direct effects of cyclosporine on target cells. Over the past few years, we have assayed interleukin-2 expression in samples from many dogs receiving cyclosporine at the same dosage (5 mg/kg [2.3 mg/lb], PO, q 12 h) used in the study by Rhoades et al and have observed marked dog-to-dog variability. In some dogs, suppression of T-cell interleukin-2 expression was minimal; in others, suppression appeared to be optimal for the desired systemic immunosuppressive effect (on the basis of clinical studies in people); and in others still, suppression was profound enough to predispose to opportunistic infection. Unfortunately, measuring blood cyclosporine concentrations and adjusting the dosage on the basis of target trough or peak drug concentrations, although helpful, do not eliminate this variability in target cell responses. Previous work with healthy dogs has demonstrated little correlation between blood cyclosporine concentration and activated T-cell cytokine expression,[2,3] and in individual dogs, trough drug concentrations markedly lower than the minimum used by Rhoades et al (250 ng/mL) can be associated with substantial suppression of cytokine expression, whereas trough concentrations as high as 400 ng/mL may be needed to reliably suppress T-cell function in most dogs.

There are undoubtedly multiple reasons for the marked dog-to-dog variability in the target cell response to cyclosporine, including variations in oral bioavailability, protein binding, drug metabolism, and duration of intracellular effects within T cells. In our opinion, given this high degree of individual variability, the likelihood of achieving optimal systemic immunosuppressive effects without an unacceptable risk of secondary infection can be maximized only if cyclosporine therapy is individualized on the basis of pharmacodynamic assays that measure effects on target T cells.

In human transplant medicine, the modern era of low rejection rates only began when steroids were added to cyclosporine for immunosuppressive regimens.[4–7] Given that the Rhoades et al study found that both cyclosporine and prednisone as sole agents were reasonably effective for the treatment of IMPA in dogs, we suspect that the combination of the two drugs would be even more effective and would allow for the use of lower prednisone dosages, which would help reduce the incidence and severity of steroid-related adverse effects. In the Rhoades et al study, the use of a single immunosuppressive agent in each treatment group was necessary for comparative purposes. In our opinion, however, their findings suggest that a combination of cyclosporine and prednisone would likely be even more successful.

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1 Rhoades AC, Vernau W, Kass PH, et al. Comparison of the efficacy of prednisone and cyclosporine for treatment of dogs with primary immune-mediated polyarthritis. *J Am Vet Med Assoc* 2016;248:395–404.
2 Archer T, Fellman C, Mackin A, et al. Pharmacodynamic monitoring of canine T-cell cytokine responses to oral cyclosporine. *J Vet Intern Med* 2011;25:1391–1397.
3. Fellman CL, Archer TM, Stokes JV, et al. Effects of oral cyclosporine on canine T-cell expression of IL-2 and IFN-gamma across a 12-h dosing interval [published online ahead of print Dec 17, 2015]. *J Vet Pharm Ther* doi:10.1111/jvp.12280.
4. Rosenthal J, Hakala T, Starzl T, et al. Cadaveric renal transplantation under cyclosporine-steroid therapy. *Surg Gynecol Obstet* 1983;157:309–315.
5. Gartner J, Zitelli B, Starzl T, et al. Orthotopic liver transplantation in children: two-year experience with 47 patients. *Pediatrics* 1984;74:140–145.
6. Gordon R, Iwatsuki S, Starzl T, et al. Cyclosporine-steroid combination therapy in 84 cadaveric renal transplants. *Am J Kidney Dis* 1985;5:307–312.
7. Demetris A, Lasky S, Dekker A, et al. Pathology of hepatic transplantation: a review of 62 adult allograft recipients immunosuppressed with a cyclosporine/steroid regimen. *Am J Pathol* 1985;118:151–161.