CVMA-SBCV Spring Session: Dermatology

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Conflicts of interest statement: In the last 5 years, I have received honoraria, consulting fees, and/or have collaborated with Royal Canin, Purina, Zoetis, and Novartis/Elanco. I am also the (volunteer) president of the Canadian Academy of Veterinary Dermatology.

About today's lectures: My presentations will include some of the resources available on the website of the Canadian Academy of Veterinary Dermatology: www.cavd.ca. Some are open-access features while others are available to members only. Membership costs \$25 for the remainder of 2019 and is open to all veterinarians and veterinary technicians in Canada. I invite you to become a member of the CAVD by visiting our website: www.cavd.ca Membership benefits include:

- The Bulletin mailed twice per year (plus online access to past issues)
- E-newsletters several times per year, keeping you up to date with the latest news, developments, and products used in veterinary dermatology
- Access to in-clinic tools for veterinarians and veterinary technicians, including:
 - o the Dog and Cat Itch Scale for scoring pruritus
 - the Cytology Scale for skin and ears
 - o a canine and feline Elimination Diet Trial client handouts
 - updated lists of foods for dogs and for cats available in Canada for elimination diet trials
 - o updated lists of topical therapies available in Canada and their indications
 - o detailed article on Interpreting Small Animal Culture and Susceptibility Reports
 - links to other client handouts (MRSP, MRSA, etc.), Compendium of Veterinary Products, the Health Canada Drug Product database and many others
- Invitations to webinars and access to archived events
- The "Head Scratcher" question bank to hone your dermatology knowledge
- Staying updated about upcoming CE events across Canada
- Discounted registration to the CAVD Dermatology Forum

The skin microbiome & 21st century pyoderma

This lecture presents the approach to patients with pyoderma and how it has changed in the last two decades since the emergence of methicillin-resistant *Staphylococcus pseudintermedius*. I will also describe the skin microbiome, which is an increasing area of interest in human and veterinary medicine.

Microbiome: The composition of all microbial genes in a community.

- your cells carry 20-25,000 genes
- your microbes carry 500 times more

Microbiota: An aggregate of microorganisms in a community, including bacteria, archaea, protists, fungi and viruses.

- you have ± 30 trillion human cells and ± 39 trillion microbial cells
- most are not pathogenic
- microbiota are essential to life

Past: culture methods (1-9% of totality)

Current: sequencing methods

Skin microbiome

- in humans, skin microbial communities tend to:
 - vary between body regions
 - be very diverse
 - be shared easily
- altered in disease states in humans and dogs
 - o has been demonstrated in atopic dermatitis: flares are associated with loss of microbial diversity

Staphylococci

part of normal cutaneous microbiota of mammals

- several species can be commensals and opportunistic pathogens
- pyoderma typically caused by the same strain found at carriage sites
- in dogs:
 - S. pseudintermedius
 - S. schleiferi (coag. variable)
 - S. aureus
- other coagulase-negative Staph (CoNS) can be highly resistant but usually not clinically relevant
 - important for your lab to ID the CoNS to species in case it is S. schleiferi

Methicillin-resistant (MR) staphylococci

- inherent resistance to all beta lactams
- commonly resistant to other antibiotics (MDR = multidrug resistant)
- MRSP has a concerning predilection to rapidly acquire further resistance
- skin infections are very common, so MRSP frequently isolated from dogs
- potential for zoonotic transmission

Spread of staphylococcal resistance

- MR and MDR staphylococci are very common in both carriers and animals with infections
- MRSP can be considered endemic rather than an emerging issue
- dominant strains can proliferate and outcompete other strains
 - · e.g. antibiotic drug obliterates colonizing strains and allows recolonization by a resistant strain
 - this is likely mechanism by which MRS spread across animal populations
 - antibiotic therapy a risk factor

Dermatology and antibiotic use

- Skin problems are the #1 cause of antibiotic use in dogs
- 23-30% of all antimicrobials prescribed

But...

- MRSP is not more pathogenic than MSSP (just harder to treat systemically)
- pyoderma presents a key opportunity for antimicrobial stewardship
- good evidence that systemic antibiotics are not needed in most cases
- pyoderma is a SECONDARY condition

Pyoderma: general approach

- 1) confirm diagnosis
 - cytology
- 2) +/- culture:
 - o <50% improvement after 2 weeks
 - o lesions after 4 weeks
 - o new lesions
 - o deep/severe pyoderma
 - o phagocytosed rods
 - suggestive history
 - o possible zoonosis
- 3) implement topical therapy
 - topical therapy with chlorhexidine products appears to be equally effective to systemic antibiotics, even when infection is caused by MRSP
 - o can consider dilute bleach soaks for patients not responding to chlorhexidine (e.g. 1:30 dilution of household bleach in water with 1/2 tsp baking soda per litre. Make fresh daily. Usually applied after shampooing and allowed to sit on the skin for 10 minues before rinsing and conditioning. Irritating to some dogs and can discolor fur and fabrics). Hopefully bleach based shampoos will come to Canada.
 - o accelerated hydrogen peroxide products such as Pure Oxygen Ultra usefulness?
 - a CAVD-sponsored study is currently ongoing investigating the use of medical grade honey for fold pyoderma
 - tips for shampooing
 - volume of shampoo to use: 1 guarter sized amount per 2 palms surface area
 - 10 minutes contact time ideal for medicated shampoos
 - 2 times weekly to start + daily chlorhexidine spray

- massage, starting with problem areas
- use cool/lukewarm water
- avoid standing water
- make it a positive experience for the dog

• 4) +/- systemic antibiotics

- Before reaching for these always consider: Do you need a deep treatment for a superficial problem?
- Indications
 - deep/severe pyoderma
 - poor response to topical therapy
 - unable to use topical therapy (e.g. bathing cats)
- o base on culture whenever possible
- o always combine with topical therapy
- o most commonly use beta-lactam drugs if isolates are not MR
- avoid empirical fluoroquinolones
- o if MR, select antibiotic carefully based on culture
 - clindamycin check erythromycin
 - potentiated sulfas
 - doxycycline or minocycline evaluate culture results separately
 - veterinary fluoroquinolone
 - What works today might not work the next time!
 - The "scary trio" if extensive resistance leaving only chloramphenicol, amikacin, and rifampin as choices
 - Think again do you really need systemic therapy given the potential for severe sideeffects? ALWAYS combine with topical therapy. Warn owners.
 - Chloramphenicol: TID therapy, GI s/e, hind limb weakness, concern for human contact
 - Amikacin: SC q24hr (stings), renal tubular necrosis, check UA for casts and protein twice weekly
 - Rifampin: good tissue penetration but resistance develops quickly, hepatotoxicity, check chemistries q 7 days
- Duration of therapy
 - usually 3 weeks for superficial pyoderma or 1 week past resolution of lesions
 - longer for deep pyoderma
 - but not based on any evidence!
 - "the idea that stopping antibiotic treatment early encourages antibiotic resistance is not supported by evidence, while taking antibiotics for longer than necessary increases the risk of resistance" Llewelyn M et al. BMJ 2017;358
 - studies are needed for pyoderma
 - consider shorter therapy if using a drug such as amikacin or rifampin
- 5) consider primary cause
 - o In 30 dogs with recurrent pyoderma (Bensignor E, Germain PA. Vet Derm 2004; 15(s1):42)
 - **18 (60%) atopic dermatitis, 2 (7%) food allergy, 2 (7%) flea allergy,** 2 (7%) hypothyroidism, 1 each hyperestrogenism, demodicosis, zinc-responsive, 2 (7%) no cause identified
 - Work-up and treatment depend on: signalment, age of onset, degree of pruritus especially when infection resolved (avoid or discontinue antipruritic therapy to assess pruritus when infection resolves), other clinical signs
 - Allergic dermatitis is most common primary cause:
 - elimination diet trial
 - treatment for allergy (Atopica®, corticosteroids, Apoquel®, Cytopoint®)
 - allergy testing and immunotherapy
 - allergen avoidance
 - skin barrier-enhancement
 - Other treatments
 - Staphage lysate® vaccine especially for idiopathic recurrent pyoderma
 - Undergoing investigation: S. pseudintermedius vaccine
 - future directions: interferons, antimicrobial peptides, bacteriophages, etc.?
- 6) client communications
 - o more on this later

- see https://www.cavd.ca/resources/in-clinic-tools for links to client handouts on MRSP and MRSA from the Worms and Germs Blog (which are balanced and practical, rather than panic-inducing)
- 7) schedule recheck
 - 2-4 weeks appropriate in most cases (2 if using systemic antimicrobials)

Major changes in my approach to pyoderma in the last 20 years

- I wear gloves to examine dermatology patients, wash my hands a lot, and wear a labcoat again (which I change if suspect resistant pyoderma)
- I'm a lot more concerned about resistance
- I'm more mindful of when and how I prescribe systemic antibiotics
- I rely a lot more on topical therapy alone
- I'm more patient
- I consider inter-animal transmission more than before, and the (low) potential for zoonotic transmission
- exam room cleaning includes floors between dermatology patients

The good news/silver lining to the emergence of MRSP: Pyoderma presents one of the key opportunities for antimicrobial stewardship in small animal practice!

Additional Resources for pyoderma/MRS: found at: https://www.cavd.ca/resources/in-clinic-tools:

- WAVD Clinical Consensus Guidelines for Methicillin-Resistant Staphylococci a very thorough open access article about MRS
- o lists of medicated veterinary shampoos, sprays, and wipes (member access) a regularly updated Canadian resource
- Interpreting Small Animal Culture and Susceptibility Reports (member access) a clinical pharmacologist's guide to interpretation
- Precautions when Handling Animals with Antimicrobial Resistant Infections (member access) a nice reminder of what we can do to improved patient and staff safety with AMRs
- o The Winter 2019 issue of the CAVD Bulletin entirely focused on Pyoderma and Methicillin-Resistant Staphylococci (https://www.cavd.ca/publications/the-bulletin, member access)

New drugs for old diseases & New uses for old drugs

This lecture reviews some of the newer therapies available in small animal dermatology and reviews uses of some older drugs as well.

Extra Label Drug Use

- The CVMA holds that Extra Label Drug Use (ELDU) is an important and legal strategy in the effective and efficient treatment of animals by licensed veterinarians when an approved veterinary product is not available or suitable
- The CVMA supports ELDU when the prescribing veterinarian has evidence to support efficacy, dosage regimen, or
 indication for the disease and species being treated, and the circumstances of the use are in accordance with the
 provincial veterinary regulatory authority's policy or guidelines
- www.canadianveterinarians.net/documents/extra-label-drug-use-eldu

Please see my review articles of new drugs:

- Gortel K. Developments in Small Animal Dermatology. Can Vet J 2018 Jan, 59(1), 85.
 - o https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5731399/
- Gortel K. An embarrassment of riches: An update on the symptomatic treatment of canine atopic dermatitis. 2018 Sept, 59(9), 1013.
 - o https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6091120/

Articles in the CVJ Dermatology Colum, a regular feature since 2018, are all archived at the CAVD website: https://www.cavd.ca/publications/canadian-veterinary-journal

Apoquel™ (Oclacitinib)

• Janus Kinase (JAK) inhibitor – inhibits the function of various cytokines

- "for the control of pruritus associated with allergic dermatitis and the control of atopic dermatitis in dogs at least 12 months of age"
- twice daily for up to 14 days, then once daily
- for short or long term use
- what about cats?
 - o not very effective at canine doses (5/12 cats responded in one study)
 - much shorter half life
 - Oclacitinib at 0.7-1.2 mg/kg BID for 28 days vs. methylprednisolone 0.5-1.0 mg/kg BID. (Noli et al. Vet Derm 2019; 30:110.)
 - not statistically different but methylprednisolone performed better
 - 4/14 oclacitinib cats tested had mild increase in renal values
 - "Oclacitinib was well tolerated by cats at 1 mg/kg and 2 mg/kg BID for 28 days and appeared to be a safe medication for this species" (Lopes NL. BMC Veterinary Research 2019; 15:137)
- what about other conditions?
 - o 1 case of good response with subepidermal blistering disease in a dog
 - o Ischemic dermatopathy in 4 young dogs (Levy BJ et al Vet Derm 2019; 30: 201):
 - severe and very refractory to therapy with GC and cyclosporine
 - rapid response allowing steroid discontinuation
- dosing
 - o aim for 0.4-0.6 mg/kg once daily long term
 - for dogs 20.0 26.9 kg, can combine half tablets to reduce cost of therapy (as per Zoetis US website)
 - o avoid long term BID use including splitting the daily dose
 - one unpublished study (abstract by Denti D et al, Vet Dermatol 2018; 29, 360) showed statistically significant reduction of neutrophils, eosinophils, and monocytes at mean dose 0.5 mg/kg BID

Cytopoint™

- Canine Atopic Dermatitis Immunotherapeutic aka. lokivetmab
- an injectable caninized monoclonal antibody that targets IL-31, a key cytokine involved in pruritus
- Cytopoint™ "aids in the reduction of clinical signs associated with atopic dermatitis in dogs"
 - US label has been expanded to include "allergic dermatitis"
- Targeted and unique
- Rapid onset of efficacy, similar to prednisolone and Apoquel™
- Long lasting (4-8 weeks) mean 37 days in one study
- Safe
 - o No immune suppression
 - o No contraindications for concurrent therapy (e.g. Apoquel™)
 - No contraindications for concurrent diseases
 - Use in dogs without age limitations or size restrictions
- field study with 135 dogs (Souza CP et al, Vet Dermatol 2018, 29: 489)
 - o overall 88% of dogs had reduced pruritus
 - o ≥50% reduction in pruritus in 77% of dogs
 - o can work well even when Apoquel™ has not
 - In 21 dogs with a partial or no response to twice daily Apoquel™, 15 (71%) responded to Cytopoint®)
 - o but dogs not responding to Apoquel are less likely to respond to Cytopoint®
 - o note: some Cytopoint® non-responders can do well with Apoquel™
- North American label dose: minimum 2.0 mg/kg q 4-8 weeks differs from European label dose: minimum 1.0 mg/kg monthly (European study with 274 dogs: Moyaert H et al. Vet Derm 2017; 28: 593.
- NOT for use in cats
- Consider Cytopoint®:
 - o concurrent disease such as systemic infection, neoplasia, demodicosis
 - o patients < 1 year of age
 - o poor client or patient compliance
 - very small dogs
 - o poor efficacy of other treatments, e.g. Apoquel™ not lasting 24 hr
 - side-effects from other treatments
 - as combination therapy
 - client preference

Isoxazolines

- 5 oral formulations for dogs
 - Simparica (sarolaner), Nexgard + Nexgard Spectra(afoxolaner), Bravecto (Fluralaner), Credelio (Lotilaner)
- 2 topical formulation for cats
 - Bravecto (Fluralaner), Revolution Plus (sarolaner)
- effective for a wide variety of ectoparasites including Demodex canis (they seem to work for everything!)
 - reconsider need for systemic antibiotics in patients with demodicosis
 - treatment trials?

Corticosteroids

These days, is it still appropriate to use corticosteroids to manage atopic dermatitis in dogs? Yes – they are old drugs but still have advantages:

- superior anti-inflammatory
- most effective treatment for otitis
- rapidly effective
- may work when other treatments fail
- short term use usually ok
- avoid long term use
- also consider topical steroids, e.g.:
 - Hydrocortisone aceponate spray (Cortavance) labeled for 7 days = flares
 - NOT the same as hydrocortisone (moderate skin potency)
 - minimal systemic effects (vs. betamethasone in Topagen)
 - if using long term, use only intermittently (ELDU)
 - e.g. "weekend therapy" atopic dogs relapsed at 115 days vs. 33 days with placebo
 - also shown to be effective in cats (ELDU)
 - monitor for skin atrophy especially thin-skinned areas with ANY topical steroid!
 - o Ears: Burow's HC solution (I use Chiron Pharmacy) daily therapy possible; one abstract using Cortavance

Cyclosporine (Atopica)

Many ELDU uses!

- Perianal fistulae, Granulomatous sebaceous adenitis, Idiopathic facial dermatitis of the Persian cat, Erythema multiforme, Sterile granuloma / pyogranuloma syndrome, Sterile nodular panniculitis, Pemphigus foliaceus, pemphigus erythematosus, Idiopathic German shepherd deep pyoderma, Proliferative otitis, Feline eosinophilic granuloma complex, Ulcerative dermatosis of the philtrum, Metatarsal fistulas of German Shepherds, Sterile nodular panniculitis, Reactive histiocytosis, Uveodermatologic syndrome (VKH-like syndrome), Feline plasma cell pododermatitis, Cutaneous lupus erythematosus
- often where you would reach for steroids, or as steroid sparing agents

Sublingual Immunotherapy

- a unique way of administering allergen-specific immunotherapy
- not just for convenience; oral cavity is a special immunological site
- efficacy not significantly different from SCIT
- easier for some clients and pets (but not all)

Pentoxifylline

- methylxanthine derivative with many immunologic and rheostatic effects, used in dogs for various indications:
 - atopic dermatitis
 - contact dermatitis
 - vascular diseases

Long acting otic preparations

- Osurnia
 - o gel florfenicol, terbinafine, betamethasone acetate
 - o applied 2x, 1 week apart
- Claro
 - o liquid florfenicol, terbinafine, mometasone furoate
 - o applied 1x
- I recommend not using these products in cats ELDU due to potential for ototoxicity

Additional Resources: found at: https://www.cavd.ca/resources/in-clinic-tools:

List of otic medications available in Canada (member access), including therapeutic choices based on cytology, and recommended volumes of administration

Dermatology Bootcamp: 1) Client communications

Client communications:

- essential for the effective delivery of veterinary care
- dermatology = often complex diagnostic + therapeutic recommendations
- effective communication = facilitates connection between client and veterinarian

History Collection

start with "open-ended inquiry" try not to interrupt move on to closed ended questions as needed

Reflective listening

- nonverbal communication as client is speaking
- paraphrase:
 - "So I understand that Barley..."
 - "... Did I miss or misinterpret anything?"
- allows client to make corrections if needed
- creates a sense of relationship-based communication

Making a clear recommendation

- how well do your clients adhere to our recommendations? estimates vary but veterinarians seem to overestimate adherence
- clients who receive a clear recommendation 7x more likely to follow it
- Some of my tips...
 - use visual aids such as pictures, diagrams, and charts
 - "chalk and talk" use a pen and paper to help explain conditions and treatments
 - lay out expectations e.g. no sure, but effective management possible
 - take care in presenting information on "methicillin-resistant Staph" as it can cause owners extreme worry.
 - Don't call methicilin-resistant S. pseudintermedius "MRSA". I prefer to tell owners that the
 culture shows a dog Staph bacterium called Staph pseudintermedius which is resistant to a
 number of antibiotics.
 - use a balanced handout such as the one from Worms and Germs Blog (can access at https://www.cavd.ca/resources/in-clinic-tools open access resources)
 - I discuss the risk of zoonotic transmission but emphasize that the risk is low
 - provide written instructions
 - specific treatments, when to recheck, general instructions (templates), and additional handouts as needed
 - use an itch scale and calendar pages for tracking treatments and progress (https://www.cavd.ca/resources/in-clinic-tools open access resources)
 - schedule recheck/follow-up and explain why
 - don't try do to this in 15 minutes! recognize the value of dermatology patients in your practice they are long term patients
 - listen and learn from your clients ©

Additional Resources:

Royal Canin has developed a series of excellent E-learning modules called "Conquering Dermatology Conversations" which pertain to client communications. They are short, mobile-friendly, and suitable to all members of the veterinary team. Access them at http://www.royalcanin.ca/ and log in under "For Veterinarians".

Dermatology Bootcamp: 2) Microscopy

A cytology scale can be very useful for quantifying the numbers of bacteria, inflammatory cells, and Malassezia on skin and ear cytology slides. You can find one at https://www.cavd.ca/resources/in-clinic-tools open access resources

Please also see the cytology handout provided separately.

Tips:

- using the condenser your microscope:
 - raise your condenser and open the iris (maximize light) for cytology
 - lower your condenser for skin scrapings (to increase contrast and make parasites more visible)
- coverslips
 - the high dry (400x) objective is intended for use with a coverslip! Images will be blurry without a coverslip, it does not mean the lens is dirty or has been dragged through immersion oil ©
 - coverslips are very helpful for examining skin scrapings by making scraped materials into a tidy square and relatively thin preparation, rather than a widespread mess of peaks and valleys. They also help to ensure you examine all collected material in a skin scraping.
- taking photos of microscopy findings
 - unless you have a specialized image capture system, an easy way is to take photos using your smartphone stabilized by a cardboard roll placed over the eyepiece (without the roll, tiny movements of your hand make the image disappear). You have to cut the roll to the appropriate length which takes some time, so once you have it, hang on to it.

Dermatology Bootcamp: 3) Literature updates

No notes for this presentation, just a quick circuit of studies I have found interesting recently.

Thank you for attending!