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ABOUT THE SPEAKERS

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CYTOLOGY AND CULTURES: SUCCESSFUL TIPS AND TECHNIQUES TO IMPLEMENT TOMORROW

James O. Noxon, DVM, DACVIM (SAIM)

Cytology is defined as the collection of cellular material and fluid for microscopic examination. Skin is ideal for this useful diagnostic procedure because it is an external organ. Thus, the lesions being evaluated are readily accessible for the diagnostic procedure. It is a great waste NOT to perform cytology in dermatologic cases. In fact, cytology is indicated in almost all patients presenting with skin disease.

Cytology provides the veterinarian with useful information about the etiology, pathogenesis, and severity of skin diseases. Cytologic techniques are especially useful as monitoring tools in dermatology cases; for example, to monitor the presence of infectious agents on the skin or ears following therapy. Lastly, cytology is a cost-effective diagnostic procedure. It generates income for a veterinary practice while providing essential information for managing patients.

There are three important aspects of cytologic tests:

- Selection of the proper lesions or locations from which to collect samples.
- Proper collection of materials and slide preparation.
- Interpretation of the findings.

SELECTION OF LESIONS

Cytology is indicated in most dermatology cases. It is extremely helpful in determining the cause of papules, pustules, epidermal collarettes, nodules, tumors, draining tracts, ulcers, or plaques. Often, it is helpful to sample lesions in each different stage of development.

COLLECTION OF MATERIALS FOR EXAMINATION

For the most part, cytology is a highly cost-effective diagnostic procedure. Other than a quality microscope, the only supplies required are swabs, syringes, needles, glass slides, a small paintbrush (nylon or camel hair), and an appropriate stain. Several stains are available for cytology. Romanovsky stains, such as Wright’s stain, and Modified Wright’s stains like Diff-Quik, are easily and quickly used. They are excellent when permanent slides are desired. Supravital stains, such as New Methylene Blue, are also easy to use and rapid. Each clinician should
choose a stain with which he/she is comfortable and become accustomed to its staining qualities.

Several techniques can be used to obtain samples:

- Fine-needle aspiration.
- Impression smears made with microscope slides pressed firmly onto the surface of cutaneous lesions, from under crusts and from cut surfaces of lesions (eg, tumors) removed from the skin.
- Impression smears made with acetate tape or adhesive microscope slides pressed firmly onto the skin.
- Scrapings of tumors or nodules.
- Lancing pustules or papules to remove contents for examination (Figures 1 and 2).
- The use of cotton-tipped applicator swabs to “roll” in difficult-to-reach areas (eg, facial folds).
- When the claw is affected, by scraping material from the claw with a scalpel blade or edge of a microscope slide.

Each technique has advantages and is best suited for specific lesions.

One common method of collecting a sample is to select an epidermal collarette and gently roll back the crust on the edge with an injection needle or the edge of a glass microscope slide (Figure 3). This technique often reveals a subtle area of moisture or seropurulent material that can be collected for cytology or culture. A direct impression can be made with a microscope slide, or an impression can be carefully made with a sterile swab for culture.

**DISTRIBUTION OF MATERIAL ON A SLIDE**

Slide preparation is an important step in cytology. It is much easier and more productive to examine a well-prepared slide. Samples can be distributed on a slide by “squash” preparations, nontraumatic imprints, or brush cytology.

- In the “squash” technique, the sample is placed on the slide, and then another slide is placed over the slide containing the sample (Figure 4). No pressure should be placed on the sample material. The top slide is

![Figure 1. Use of a sterile needle to open a pustule and collect material for cytology or culture.](image1)

![Figure 2. After material is collected, it can be placed directly onto a slide for cytology or onto a sterile swab for culture.](image2)

![Figure 3. Epidermal collarette. After the hair is carefully removed to avoid contamination, the crust around the edge can be rolled back with a sterile needle for sampling.](image3)
then gently pulled away from the slide containing the sample, leaving the specimen distributed across the slide (Figure 5).

- Alternatively, after the sample is collected by an imprint or by aspiration, a camel hair or nylon paintbrush can be used to distribute the sample on the slide (eg, painting the sample). When performed properly, this technique gives single cell layer distribution on the slide, with minimal trauma to the sample (Figure 6). The brush is rinsed well with tap water before and after each use to prevent contamination.

- When a cotton-tipped applicator is used to collect material, the swab should be “rolled” onto the glass slide, not rubbed back and forth on the slide. Rolling minimizes the cellular disruption that leads to “nuclear streaming,” which appears as long filamentous strands of nuclear material on a slide. This material is distracting and often mimics infectious materials.

Slides should then be fixed and stained. The method used to fix the slide varies with the sample collected. Although controversial, heat fixing may help some material, such as greasy or waxy exudate, adhere to the slide. Heat fixing is a gentle warming of the slide. Care should be taken not to overheat the slide, which will damage or destroy some infectious agents and render the sample less useful. One slide should be left unstained in case a special stain is needed. As mentioned previously, there are multiple options for staining cytologic specimens. Most clinicians prefer a Romanovsky-type stain (Wright’s stain, Giemsa stain, or Modified Wright-Giemsa [Diff-Quik] stain).1-3

**SLIDE EXAMINATION**

The entire slide should first be examined under low (scanning) power. On most microscopes the lowest power is 40× (a 4-power objective); however, lower power objectives (eg, 2×) are available. The scan is performed to evaluate the staining of the slide, to identify areas that should be examined more closely, and to identify large structures (eg, foreign bodies, hyphae, and Demodex species mites) that may be missed under higher power. After the scan is completed, the slide should be examined using low power (10× objective = 100×) and oil immersion (50× to 100× = 500× to 1000×) objectives. See “Tips” box on page 8.
TIPS FOR MICROSCOPIC EXAMINATION

Tip 1: Always keep one hand on the fine-focus knob while scanning a slide. You should be slowly moving that knob back and forth, adjusting the focal plane to enable you to see materials at different depths of the slide. This is especially critical with cutaneous impressions and slides where the material is somewhat thick.

Tip 2: Most microscopes have a “high dry” objective, usually a 400 objective giving a total magnification of 400x. These objectives are designed to work best when the slide has a cover slip. Otherwise the image is slightly blurred. So, place a drop of immersion oil on the sample, and then add a cover slip, if you use this objective. Author’s Note: You will be impressed by the difference!

Tip 3: Increase refractivity to highlight parasites, foreign bodies, or (eosinophilic) granules by either (1) lowering the condenser stage or (2) closing the aperture diaphragm. Either of these steps increases “glare” and allows light to bounce off of the structures, making them easier to see. Author’s Note: Really!

INTERPRETATION OF CYTOLOGY

When examining any cytologic preparation, the viewer is determining:

- If inflammation is present and, if so, what cell types are involved.
- If parasites or microorganisms are present and, if so, what types and relative numbers are present.
- What cells are present and whether they exhibit normal characteristics of cells found in the lesion sampled (noting any cellular atypia, clumping of cells, characteristics of neoplasia, etc).

The microscopic findings on the slide are always interpreted in light of the clinical findings.

THE MICROSCOPE

Microscopes are indispensable instruments for a veterinary practice. When purchasing a microscope, the veterinarian should consider buying one that is double-headed, which enables two viewers to see the images at one time. This dual function is very helpful for quality control—an absolutely necessary aspect for the veterinarian, other veterinarians in the practice, and the veterinary technicians. A camera that allows viewing on a monitor is also useful, but the resolution is not as high-quality as is seen when looking directly through the scope. The monitor system does, however, allow for excellent client education.

The author frequently escorts clients into his clinic's lab to view parasites, bacteria, neoplastic cells, yeast, and other obvious microscopic items of interest (a simple, effective educational technique). Client compliance—and willingness to proceed with other tests or treatment—tends to increase dramatically after clients have “seen” what is going on with their pets.

General Rules in Microscopy

- Keep the scope clean. Scopes should be thoroughly cleaned once daily by a veterinary technician. In addition, it is helpful to have the scope professionally cleaned and lubricated 1-2 times yearly. Professional cleaning makes a huge difference in the functionality of the instrument.
- Keep the scope covered when not in use. All hospitals inevitably tend to be dusty and have hair floating in the environment, which can damage the scope.
- Use a different microscope for fecal examinations. Fecal solutions (sugars, salt solutions) are quite caustic if they come in contact with the microscope lens or are “spilled” onto the slide platform.
- Adjust the scope for Kohler illumination (at least once daily; see next section). Doing this helps to “focus” the scope for use.

Tuning the Microscope for Maximum Clarity (Kohler illumination)

- Tune the microscope using the 10 power objective.
Focus on a slide (cytology or histopathology) to give a baseline image.

Lower the condenser/stage to the bottom.

Close the aperture (field diaphragm) on the base of the microscope and the condenser aperture. A small circle of light should appear in the visual field.

Next raise the condenser stage (while watching through the scope) until the circle of light is at its smallest and has sharp borders. This occurs when the condenser is near the top.

Center the circle of light using the set screws on the condenser stage (usually two, one at the 4 o’clock and one at the 8 o’clock positions).

Open the aperture ring (field diaphragm) on the base of the microscope until the light just fills the visual field.

Adjust the condenser aperture ring (on the condenser) according to the objective being used. For lower objectives (2-power and 4-power), the ring should be set at approximately the 0.2 position. For higher objectives, the ring is set higher (0.4 for the 10-power; 0.6 for the 40-power; 0.6-0.8 for the oil immersion 100-power objective).

To increase contrast (eg, to help visualize eosinophil granules or parasites), close the condenser aperture diaphragm or lower the condenser.

Avoiding Sample Contamination

The key to sampling is to use sterile technique to the extent possible. Contamination from skin surrounding a lesion or from hair invalidates the desired information. Hair should be carefully clipped from around the lesion to be sampled to facilitate collection, without brushing the swab on the hair. If an intact lesion is selected for sampling, it may be gently wiped with alcohol to remove debris; however, if there is any doubt about the integrity of the lesion, it is best to sample without any decontamination. The lesion should not be scrubbed, with one exception stated in the following text. Adjacent skin should also be avoided during the sampling procedure.

The material can first be collected on a sterile needle and then transferred onto a sterile swab for culture, or the swab can be used to collect material directly from the lesion, if it can be done without contaminating the swab. The sample should be carefully placed into a sterile culture container or Petri dish, and the container should be sealed to prevent contamination during shipping (contact the laboratory for its recommended best practices when shipping samples).

Many skin problems need a culture but may not have an ideal lesion for sampling. These include such lesions as those associated with acral lick dermatitis (eg, lick granuloma); deep skin infections, with or without draining tracts; or granulomas. In these examples, a skin sample can be taken steriley with a biopsy punch or an excisional biopsy and the sample submitted to a laboratory, where it will be macerated, minced, and cultured. Ideally, a very small amount of the surface should be removed with a sterile blade before submitting the remainder of the sample (in most cases dermis and subcutis) for maceration and culture. This may not be possible in some cases, however.

Technique for Sterile Sampling

The area to be sampled is gently scrubbed with an antiseptic solution (Figure 7).

The area that has been scrubbed is then rinsed with sterile saline (Figure 8). It is important not to contaminate the site that has just been scrubbed. The saline rinse should start at the center of the scrubbed
area and then move toward the periphery. It is important to avoid allowing material from unscrubbed areas to flow back over the area prepared for biopsy. The saline is allowed to dry before proceeding.

- A sterile biopsy punch is used to collect a tissue sample (Figure 9).

- The sample (biopsy punch) is handled carefully (ie, steriley) to avoid contamination.

- The sample is placed into a sterile container for transport to the laboratory of choice. It is always best to collaborate directly with the laboratory regarding the best practices for successfully transporting the sample.

Many of the lesions to be sampled in this manner have an open area. The sample should be taken in an adjacent area, not directly through the open lesion, if possible. Deeper tissues involved can be palpated. The biopsy site is selected to sample an affected area around the draining or open lesion.

**SUMMARY**

Cytology is one of the most useful diagnostic tools in dermatology. Virtually every dermatology case presents with multiple opportunities for cytologic evaluation, and the information that cytology provides is often the key diagnostic information that marks the therapeutic path for the patient. Cultures are important diagnostic tools also. The usefulness of the culture is dependent on proper lesion selection and technique.

**REFERENCES**


Additional references are available from the author.
FROM NOSE TO TAIL: WORKING UP THE ITCHY DOG

Valerie A. Fadok, DVM, PhD, DACVD

Itch is one of the most frustrating clinical signs pet patients experience. The constant scratching, licking, chewing, rubbing, and slurping drives clients wild! There are several ways to approach itch. Clearly, the major priority is to stop it, but finding the cause is critical. It is possible to control itch in the short term pharmacologically, but in the long term it is essential to treat the underlying disease.

In her symposium presentation, Dr. Fadok takes the diagnostic approach to itch, using the affected region of the body to give clues to the underlying cause. As the process evolves, a great deal of overlap occurs; but this manner of pattern analysis can be quite helpful. The criterion in the described approach is where the disease starts, as many diseases causing itch can become generalized over time.

First, a few new, exciting facts have recently been learned about itch. For years, researchers studying itch have thought that the condition was a poor cousin of pain, sharing nerve pathways. It was never clear why some stimuli cause itch and others pain. Today it is understood that itch has its own receptors and its own pathways. This knowledge is important because it will lead to highly targeted itch control that will not impair reactivity to pain. The veterinary community—and the patients within it—can look forward to much relief.
## REGIONAL APPROACH TO CAUSES OF CANINE ITCH

### FACE AND HEAD (FIGURES 1–3)

<table>
<thead>
<tr>
<th>Region Affected</th>
<th>Differential Diagnosis</th>
<th>Clinical Signs</th>
<th>Diagnostic Tests</th>
</tr>
</thead>
</table>
| Periocular          | • Demodicosis (often pruritus associated with bacterial infection, but in some dogs pruritus is seen in the absence of infection)  
                      • Atopic dermatitis  
                      • Food allergy  
                      • Bacterial infection  
                      • *Malassezia* species  
                      • Dermatophytosis            | • Alopecia  
                      • +/- Crusts  
                      • +/- Erythema  
                      • +/- Lichenification  
                      • +/- Hyperpigmentaion      | • Skin scrapings or hair plucks  
                      • Cytology  
                      • +/- Fungal culture  
                      • Bacterial culture  
                      • Allergy testing*  
                      • Diet trial |
| Perioral             | • Demodicosis  
                      • Atopic dermatitis  
                      • *Malassezia* species  
                      • Mucocutaneous pyoderma | • Alopecia  
                      • Erythema  
                      • Erosions  
                      • Ulcers  
                      • Fissures                  | • Skin scrapes or hair plucks  
                      • Cytologies  
                      • Biopsies**  
                      • Allergy workup          |
| Dorsum of muzzle    | • Demodicosis  
                      • Dermatophytosis  
                      • Eosinophilic furunculosis  
                      • Bacterial infection  
                      • Pemphigus foliaceus     | • Alopecia  
                      • Erythema  
                      • Crusting  
                      • Papular/nodular eruptions | • Skin scrapings  
                      • Cytologies  
                      • Fungal culture  
                      • Biopsy          |

* Allergy testing is done specifically to select allergens for immunotherapy and is not a diagnostic test per se.

** Biopsies of the perioral area are indicated for blistering or erosive disease, after infection is ruled out, to determine if an autoimmune disease is present.

---

**Figure 1.** Dog with sarcoptic mange affecting the face and ear margins. A positive pinnal-pedal reflex was present.

**Figure 2.** Dermatophytosis as the cause of facial itch and crusting in a Maltese crossbreed.

**Figure 3.** Facial demodicosis associated with pruritus.
# EARS (FIGURES 4 AND 5)

<table>
<thead>
<tr>
<th>Region Affected</th>
<th>Differential Diagnosis</th>
<th>Clinical Signs</th>
<th>Diagnostic Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pinna</td>
<td>• Scabies • Yeast dermatitis • Bacterial dermatitis • Atopic dermatitis • Food allergy • Vasculitis/vasculopathy</td>
<td>• Crusting at the margins with scale • Erythema +/- papules • Pinnal-pedal reflex • Ulceration, notching, bleeding</td>
<td>• Scrapings; response to treatment • Cytology • Biopsy • Diet trial • Allergy testing</td>
</tr>
<tr>
<td>Canal</td>
<td>• Atopic dermatitis • Food allergy • <em>Malassezia</em> otitis externa • Staphylococcal otitis externa • Topical drug reaction • Demodectic otitis externa</td>
<td>• Erythema, edema • Brownish, waxy exudate • Yellow thick exudate</td>
<td>• Cytology • +/- Biopsy • +/- Culture</td>
</tr>
</tbody>
</table>

Figure 4. Ear-tip vasculitis associated with erythema and itch.

Figure 5. Pinnal and canal disease associated with *Malassezia* species.
### FEET (FIGURES 6 AND 7)

<table>
<thead>
<tr>
<th>Region Affected</th>
<th>Differential Diagnosis</th>
<th>Clinical Signs</th>
<th>Diagnostic Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorsal aspect of the feet</td>
<td>• Demodicosis • Scabies • Atopic dermatitis • Food allergy • Bacterial dermatitis • Dermatophytosis • “Interdigital cysts” (in the dorsal web)</td>
<td>• Alopecia • Erythema • +/- Lichenification • +/- Exudation</td>
<td>• Scrapings • Cytology • Biopsy • Diet trial or allergy testing as indicated • Response to parasiticide</td>
</tr>
<tr>
<td>Ventral aspect of the feet</td>
<td>• Demodicosis • Scabies • Atopic dermatitis • Food allergy • Contact dermatitis • <em>Malassezia</em> dermatitis • Bacterial dermatitis • Contact allergy</td>
<td>• Alopecia • Erythema • Lichenification • +/- Waxy exudate</td>
<td>• Scrapings • Cytology • +/- Biopsy • Allergy testing or diet trial</td>
</tr>
</tbody>
</table>

Figure 6. Demodicosis on the feet.

Figure 7. *Malassezia* pododermatitis associated with atopic dermatitis in a golden retriever.
### DORSUM / BACK (FIGURE 8)

<table>
<thead>
<tr>
<th>Region Affected</th>
<th>Differential Diagnosis</th>
<th>Clinical Signs</th>
<th>Diagnostic Tests</th>
</tr>
</thead>
</table>
| Anterior back*  | • Injection-site reaction  
• Topical flea medication reaction  
• Cheyletiellosis  
• Lice  
• Pemphigus foliaceus/erythema multiforme | • Alopecia  
• Erythema  
• Crusting  
• Erosions  
• Swelling | • Skin scrapings and cytologies to rule out mites, infection  
• Biopsy |
| Caudal back     | • Flea allergy dermatitis  
• Cheyletiellosis  
• Food allergy  
• Secondary bacterial and/or yeast infections | • Alopecia  
• Erythema  
• +/- Crusts  
• +/- Erosions | • Skin scrapings and cytologies to rule out mites and infection  
• Response to flea control  
• Diet trial |

*Not a commonly affected area.

---

**Figure 8.** Pemphigus foliaceus secondary to use of topical fipronil with amitraz.

---

### VENTRUM / CHEST AND BELLY (FIGURE 9)

<table>
<thead>
<tr>
<th>Region Affected</th>
<th>Differential Diagnosis</th>
<th>Clinical Signs</th>
<th>Diagnostic Tests</th>
</tr>
</thead>
</table>
| Anterior back*  | • Scabies  
• Demodicosis  
• Pyoderma  
• Malassezia dermatitis  
• Infected callus | • Alopecia  
• Erythema  
• Crusting  
• Swelling  
• Hyperkeratosis | • Skin scrapings  
• Cytologies  
• +/- Biopsies |
| Abdomen         | • Parasites (eg, scabies, demodicosis)  
• Atopic dermatitis  
• Food allergy  
• Bacterial infection  
• Yeast infection  
• Contact allergy | • Alopecia  
• Erythema  
• +/- Scale/crust  
• +/- Lichenification | • Skin scrapings and cytologies  
• Allergy testing  
• Diet trial  
• Response to scabies treatment |

**Figure 9.** Erythema and severe itch associated with scabies on the abdomen of a Saint Bernard with a poor response to oclacitinib (Apoquel – Zoetis).
TREATMENT BASED ON DIAGNOSIS

Scabies
- Selamectin (Revolution – Zoetis) every 2-4 weeks for three treatments (treat all in-contact dogs). Labeled for use every 30 days but has been safe when used off-label every 2 weeks.
- Imidacloprid + moxidectin (Advantage Multi – Bayer) every 2 weeks for three treatments (treat all in-contact dogs).
- For avermectin-resistant scabies: lime sulfur dips or fipronil spray weekly.

Demodicosis
- Oral ivermectin, 0.4-0.6 mg/kg/day
- Oral moxidectin, 0.4-0.6 mg/kg/day
- Weekly doramectin, 0.4-0.6 mg/kg subcutaneously
- Amitraz dips every 1 to 2 weeks
- Treat until achievement of two negative scrapings 1 month apart; watch for avermectin-sensitive breeds.

Demodicosis
- Oral ivermectin, 0.4-0.6 mg/kg/day
- Oral moxidectin, 0.4-0.6 mg/kg/day
- Weekly doramectin, 0.4-0.6 mg/kg subcutaneously
- Amitraz dips every 1 to 2 weeks
- Treat until achievement of two negative scrapings 1 month apart; watch for avermectin-sensitive breeds.

Staphylococcal Pyoderma
- Antibiotic therapy
  - Always consider efficacy, safety, and compliance when choosing antibiotics
  - If empirical, avoid tetracyclines, penicillins, fluoroquinolones
  - Cephalosporins often recommended as the treatment of choice: cefovecin (Convenia – Zoetis), cefpodoxime (Simplicef – Zoetis), cephalexin (Rilexine – Virbac Animal Health)
  - If poor response, culture and sensitivity test required, as methicillin-resistant staphylococcal infections are relatively common
- Bathing with chlorhexidine shampoo or accelerated hydrogen peroxide (Pure Oxygen – Ogena Solutions) critical to speed recovery and reduce the duration of antibiotic therapy

Malassezia Dermatitis
- Oral antifungal medication
  - Ketoconazole, fluconazole, itraconazole, 5 mg/kg/day
  - Terbinafine, 30-40 mg/kg/day
- Bathing with imidazole or 3% chlorhexidine shampoo
Dermatophytosis

- Systemic antifungal agent
  - Itraconazole, 5-10 mg/kg/day
  - Terbinafine, 30-40 mg/kg/day
- Topical therapy
  - Lime sulfur dips once to twice weekly
  - Bathing with miconazole (Malaseb – Bayer) or climbazole (Douxo Chlorhexidine + Climbazole + Phytosphingosine – Sogeval) three times a week
  - Accelerated hydrogen peroxide (Pure Oxygen)?

Eosinophilic Folliculitis and Furunculosis

- Glucocorticoids
  - Prednisone or prednisolone, 1 mg/kg/day
  - Methylprednisolone, 0.8-1 mg/kg/day

- Flea allergy dermatitis
  - Oral flea control preferred if dogs are bathed more than once weekly
    - Nitenpyram (Capstar – Novartis Animal health) trial: give every other day or three times a week for 1 month. If itch resolves, flea allergy confirmed
  - Topical flea control

Atopic Dermatitis

- Avoidance of what can be avoided (food triggers, fleas)
- Allergen-specific immunotherapy to change the immune response
  - Injection
  - Sublingual immunotherapy
- Infection control
  - Bathing
  - Antibiotics and antifungal medications, if needed
- Skin barrier repair
  - Premium diet
  - Oral fatty acids
  - Topical lipids
- Itch control
  - Glucocorticoids
    - Cyclosporine (Atopica – Novartis Animal Health)
    - Oclacitinib (Apoquel – Zoetis)
- Topical tacrolimus (0.1% Protopic – Astellas Pharma) applied once to twice daily

Food Allergy

- Diet trial based on previous diet history
- Challenges to identify the allergens
- Avoidance

Contact Allergy

- Avoidance
- Glucocorticoids
- Pentoxyfylline

Topical Drug Eruption

- Stop the drug
- Control infection, if present
- Glucocorticoids to reduce inflammation

Vasculitis/Vasculopathy

- Determined by severity
- Pentoxyfylline, 20-30 mg/kg every 12 hours
- Glucocorticoids for a rapid response
- Topical tacrolimus (0.1% Protopic – Astellas Pharma) applied once to twice daily

A REVIEW OF ANTI-ITCH TREATMENTS FOR DOGS

Short-term Control

Short-term itch control in dogs may be critical to ensure that clients stay on a long-term plan. With few exceptions, most skin diseases are chronic, requiring ongoing management rather than achieving a cure.

Itch control in the short term usually involves the use of antihistamines and steroids. For most dogs with moderate to severe itch, antihistamines provide limited relief. In veterinary medicine, evidence for their use is poor as few quality trials have been published. None of the H1 blockers has been shown to be superior to any other. Thus, these medications are used by trial and error. The older generation agents have significant sedating effects, which may be exploited at night. Physicians choosing antihistamines to control itch often advocate using four times the dose used to treat upper respiratory allergies. New antihistamines are less sedating, but there is no evidence that they have superior activity. Some of the antidepressant medications (amitriptyline, doxepin, mirtazapine) have been used, as they have antihistaminic activity.

Oral or injectable glucocorticoids are often used for short-term control of itch and can be used long-term, although their side effects make them less desirable. Glucocorticoids have a number of cellular and molecular targets, which enables them to reduce itch and
inflammation very effectively. Topical steroids can be helpful when itch is focal. Hydrocortisone aceponate (Cortavance – Virbac Animal Health) or triamcinolone (Genesis – Virbac Animal Health) are sprays that can be used initially twice daily then tapered to every other day. Topical creams, such as betamethasone, can also be used for 7-10 days, but should not be used for long periods of time, as they can cause cutaneous atrophy and even systemic signs of hyperadrenocorticism.

For focal itch, topical tacrolimus (0.1%, Protopic) can be helpful in some patients. This calcineurin inhibitor is best used twice daily for the first week, then once daily or as needed. It does not work rapidly to reduce itch and can cause irritation and itch in some patients.

In most patients, steroids are used systemically. Short-term side effects can include polyuria, polydipsia, polyphagia, and behavior changes. When using prednisone or prednisolone, 0.5 mg/kg can be given every 12 hours initially and then tapered according to response. Methylprednisolone can be administered to help reduce the polyuria and polydipsia associated with steroid use. Rarely, oral triamcinolone (0.2 mg/kg) or oral dexamethasone (0.1 mg/kg) can be used if animals have become refractory to prednisone. These steroids are potent and not recommended for long-term treatment. Of notable interest, a recent publication showed that dogs with suboptimal serum levels of vitamin D were less responsive to prednisolone. Some dermatologists supplement atopic dogs with oral vitamin D and believe it has a benefit; these empirical findings require further testing. Often dermatologists use an intravenous injection of dexamethasone sodium phosphate for quick relief, which may last up to 72 hours in some patients.

Long-term Management

When opting for long-term steroid treatment, the author and colleagues recommend using the “safe steroid dose” calculation popularized by Dr. Candace Sousa. The patient’s body weight in kilograms (kg) is multiplied by 30 to give the annual dose of prednisone or prednisolone in milligrams (mg). Thus, a 10 kg dog is given 300 mg of a steroid agent per year; if trimeprazine/prednisolone is used (Temaril-P – Zoetis, with 2 mg prednisolone per tablet), the safe dose is 150 tablets per year or about 1 tablet every other day. Many dogs can live on this dosage throughout the year with minimal long-term steroid side effects (eg, liver enzyme elevation, muscle wasting). Clients often object to behavioral side effects when they occur, and numerous dogs still gain weight and have dry skin even with low dosing.

For long-term management of atopic dermatitis in some dogs (failure to respond to immunotherapy, elderly), it is preferable to use cyclosporine (Atopica), as it has fewer side effects when used long-term. It is a fungal metabolite that binds to a protein in the cell called cyclophilin; this complex inhibits the enzyme calcineurin, which ultimately blocks the production of IL-2 and other upstream cytokines critical for lymphocyte proliferation and function. Calcineurin is a serine/threonine phosphatase that dephosphorylates the NFAT (nuclear factor of activated T cells) family of transcription factors, which activate production of IL-2 and other cytokines. Cyclosporine revolutionized the treatment of atopic itch, as it allowed veterinarians to control atopic itch in dogs and cats in which glucocorticoids were no longer effective or in which glucocorticoids were contraindicated. The drug can be expensive for larger dogs and does take 4-6 weeks to be fully effective, because of its mechanism of action. It is given initially at 5-7 mg/kg/day for 4-6 weeks and then decreased slowly to the frequency that controls the disease. Some animals may need daily therapy indefinitely.

Short-term side effects of nausea and vomiting are common and can be prevented by using maropitant (Cerenia – Zoetis) initially for 4 days or by initially giving with food then transitioning to administration on an empty stomach. Long-term side effects can include chronic loose stools and risk of opportunistic infections. Gingival hyperplasia, papillomas, lichenoid cutaneous reactions, hypertrichosis, and some unusual neurologic signs have also been seen. Because cyclosporine is an immunomodulatory drug, it is best to avoid use in dogs and cats less than 1 year of age and in dogs with a previous history of malignant neoplasia.

Newest Innovative Treatment

The newest and most innovative treatment for itch control in canine allergic skin disease is oclacitinib (Apoquel). This drug, given orally, works very rapidly to stop itch and can therefore be used for short-term and long-term itch control. Oclacitinib is a Janus kinase inhibitor that is targeted to those cytokines utilizing JAK1 as their major signal transduction pathway. Its primary target for itch control in allergic disease is the T helper 2
cytokine IL-31. Release of IL-31 is part of the skewed Type 2 lymphocyte response in allergic disease, and the IL-31 can bind directly to nerves to cause itch. In addition, the cytokine TSLP (thymic stromal lymphopoietin), which is produced by keratinocytes, also binds directly to nerves to stimulate itch. It, too, utilizes JAK1 as part of its signal transduction mechanism.

Studies have shown that oclacitinib is effective in flea allergy, food allergy, atopic dermatitis, and contact allergy. The drug has provided excellent itch control in dogs with chronic atopic dermatitis that has failed to respond to immunotherapy and/or cyclosporine and in those dogs who cannot tolerate glucocorticoids or that have become refractory to them. It is critical to remember than oclacitinib is meant for allergic itch. It will not control the itch associated with infection; and, thus, it is important that infection and ectoparasite control be addressed if oclacitinib is to be used chronically. The most common side effects seen with oclacitinib (in less than 5% of dogs) were gastrointestinal. Complete information can be found on the product insert.

Oclacitinib is given orally at 0.4-0.6 mg/kg every 12 hours for up to 14 days, then once daily if used chronically. Some dogs have a mild relapse of itch when the dose is dropped to once daily; the author has found that giving the medication in the early evening works best. Other dogs have a more serious relapse and may need to take the medication twice daily for a longer period of time. Prolonged BID dosing is off-label, and dogs on this regimen should be monitored for changes in CBC. Some owners have found that splitting the once-daily dose into a half dose twice daily works better for their pet.

**SUGGESTED READING**


Steps forward that in the past seemed esoteric, or like distant possibilities, are becoming commonplace as research rapidly advances.

GLOBAL INNOVATIONS IN DERMATOLOGY
KEY RESEARCH ADVANCES THAT WILL IMPACT DAILY PRACTICE

Douglas J. DeBoer, DVM, DACVD

What’s new—and cool!—this year in the world of veterinary dermatology? Steps forward that in the past seemed esoteric, or like distant possibilities, are becoming commonplace as research rapidly advances. Many of these findings will lead to new diagnostic and treatment products that will be invaluable in everyday practice. It is therefore important to learn about and understand the developments that are taking place, and how they will impact veterinary practice in the future. Three themes are currently changing the approach to treating skin disease in both pets and people.

CYTOKINES IN DERMATOLOGY

- Cytokines are small protein molecules used as “chemical messengers” to enable cells to communicate with each other. Familiar examples of cytokines include the interferons and interleukins (IL-2, IL-4, etc).

- Cytokines cause their effects by being produced by one cell, traveling to another cell, and interacting with a cell-surface receptor.

- Though it was originally thought that cytokines were used only by cells of the immune system to direct the immune response (which is true!), it is now known that many different kinds of cells can produce and react to cytokines.

- This diversity includes cells of the immune system, skin, endocrine system, and nervous system—creating a sort of network that enables cells of many different organ systems to communicate.

- One example is the recent finding that, during the allergic response, cytokines directly affect epidermal cells, causing them to produce lower amounts of critical structural proteins and antimicrobial peptides … leading to increased permeability of skin and more infections.1

- A second example is the recent finding that interleukin-31 (IL-31) is a key cytokine in serum.2 IL-31 can directly stimulate pruritus by binding to receptors on nerve cells as well as acting on lymphocytes to augment the allergic state.

- Blocking the action of IL-31 can produce dramatic relief of pruritus in dogs. Oclacitinib (Apoquel – Zoetis) blocks the action of IL-31 (and several other cytokines) by inhibiting the signaling function of its receptor. The drug may also inhibit production of IL-31 by cells of the immune system.3 Recent studies show these actions can provide allergic patients with clinical benefits that are at least equivalent to those of corticosteroids or ciclosporin.4,5
BIOLOGICAL THERAPIES

- Various new therapies on the market and in development rely on a biological product rather than a chemical drug.

- Examples of these therapies include recombinant cytokines, cytokine receptor fragments, and monoclonal antibodies. Many of these molecules are on the human medical market, aimed at such diseases as rheumatoid arthritis, psoriasis, autoimmune diseases, and cancers. Many more are in development.

- The monoclonal antibody products bind to (and therefore prevent action of) such molecules as IL-2, TNF-alpha, cytokine receptors, and IgE.

- These products are prepared by producing a monoclonal antibody in a mouse, then “grafting” the binding site of the antibody onto human IgG, producing a “humanized” monoclonal antibody that persists in a person’s body for a prolonged period without being recognized as a foreign protein.

- In the past, development and use of these therapies has been limited (especially in veterinary medicine) by the extreme expense of manufacturing them. As time passes, however, production costs continually decline and are reaching the point where such treatments as monoclonal antibody therapy may be economically realistic in veterinary practice.

- Therapies that may benefit skin diseases include anti-TNF-alpha (adalimumab) for psoriasis; also anti-IL-4/13 receptor (dupilumab) and anti-IL-31 (in human clinical trials) for atopic dermatitis. Two recent studies reported the production of a “canine-ized” version of monoclonal anti-IL-31. In preclinical laboratory models, this monoclonal was capable of reducing pruritus in dogs for more than 3 weeks after a single injection.

- It is important for practitioners to be aware of and understand these therapies, as they are more and more likely to become routine in the years ahead.

METHICILLIN-RESISTANT STAPHYLOCOCCAL SKIN INFECTIONS: THE STORY CONTINUES

- The prevalence of antibiotic-resistant staphylococci (in dogs, chiefly Staphylococcus pseudintermedius) has increased substantially in recent years.8

- It is important to keep terminology correct: “MRS” (methicillin-resistant Staphylococcus) versus “MRSP” (methicillin-resistant Staphylococcus pseudintermedius) versus “MRSA” (methicillin-resistant Staphylococcus aureus) to avoid client confusion and distress.

- Clinical implication: if a dog is treated with an empirically chosen beta-lactam antibiotic (cephalosporin or amoxicillin/clavulanic acid) and there is limited or no response, culture and susceptibility testing should be performed. It is impossible to predict empirically which antibiotics are indicated; and “antibiotic-hopping” is hazardous, as with each cycle of treatment multiple-drug resistance becomes more likely.

- When performing a culture, it is important for the lab to report the species of Staphylococcus with which you are dealing (ie, a canine versus human strain) so that the appropriate measures can be taken. What are “appropriate measures” is currently the subject of debate among authorities, however!

- Recent studies point to the possibility that the home environment itself may be a source of recolonization, as staphylococci can survive on surfaces for weeks to months.9

- Experts do not currently agree as to the advisability and effectiveness of decolonization procedures when infections have been recurrent.

- Recent studies demonstrate that it is possible to eliminate active superficial staphylococcal infections (even MRS) from the skin by using topical products as the primary treatment, without antibiotics. For example, products containing 2%-4% chlorhexidine, when applied daily, can resolve mild to moderate superficial pyoderma as rapidly as systemic antibiotics.

- Other treatments that are being discussed for topical treatment in dogs include hypochlorite-ion–based products, alcohol gel hand sanitizer, herbal oils, and accelerated hydrogen peroxide products. The
veterinary community awaits publication of studies before making conclusions about the efficacy and safety of these products.

- Spray-on, wipe-on, leave-on, or mousse products are often preferable to shampoos for frequent or long-term use, as they provide residual effect and improve client compliance. If a shampoo is used, a total of 10 minutes of contact time is important.

- MRS is spreading fast in the human and veterinary worlds. For practitioners who have not already done so, it is time to start taking every precaution to prevent transmission of MRSP strains in the clinic and prevent colonization of humans by MRSA.

- Key sanitation measures have been developed by expert panels and include handwashing and disinfection, gloves, protective clothing with frequent laundering, cleaning and disinfection of premises, and education of staff and pet owners.

### REFERENCES


