What's New in Veterinary Dermatology

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Every spring, the American College of Veterinary Dermatology (ACVD) and the American Academy of Veterinary Dermatology (AAVD) host a North American Veterinary Dermatology Forum (NAVDF). This April the NAVDF was held in Nashville, TN. The NAVDF is open to everyone with an interest in veterinary dermatology, including both boarded and non-boarded veterinarians, technicians and veterinary students. The three-day conference presents the latest research in veterinary dermatology as well as clinical updates to aid veterinarians and specialists in diagnosing and treating dermatologic diseases. Many of the research abstracts and poster presentations presented at the NAVDF will not be published for months to years after the conference, so I have tried to summarize the more clinically relevant information.

Research Abstracts

Stability and pharmacokinetics of Atopica® capsules stored at -20°C. Bachtel J, *et al.*

Many veterinarians recommend freezing Atopica® or generic ciclosporin capsules before oral administration to reduce the incidence of vomiting in dogs. Although freezing does not seem to affect the clinical efficacy of ciclosporin, no one has studied the impact on ciclosporin stability. This study looked at ciclosporin concentrations of all available Atopica® capsule strengths (10 mg, 25 mg, 50 mg, and 100 mg). Ciclosporin concentrations were assessed after -20°C storage at five time points (1 hour, 1 day, 7 days, 15 days, and 30 days) and at package insert recommendations (15–25°C). A blinded, randomized cross-over study was also performed to compare blood concentrations of ciclosporin dosed in eight healthy beagle dogs (4.9–5.3 mg/kg PO) after Atopica® storage for 28 days at -20°C versus storage at 15–25°C with a 7 day washout period. They found no significant difference between ciclosporin concentrations of frozen Atopica® capsules compared those stored at the recommended temperature range ($p = 0.80$). In the crossover study, there were no significant differences in pharmacokinetics. Thus, Atopica® capsules can be administered to dogs after storage at -20°C for approximately one month without significant impact on drug stability or pharmacokinetics. Although this study did not evaluate generic modified ciclosporin capsules, which is commonly used for cost reasons, my opinion is that there would likely be similar findings.

Aspergillus* spp. otitis in small animals - a retrospective study of 17 cases. Goodale EC, *et al.

Aspergillus spp. are common saprophytic opportunistic fungal organisms and can cause otomycosis in humans as well as dogs. This retrospective review of medical records from 1989–2014 identified eight dogs and nine cats diagnosed with *Aspergillus* otitis based on culture. All dogs weighed greater than 23 kg. The most common predisposing causes identified were concurrent disease or therapy causing immunosuppression (3/8 dogs, 3/9 cats), historical otic foreign bodies (3/8 dogs) and previous fluoroquinolone usage (topical or systemic) (3/8 dogs, 7/9 cats). *Aspergillus* otitis was unilateral in all dogs and usually unilateral in cats; two cats had bilateral disease. Concurrent otitis media was identified in three dogs and one cat and suspected in two cats. *Aspergillus fumigatus* was the most common isolate and was more common in cats (1/8 dogs, 5/9 cats). *Aspergillus niger* (3/8 dogs) and *Aspergillus terreus* (3/8 dogs) were most commonly cultured from dogs. Animals received various topical and systemic antifungal medications however otic lavages under anesthesia and/or surgical intervention increased the likelihood of resolution. *Aspergillus* otitis is uncommon, typically seen as unilateral otitis externa in cats and larger breed dogs and may have an association with immunosuppression, otic foreign bodies and previous fluoroquinolone usage.

Comparison of minocycline and doxycycline susceptibilities of MRSP isolates using current and revised breakpoints. Hnot ML, *et al.*

This study compared the current published Clinical and Laboratory Standards Institute (CLSI) breakpoints to predict minocycline and doxycycline susceptibility of *Staphylococcus pseudintermedius* to recently proposed breakpoints, which are four dilutions lower than current breakpoints. This study

measured minimum inhibitory concentrations (MICs) of minocycline and doxycycline in 100 canine meticillin-resistant *S. pseudintermedius* clinical isolates and compared their susceptibilities to minocycline and doxycycline based on current and proposed standards. Use of the current published breakpoints misclassified 45 and 5 of the isolates as susceptible to minocycline and doxycycline, respectively. These results underscore the importance of utilizing the proposed minocycline and accepted doxycycline breakpoints in place of current tetracycline breakpoints.

Effect of food on pharmacokinetics of minocycline in healthy research dogs. Hnot ML, *et al*.
Tetracyclines are recommended to be given on an empty stomach in people but no studies have looked at whether this is true in dogs. Since doxycycline has become harder to obtain, many veterinarians have started prescribing minocycline. Ten research hounds were administered oral minocycline (approximately 5 mg/kg) with and without food, in a crossover study, with a one-week washout between treatments. Blood samples were collected immediately prior to minocycline administration and over 24 hours. Minocycline plasma drug concentrations were measured. A significant difference was found for C_{MAX} ($P = 0.0059$), with fasted dogs attaining a higher C_{MAX}. Since feeding was a significant source of variation for the population's primary pharmacokinetic parameters ($P < 0.01$) and fasted dogs had higher minocycline concentrations, they recommend administering minocycline without food. They also recommended giving water after administration to avoid esophageal irritation.

Investigation of the effects of 30 day administration of oclacitinib (Apoquel®) on intradermal and allergen-specific IgE serology testing in atopic dogs. Clear V, *et al*.
We have found oclacitinib to be very helpful in weaning dogs off of glucocorticoids for the requisite 30 days before intradermal allergy testing (IDT) and have clinically found no effect on IDT results. The following study helped confirm or clinical findings. This study looked at the effects of 30 day administration of oclacitinib on IDT reactivity and IgE serology in 22 dogs with confirmed atopic dermatitis (AD) and initial positive test reactions in a randomized, double-blinded, placebo-controlled study. Eleven dogs were treated with oclacitinib at a dose of 0.4–0.6 mg/kg orally every 12 hours for 14 days, then every 24 hours for 16 days. Eleven dogs were treated in the same fashion with oral placebo. IDT was performed at day 0 and day 30 using a panel of 56 aqueous allergens. Serum was collected for IgE serology (Heska-ALLERCEPT®) at day 0 and day 30. At day 30, oclacitinib did not have a statistically significant effect on IDT or IgE serology reactivity.

Sterile nodular panniculitis: a retrospective study of 39 dogs. Contreary CL.
Sterile nodular panniculitis is a rare skin disease that appears as multiple, variably sized subcutaneous nodules/masses that sometimes drain. Thirty nine dogs were studied in this retrospective case series, all with negative special stains for infectious organisms. Bacterial culture results were negative (24/30) or isolated rare numbers of *Staphylococi* (6/30). The breed distribution was compared between dogs with sterile nodular panniculitis and all other dogs examined at the teaching hospital over the same time period. Australian Shepherd dogs, Brittany Spaniels, Dalmatians, Pomeranians, and Chihuahuas were significantly overrepresented ($P < 0.05$). Thirty two dogs (82.1%) had no concurrent systemic illness at the time of initial diagnosis or during documented follow-up. The concurrent diseases diagnosed in 7 dogs included polyarthritis (4), diabetes mellitus (1) and historical seizures (2). Interestingly, halogen panniculitis has been reported in people on KBr therapy for epilepsy and a recent case report of two dogs with KBr-associated panniculitis was published in JSAP.

A prospective, randomized, double-blinded, placebo-controlled trial evaluating the effects of a natural triglyceride omega-3 supplement on atopic dermatitis and erythrocyte membrane fatty acid concentrations in dogs. Palmieiro BS, *et al*.
There is a dearth of well-designed studies looking at efficacy of fatty acid (FA) supplements in dogs and I am often at a loss when people ask which fatty acid supplements to recommend. This study evaluated the efficacy of a triglyceride form omega-3 supplement (Canine Omega Benefits) for atopic dermatitis in dogs and to evaluate its effect on canine erythrocyte membrane fatty acid concentrations, compared to placebo. Seventy-two dogs with a clinical diagnosis of AD were evaluated by one of two veterinary dermatologists on days 0, 42 and 84; Lesion scores and pruritus scores were measured and blood was obtained to

measure erythrocyte membrane fatty acid concentrations. Overall improvement was assessed in 68 dogs completed. On days 42 and 84, treated dogs had a significant reduction in lesion scores. On day 84, significantly more treated dogs (60%) had reduction in pruritus scores. A significant increase in omega-3-index (EPA+DHA/total erythrocyte FA) levels and reductions in Arachidonic Acid:EPA and Omega-6:Omega-3 ratios were found on days 42 and 84 compared to placebo. The authors suggested that COB was an effective treatment for the reduction for pruritus and skin lesions associated with AD and improved EM FA concentrations in dogs.

Evaluation of cyclosporine-sparing effects of polyunsaturated fatty acids in the treatment of canine atopic dermatitis. Muller R, *et al*.
Here is another well-designed study looked at FA use in dogs. This was a randomised, double-blinded, placebo-controlled trial with atopic 36 dogs. Dogs were stable on their individual cyclosporine dosage and received either a combined omega-3/omega-6 fatty acid product or placebo orally for 12 weeks. Lesion scores were examined monthly. Pruritus, quality of life, global condition and coat quality were scored by the owner. If the dog's lesion score and/or pruritus score improved by at least 25% compared to the previous visit, the cyclosporine dosage was decreased by approximately 25%. If the scores deteriorated by at least 25%, the cyclosporine dosage was increased by the same percentage. There was a significant decrease in median daily cyclosporine dosage in the treatment group as well as significant improvement in pruritus. This study supports the use of FA in atopic dogs. The question remains as to the best form we should recommend. There are many FA supplements strengths and formulations to choose from as well as new dog foods loaded with FA.

Identification and characterization of ZTS-00103289, a monoclonal antibody neutralizing IL-31-mediated pruritus, in beagle dogs. Fleck TJ, *et al*.
Zoetis continues their search for targeted therapies for canine atopic dermatitis. Therapy with monoclonal antibodies (mabs) has been successfully used clinically in humans for multiple chronic conditions including rheumatoid arthritis, asthma and psoriasis. Their latest study molecule is a mab called ZTS-00103289. Interleukin-31 (IL-31) has been shown to induce pruritus in multiple species and Il-31 is increased in people with atopic dermatitis. This study looked at the role of IL-31 in canine atopic dermatitis. They created a caninized monoclonal antibody (mAb), ZTS-00103289, that inhibits IL-31 mediated cell-based signaling. A single subcutaneous dose of mAb or placebo was administered to dogs (n = 18/group) at a dose of 1 mg/kg. The dogs were challenged with IL-31 on days 1, 28 and 56 and pruritus was measured The mean pruritus scores for treated dogs were significantly lower than for placebo dogs on days 1 and 28 but not on day 56. The authors suggest that these results support the use of 1.0 mg ZTS-00103289/kg, SC to achieve a one-month duration of efficacy in this model.

Laboratory dose titration efficacy study of ZTS-00103289, a caninized anti-IL-31 monoclonal antibody, in a canine model of IL-31-induced pruritus. Walters RR, *et al*.
This study looked at the duration of activity of ZTS-00103289. A single subcutaneous injection of mAb was administered at 0, 0.125, 0.50, or 2.0 mg/kg to groups of six beagle dogs on day 0. IL-31 challenges were performed on days -7, 1, 7, 14, 28, 42, and 56. Their pharmacokinetic and pharmacodynamic modeling predicted that 95% of animals given a 2 mg/kg dose would be expected to have serum mAb concentrations above the EC_{50} for 28 days. There were no significant levels of anti-drug antibodies in any group. A separate study using ZTS-00103289 in cats showed high levels of anti-drug antibodies, showing an immunogenicity that would likely cause problems if this drug was used in cats.

Proof of concept efficacy and safety study of an anti-IL-31 monoclonal antibody for the treatment of atopic dermatitis in client-owned dogs. Michels GM, *et al*.
The next step in the evaluation of new drug is proof of concept studies in the field. They looked at the efficacy and safety of ZTS-00103289 dosed twice subcutaneously at a 14-day interval in dogs with atopic dermatitis in a masked, placebo-controlled, 42-day study. Owner assessment of pruritus dermatologist assessment of lesions scores were measured. Seventy-eight dogs from six veterinary dermatology practices were randomized to one of two treatment groups, ZTS-00103289 or placebo, at a 2:1 ratio. Dogs treated with ZTS- 00103289 had a significantly greater reduction from baseline in owner-assessed

pruritus VAS at all assessments. There were no serious adverse events reported during the study and no hypersensitivity reactions immediately post dosing. The most frequent adverse events in order of prevalence included vomiting, diarrhea, and lethargy. The authors suggest that the results of this study support the effectiveness and safety of ZTS-00103289 for treatment of dogs with atopic dermatitis.

The skin microbiome in an allergen sensitized canine model of atopic dermatitis. Pierezan F, *et al*.

The skin and gut microbiome is a hot topic now and studies in atopic people have shown they have altered skin flora compared to non-atopic people. This study evaluated changes in the skin microbiome in atopic dogs and compared the skin microbiome between atopic dogs (n = 8) and healthy dogs (n = 8). The atopic dogs were sensitized with a suspension of house dust mites and samples were collected prior to and at several timepoints after the challenge. The atopic dogs displayed differences in bacterial groups on the allergen sensitized skin site, with increases in the proportions of *Staphylococcaceae*, *Streptococcaceae*, and decreased proportions of *Fusobacteriaceae*. The pre-sensitized samples from the atopic dogs were significantly different from healthy pet dogs, with increases in *Firmicutes* and *Actinobacteria*, and decreases in *Gammaproteobacteria*. The authors suggest that given the many similarities between human and canine atopy, dog models could be used as a tool to study the role of the skin microbiome.

A diagnostic tool for the veterinary dermatologist and pathologist: panfungal polymerase chain reaction (PCR) on formalin-fixed paraffin embedded (FFPE) tissues to classify fungal organisms found histologically. Smith CM, *et al*.

Diagnosing fungal diseases can be challenging due to culturing difficulties and false negatives on pathology. This study looked to validate the use of panfungal primers via PCR to classify fungal organisms on FFPE tissues. Samples from nineteen cases where fungal organisms were observed histologically were selected and included in this study. These included tissues from canine, feline, equine and bovine with cutaneous, nasal, and pulmonary fungal infections. DNA was extracted and isolated from FFPE tissues using the BiOstic FFPE Tissue DNA isolation kit. PCR was performed. Of the 19 cases, 15 (79%) were PCR positive, nine confirmed the histologic diagnosis to the species level, three cases had an identity match where fungal organisms were seen, but morphology did not allow histologic classification, and three had inconclusive sequencing results. Of these cases, 4 were confirmed with immunohistochemistry and one was confirmed with fungal culture. The authors plan further studies looking at cases confirmed by fungal culture and other ancillary tests to continue to validate this protocol.

Development of a real-time PCR technique to detect *Sarcoptes scabiei* in canine samples. Zewe CM, *et al*.

Sarcoptes diagnosis in dogs is often made on clinical signs and history due to the poor sensitivity of skin scrapings. This study attempted to develop a highly sensitive PCR test to diagnose scabies in dogs. DNA was extracted from skin scrapings and skin biopsies of dogs with scabies Different sets of primers targeting the mitochondrial r16S DNA of *S. scabiei* were tested. Test runs showed uniform and consistent peaks on known positive skin scrapings and paraffin-embedded biopsy samples. No amplification was observed on negative samples. This test may become available in the next few years to help us more accurately diagnose canine scabies.

Deep pyoderma caused by *Burkholderia cepacia* complex in dogs associated with ciclosporin administration in dogs: a case series. Banovic F, *et al*.

Burkholderia cepacia are ubiquitous gram-negative bacilli associated with fatal nosocomial infections in humans; and are often resistant to many antibiotics. This retrospective identified six dogs with *Burkholderia*-associated deep skin infections. All dogs were receiving oral ciclosporin at the time of skin infection development. All dogs were castrated males and 4 of 6 (67%) were West Highland white terriers. The skin lesions looked like the typical lesions seen with deep pyoderma and were confined mainly to the trunk. Skin cytology in all cases showed inflammatory cells (neutrophils and macrophages) and a moderate to abundant amount of intracellular and extracellular bacilli. In three dogs, histopathology showed a multifocal, nodular to coalescing pyogranulomatous dermatitis associated with

multifocal folliculitis and furunculosis. Aerobic cultures showed multidrug-resistant *Burkholderia* strains with sensitivity to trimethoprim/sulfonamides in all dogs and marbofloxacin, piperacillin and ceftazidime in three dogs. Complete remission was achieved in all dogs using either trimethoprim/sulfonamides, quinolones (marbofloxacin, ciprofloxacin) or doxycycline in conjunction with ciclosporin withdrawal. The authors suggest that veterinarians be aware of the rare potential for *Burkholderia*-associated deep skin infections in dogs receiving oral ciclosporin. These infections, although rare, are important because of potential transmission risk to humans or other animals.

Suspected zinc-responsive dermatosis in nine Boston terrier dogs. Lee FF, *et al*.
Zinc-responsive dermatosis is mostly associated with Siberian Huskies. This retrospective study found nine Boston terriers with hyperkeratotic lesions localized to the face and pressure points documented from 2004–2014. The median age of onset of lesions was 3.5-months-old (range 1–24 months). Symmetrical alopecia with thick scale or hyperkeratotic plaques was noted on the haired skin of the dorsal muzzle (5/9), the margins and concave aspects of the pinnae (8/9), the hocks (2/9), and the elbows (1/9). Skin biopsies were consistent with zinc-responsive dermatosis. Five dogs were treated with zinc supplementation (sulfate, gluconate, methionine), and four were known to clinically improve or resolve within 1–4 months. Although the underlying causes and were not definitively there are histologic and clinical similarities to zinc-responsive dermatosis and my clinical experience fits with Boston terriers being possible over-represented in cases of zinc-responsive dermatosis.

Sterile pustular erythroderma of miniature schnauzers: a retrospective study of seven cases. Lam ATH, *et al*.
Sterile pustular erythroderma of miniature schnauzers is a rare and often fatal condition presenting with malaise and often fever with erythema, pustules or epidermal collarettes, and/or wheals. Most cases have been associated with bathing. This retrospective study compared clinical and pathologic features of this condition in dogs that survived with those that did not. Six cases were diagnosed via histopathologic findings from IDEXX Laboratories and one from UC Davis. All affected dogs were female miniature schnauzers, from three to 11 years of age. All dogs initially presented with truncal erythema progressing to generalized wheals or papules/pustules with only one dog having a history of bathing. Systemic signs were seen in five dogs and included lethargy (4/5), vomiting (2/5) and fever (2/5). One dog was an uncontrolled diabetic. Lab work was performed were in six dogs with four dogs having a moderate leukocytosis and two having a non-regenerative anemia and five dogs having elevated ALP and ALT levels. Histology was similar in all cases with intraepidermal, panfollicular neutrophilic and eosinophilic pustulation, and adnexal and follicular infiltration. Four dogs were treated with corticosteroids and intravenous fluids, five with systemic antibiotics. Four dogs survived and two dogs died from respiratory arrest, one with concurrent DIC. There was no relationship between patient history, clinical or diagnostic findings or how they were managed and their outcomes. This is a rare disease that hopefully clinicians may have on their list of differentials if they see an acutely sick schnauzer with skin lesions.

References

1. All abstracts were from The *Proceedings of The North American Veterinary Dermatology Forum* 2015.

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