Bayer Dermatology Symposium

Cytologic Clues to Skin Disease
Dr. Wayne S. Rosenkrantz

flies, lice, and mosquitoes, oh my!
Dr. Randall C. Thomas

Update from the 2009 23rd Annual Congress of the ESVD/ECVD
Dr. Wayne S. Rosenkrantz

Cutaneous Manifestations of Systemic Disease
Dr. Randall C. Thomas
Cytologic Clues to Skin Disease

Cutaneous cytology, the microscopic evaluation of cells and organisms found on the surface of the skin or from skin lesions, provides a rapid and inexpensive means for obtaining significant diagnostic information. Taking samples is easily accomplished with minimal equipment, and in-house cytologic evaluation enables the clinician to confirm a diagnosis more rapidly and initiate appropriate therapy without delay. Sending samples only to an outside clinical pathologist eliminates the advantage of rapid results that allow decision-making while the client is still at the clinic. Veterinarians have much to gain by building their skills in cytologic evaluation.

SAMPLE COLLECTION
The most commonly used techniques for gathering samples for cytologic examination include: direct smears of fluid aspirated from a lesion, impression smears, swab smears, scrapings, fine-needle aspiration, and fluid aspiration (from the ear). Usually, no skin preparation is warranted unless hair clipping would facilitate sample collection. Cleansing with alcohol or disinfectants is done only for fine-needle aspiration of a mass lesion.

Direct Smears
For direct evaluation of fluid-filled lesions, a small amount of fluid is collected with the corner of a slide or tip of a needle, then smeared on the microscope slide. The impression smear, another direct technique, can be used to evaluate normal-appearing skin, moist or greasy skin lesions, macules, plaques, or areas of lichenification. This technique is also used after removal of crusts or after gently opening the surface of papules, pustules, or vesicles. To obtain the sample, a microscope slide is pressed directly against the site. For dry macules and plaques, rotating the slide over the lesion will produce streaking artifacts but will often yield more material to examine. Too much pressure may result in a broken slide. This technique

The Cytology Toolbox
- Binocular microscope with a strong light source and high-quality lenses (low-power scanning objective [40×] and oil immersion [100×])
- Glass slides (with frosted ends or adhesive coating)
- Coverslips and permanent mounting media
- Syringes and hypodermic needles
- Spatulas
- Curettes
- Scalpel blades
- Cotton-tipped wood applicator
- Clear adhesive tape
- Diff Quik (Romanowsky) or methylene blue stain materials

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does not readily yield a textbook-perfect sample, but the method is highly practical. Several sites may be sampled on one slide.

Transparent acetate tape impressions can also be taken from the skin surface and are particularly useful for obtaining samples from hard-to-reach areas. They are best for obtaining epidermal debris from dry lesions. Slides with one side containing an adhesive are also available for direct impressions.

**Swab Smears**
Swab smears are used most often for sampling of ear canals, draining tracts or sinuses, interdigital webs, and dry crusty surface lesions. The cotton-tipped applicator is moistened then inserted into the tract, sinus, or ear canal. For dry lesions and interdigital webs, the moistened cotton tip is rubbed briskly over the skin surface. The cotton tip is then rolled over the surface of the microscope slide.

**Scrapings**
Used primarily to sample underneath crusts, vesicles, and peeling stratum corneum, scrapings are also helpful for collecting additional cells from surgically removed biopsy specimens. The skin is scraped with a scalpel blade held at 15- to 90-degree angle to the surface, and the collected material is then gently wiped onto the slide. The sharp edge of a broken wooden swab may be used to gently scrape the surface of some lesions that are located in claw folds, interdigital webs, and ventral paws.

**Fine-Needle Aspiration**
Fine-needle aspiration is used to sample nodules, tumors, cysts, pustules, vesicles, or bullae. Fluid-filled lesions can be aspirated with 21- or 22-gauge needles and a 3-mL syringe; whereas 21-gauge needles and 6- or 10-mL syringes should be used for firm lesions to obtain a more representative sample. After the needle penetrates the lesion, even continuous aspiration should be applied by withdrawing the plunger of the syringe; very little suction is required in fluid-filled lesions, and the material within the needle will be sufficient. In some mycobacterium cases, the needle may need to be redirected to find the fluid-filled area. For firmer nodules, suction should be interrupted while the needle is redirected into another area of the mass, repeating this procedure 3 or 4 times or as needed. Suction should then be released and the needle withdrawn from the lesion. The syringe and needle should be separated to introduce air into the syringe, then reattached to expel the needle’s contents onto a slide. A second slide can be used to streak the material across the surface.

**SLIDE PREPARATION**
For Romanowsky staining, the collected materials should be allowed to dry on the slide, and the sample side should not be heated directly or wiped during preparation. Oily, waxy, or dry skin samples collected by direct impression or moistened cotton applicators should be lightly heat-fixed before staining by holding the clear side of the slide over the flame from a match or butane lighter. Any smoke residue should be wiped from the clear surface of the slide.

Diff Quik staining requires five 1-second dips of the slide into each of the three solutions. The slide is then rinsed with distilled water and allowed to dry naturally or can be blotted or blown dry. For samples obtained on acetate tape, the tape can be either stained directly (skipping the clear fixation solution, which would prevent the tape from laying flat on the slide) or by placing a drop of the third solution (the purple stain) onto a glass slide before placing the unstained tape directly over the stain.

After staining, a coverslip may be placed if desired. Low-power objectives (40×) are usually sufficient to determine cell types, but oil immersion (100×) is preferred for assessing the presence of bacteria or yeast.

**CYTOLOGY EVALUATION**
Clinicians should learn the value of low-power scanning of the whole slide to view the entire area of each sample collected. Different body sites may yield different findings, and this information will
be missed if only the first area found is examined. In addition, a low-power scan will detect areas of blue staining demonstrating inflammatory cell nuclei, nuclear debris, protein, or evidence of a specific inflammatory response. Non–fluid-filled samples will often have inflammatory cells in small microfoci that are critical to assessing infection versus bacterial overgrowth. Complete evaluation requires focusing up and down as sample sites are evaluated to ensure that important details are not missed.

**Normal Findings**

To recognize abnormalities, clinicians must first understand what normal looks like—particularly in relation to the skin, ears, and anal sacs. Direct impressions or swab smears should be taken from the ear canals, ventral neck, axillae, and interdigital areas of healthy dogs and cats to appreciate the spectrum of normal-appearing cells. For example, mature keratinocytes that have finished their migration to the stratum corneum have lost their nuclei and keratohyaline granules. Nucleated keratinocytes, wax and lipid from ear canals, and surface debris are other common normal findings. Melanin granules should not be mistaken for bacteria. Such normal artifacts as stain precipitate, cotton fibers, pollen grains, and hairs may be missed if only the first area found is examined. In addition, a low-power scan will detect areas of blue staining demonstrating inflammatory cell nuclei, nuclear debris, protein, or evidence of a specific inflammatory response. Non–fluid-filled samples will often have inflammatory cells in small microfoci that are critical to assessing infection versus bacterial overgrowth. Complete evaluation requires focusing up and down as sample sites are evaluated to ensure that important details are not missed.

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**Table 1. Common Types of Abnormal Cells/Findings**

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Appearance</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleated keratinocytes</td>
<td>Round, lacking desmosomal attachments</td>
<td>Possible parakeratosis or erosions*</td>
</tr>
<tr>
<td>Acantholytic keratinocytes</td>
<td>Round, lacking desmosomal attachments</td>
<td>Pemphigus (numerous); subcorneal pustular dermatitis [rare]; eosinophilic pustular dermatitis or folliculitis [moderate]; Trichophyton and other dermatophyte infections [occasional]</td>
</tr>
<tr>
<td>Protein</td>
<td>Stains fine, granular pink or light blue</td>
<td>Serum or cutaneous leakage</td>
</tr>
<tr>
<td>Inflammatory cells</td>
<td></td>
<td>Variable combinations determine which type of exudate is present</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>Clear to slightly eosinophilic cytoplasm;</td>
<td>Pyoderma; pemphigus; subcorneal pustular dermatosis [rare]</td>
</tr>
<tr>
<td></td>
<td>multilobed nucleus</td>
<td></td>
</tr>
<tr>
<td>Eosinophils</td>
<td>Contain eosinophilic granules</td>
<td>Granulomatous inflammation; if large and atypical lymphocytes, consider lymphoma</td>
</tr>
<tr>
<td>Mononuclear cells</td>
<td>Monocytes stain light blue and have kidney-</td>
<td>Chronic infections or strong local antigenic stimulus; plasmacytic pododermatitis (cats); lupus erythematosus (dogs); mucocutaneous inflammation</td>
</tr>
<tr>
<td>(monocytes or lymphocytes)</td>
<td>bean shaped nuclei; lymphocytes stain dark</td>
<td></td>
</tr>
<tr>
<td></td>
<td>blue and have indented, round nuclei</td>
<td></td>
</tr>
<tr>
<td>Plasma cells</td>
<td>Round, eccentrically located nuclei with</td>
<td>Infectious response or foreign body reactions; if mainly histiocytic, consider neoplasia or cutaneous histiocytosis</td>
</tr>
<tr>
<td></td>
<td>adjacent halo and dark blue–staining cytoplasm</td>
<td></td>
</tr>
<tr>
<td>Macrophages/histiocytes/</td>
<td>Abundant vacuolated cytoplasm; may contain</td>
<td>Dermal sample site, possible ulceration [dogs]; intraepidermal site indicating possible allergic disease [cats]; if large numbers, consider mastocytoma</td>
</tr>
<tr>
<td>multinucleated giant cells</td>
<td>melanosomes, nuclear debris, or old red blood</td>
<td></td>
</tr>
<tr>
<td>Mast cells</td>
<td>Mononuclear; dense blue granules may obscurer</td>
<td></td>
</tr>
</tbody>
</table>

*The presence of nucleated keratinocytes may also indicate that the sample was obtained from below the stratum corneum; therefore, knowing how the sample was collected is important to interpretation.
Evaluation of healthy skin sites also allows the practitioner to visualize normal surface bacteria and yeast. No more than 1 of each type of organism (yeast, coccus, or rod) is generally seen per oil immersion field (oif) in skin samples, but yeast is believed to be more prevalent in the ear canals of dogs. Inflammatory cells are not usually found in skin and ear canal specimens, so the presence of these cells makes any bacterial findings very significant (particularly if intracellular or toxic neutrophils are seen). Normal anal sacs do have inflammatory cells and bacteria, but intracellular bacteria are rare. Yeast may be seen ($\leq 10/oif$), but red blood cells are not prevalent in normal anal sacs.

### Abnormal Findings

In optimum surface collection techniques, abnormal cells would be defined to include all inflammatory cells and all nucleated keratinocytes (Table 1). Inflammatory exudates may be suppurative, eosinophilic, or granulomatous. Fibroblasts in mixed suppurative or pyogranulomatous infiltrates suggest that longer-term antibiotic therapy may be needed to combat fibrosis. Plasma cells are most commonly seen when a local antigenic stimulus is present, but they may also be seen in mucocutaneous inflammation. Neutrophilic infiltrates most commonly are seen with pyoderma, but sterile suppurative disorders should be suspected if no bacteria or other infectious organisms are seen.

The presence of eosinophils is also very telling. Small clusters of these cells are typical of insect hypersensitivity or free keratin reactions, whereas a smaller number suggests atopic dermatitis or adverse food reactions (cats with allergic skin disease frequently have tissue eosinophilia). If eosinophils are seen in combination with degenerate neutrophils and intracellular bacteria, furunculosis is most likely present. Without bacteria, dermatophytosis should be considered. Importantly, eosinophils may be completely absent in inflammatory exudates from animals receiving glucocorticoids.

Granulomatous infiltrates are most commonly seen with infectious diseases, furunculosis, or sterile granulomatous disorders. More chronic or deep lesions tend to be pyogranulomatous with numerous mononuclear cells; macrophages, histiocytes, and multinucleated giant cells may also be present. Red blood cells also suggest deep lesions, such as furunculosis or vasculitis. Phagocytized nuclear debris may just represent chronic lesions and is not usually indicative of an autoimmune disease.

### Microorganisms

When evaluating microorganisms, relative numbers are as important as the associated tissue response. Bacterial and yeast overgrowth may occur without inducing a true infection that is associated with an inflammatory cell response directed at the organism. The evidence that the inflammation is directed at the organism is the presence of intracellular organisms, most often in neutrophils or macrophages. Common cytology findings include cocci, rods, and (rarely) filamentous organisms (Table 2). Infectious organisms that are too small to see include Mycoplasma, Rickettsia, L-forms (bacteria without cell walls that can change size and shape), and some spirochetes.

If bacteria and inflammatory cells are found in the same preparation, the presence of phagocytosis should also be noted. If neither granulocytes nor intracellular bacteria are seen, large

### Table 2. Examples of Microorganisms Seen on Cytology

<table>
<thead>
<tr>
<th>Finding</th>
<th>Possible Identity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocci</td>
<td><em>Staphylococcus intermedius</em></td>
</tr>
<tr>
<td>Rods</td>
<td><em>Proteus species</em></td>
</tr>
<tr>
<td>Round spheres surrounded by halo-like capsules*</td>
<td><em>Dermatophyte spores</em></td>
</tr>
<tr>
<td>Uniform filamentous structures (2–3 μm)</td>
<td><em>Dermatophyte hyphae</em></td>
</tr>
</tbody>
</table>

*More easily identified in samples from cats than in those from dogs*
numbers of bacteria may represent overgrowth that may respond to antibiotic or topical therapy to alleviate crusting, pruritus, and odor. If no bacteria are found in the stained fluid, pyoderma is less likely. However, the bacteria found in deep infections are generally few in number and sometimes difficult to find. Deep infections will also have a mixed cellular infiltrate with numerous histiocytes, macrophages, lymphocytes, and plasma cells—suggesting that long-term antibiotic therapy will be required. Large numbers of intracellular and extracellular cocci are seen more commonly in cases of impetigo or in dogs with bacterial infections secondary to immunosuppression (eg, in cases of iatrogenic or natural Cushing’s disease).

The most commonly found yeast is Malassezia, although Candida may be seen rarely. Malassezia pachydermatis inhabits the skin of most normal dogs and cats, but the yeast is difficult to find by examining direct impression smears. Although the presence of >1 yeast/oif alone does not diagnose Malassezia dermatitis, this finding indicates that yeast may be a contributing factor—especially in cases of hypersensitivity reaction.

Candida species identified on cytology will appear as yeast and pseudohyphae. Round to ovoid instead of peanut-shaped, Candida does not match the typical yeast description. Candida and concurrent bacterial rods are most frequently found in a toxic degenerative suppurative infiltrate obtained from ear samples.

**SUGGESTED READING**


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**Subcutaneous, Deep Fungal, and Protozoal Organisms Identified with Exfoliative or Aspiration Cytology**

- Cryptococcus species
- Coccidioides species
- Pythium insidiosum
- Sporothrix schenckii
- Blastomyces dermatitidis
- Histoplasma capsulatum
- Leishmania species
Flies, Lice, and Mosquitoes, Oh My!

Numerous insects can affect the skin of dogs and cats. Although fleas and ticks receive the most attention, several other insects and ectoparasites are capable of producing generalized or localized skin disease in our companion animals.

LICE
Infestation with lice, or pediculosis, occurs in mammals and avian species throughout the world. Lice are wingless ectoparasites that are generally considered to be host specific. In the United States, pediculosis is relatively uncommon, most likely because these pests are susceptible to many of the commonly used parasiticides. Lice are obligate parasites that are able to complete the entire life cycle with one host. Adult females cement their eggs to the hairs of the host. Although lice eggs, or nits, are similar in appearance to eggs of another ectoparasite, Cheyletiella species, they are generally larger and found more firmly attached to the hairs. Nymphs hatch and undergo three molts before reaching adulthood, and 3 to 5 weeks are required to complete the life cycle. Lice are primarily transmitted from host to host by direct contact, but infestation can also occur through contact with infested bedding or grooming tools. Pediculosis tends to be a disease of poor housing conditions, and its increased prevalence during the winter months may be due to heavier hair coats and animals having closer contact.

Lice species are divided into two orders: Anoplura (sucking) and Mallophaga (biting or chewing) lice (Table 1). Anoplura lice are blood-feeding ectoparasites with mouthparts that have specifically adapted to pierce the skin; Linognathus setosus is the only sucking louse of importance in dogs and cats. Some Mallophaga lice are also blood-feeders, but most have mouthparts that have adapted to chewing; consequently, most biting lice feed on debris from the skin and hair coat. Analyses have shown multiple species of biting lice obtained from dogs and cats. Although lice are considered to be species-specific, one case has been reported in which a dog was infested with Phthirus pubis, the human crab louse.

Clinical Signs
The clinical signs of pediculosis are variable, and some animals may not show any sign of discomfort. Sucking lice are not particularly active, so they are easy to observe in most cases. With heavy infestations, anemia and weakness may occur, especially in young animals. Restlessness and agitation may occur due to chronic irrita-
tion. Biting lice are more mobile and therefore more difficult to see. Most clinical signs are secondary to skin irritation, with nonspecific pruritus and excoriations being common. A poor, unkempt hair coat and seborrhea are characteristic, and traumatic alopecia may be seen in severe cases. Cats infested with *Felicola subrostratus* may present with pruritus and miliary dermatitis. In dogs, *Trichodectes canis* can serve as an intermediate host for the tapeworm, *Dipylidium caninum.*

**Diagnosis**

Pediculosis is a rare diagnosis in clinical practice but should be suspected in poorly managed patients or recent strays. Because the signs are nonspecific, differentials should include other ectoparasites that are commonly seen in dogs and cats. A diagnosis of pediculosis is usually confirmed through careful observation of lice or nits on the affected dog or cat (*Figure 1*). In some instances, an acetate tape impression of hair and debris may assist in identification of the parasite.

**Treatment**

Lice appear to be susceptible to many commonly used antiparasitic products but not all of the products are effective against the nit stages and may require multiple treatments. (*Figure 2*) Historically, pyrethrin-containing shampoos and sprays were used for treatment of lice infestation. Topical treatment with lime-sulfur (2%) is also effective against these parasites. These treatments should be repeated 2 to 3 times at 10- to 14-day intervals to resolve all stages of the life cycle.

Advantage® and Frontline® products are labeled as effective treatment for lice infestations and remain effective for all life stages with a single application. In one field study, imidacloprid (as Advantage 10% spot-on, animalhealth.bayerhealthcare.com) was evaluated against naturally occurring infestation with *L. setosus* and *T. canis* in dogs, and was 100% effective against both lice species after one application.³

In separate studies, the efficacy of fipronil (as .25% Frontline Spray, 10% Frontline Spot-on, and Frontline Spot-on Plus, Merial Ltd) was assessed against *T. canis* and *F. subrostratus* in dogs and cats, respectively. Single as well as two applications (28-day intervals) were found to be 100% effective against the two species of louse.⁴,⁵

Other products have demonstrated efficacy but no label claim. A single treatment with ivermectin (0.2 mg/kg SC) has been reported to be effective. The efficacy of selamectin (Revolution®) against *T. canis* and *F. subrostratus* were evaluated in dogs and cats, respectively. Selamectin was 100% effective against the lice after a single application.⁶

<table>
<thead>
<tr>
<th>Classification</th>
<th>Species</th>
<th>Known Targets</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anoplura (sucking)</td>
<td><em>Linognathus setosus</em></td>
<td>Dogs</td>
<td></td>
</tr>
<tr>
<td>Mallophaga (biting)</td>
<td><em>Trichodectes canis</em></td>
<td>Dogs, wolves, foxes, other canids</td>
<td>Most common</td>
</tr>
<tr>
<td></td>
<td><em>Heterodoxus spiniger</em></td>
<td>Dogs</td>
<td>Reported in warm climates</td>
</tr>
<tr>
<td></td>
<td><em>Felicola subrostratus</em></td>
<td>Cats</td>
<td>Only biting species known to affect cats</td>
</tr>
</tbody>
</table>

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**Figure 1**

*Trichodectes canis* feeding on a dog. Note the nits. Inset: *Trichodectes canis*

**Figure 2**

Lice nit
variable repellent activity against three mosquito species found in the United States, but the product consistently reduced feeding and increased mortality in mosquito species that were not repelled.7 K9 Advantix® (8.8% imidacloprid with 44% permethrin; animalhealth.bayerhealthcare.com) has been evaluated against Aedes aegypti mosquitoes, one of the most common vectors for both human and animal pathogens. This product significantly reduced feeding success of mosquitoes on treated patients for 28 days.8 Knockout Pet Treatment® (2% permethrin with pyriproxifen, virbacanimalhealth.com) is a flea spray that may also be useful as a mosquito repellent.

Feline Mosquito-Bite Hypersensitivity
Feline mosquito-bite hypersensitivity is uncommon, primarily affecting outdoor cats with dark hair on their pinnae.9,10 Clinical signs are distinctively seasonal and typically manifest as erythematous papules on the outer aspects of the pinnae and the bridge of the nose (Figure 3). Over time, these lesions may crust and coalesce into a larger, erosive to ulcerative plaque lesion that involves the entire bridge of the nose, sometimes including the nasal planum and rostral portion of the muzzle. Pruritus of variable intensity is often present, and, in some cases, periocular and footpad lesions may be seen. Affected footpads may be swollen and hyperkeratotic with erosions and ulceration. Histopathologic findings tend to overlap with other allergic diseases, but eosinophilic folliculitis and furunculosis are more often associated with insect exposure.10

Corticosteroids are the most effective treatment for active lesions. Methylprednisolone acetate (20 mg/cat or 5 mg/kg) by injection is commonly used. Oral prednisolone (2.2 mg/kg, PO Q 24 H until remission, then tapered) is also effective. For prevention, confinement during mosquito season is strongly recommended. Safe use of mosquito repellents with cats is difficult, although DEET-containing products have been reported to be useful in some cases. Spot-on, permethrin-containing products are highly toxic to cats.

FLIES
With local irritation from bite wounds being
Fly-bite dermatitis most often occurs in dogs that are chained outside or otherwise confined such that they cannot find shelter from the biting flies.

Fly-bite dermatitis
Fly-bite dermatitis is a localized irritation caused by the bite of multiple adult stable flies (*Stomoxys calcitrans*; Figure 4). These daytime-feeding, blood-sucking flies cause significant discomfort when they bite. They typically feed on the dorsal muzzle and ears in dogs. Lesions are typically found on the tips of the ears in dogs with erect pinnae, or on the outer fold of the pinnae in dogs with tipped ears. Lesions begin as areas of erythema and pinpoint hemorrhages that progress to coalescing areas of alopecia with hemorrhagic crusts. Fly-bite dermatitis most often occurs in dogs that are chained outside or otherwise confined such that they cannot find shelter from the biting flies.

Local treatments with topical antibiotics (mupirocin) or combination products (such as Panalog®) are often effective in resolving active lesions. Management changes to decrease fly exposure are the best preventative. A combination of imidacloprid with permethrin (K9 Advantix, animalhealth.bayerhealthcare.com) has been shown to decrease feeding of *S calcitrans* flies by 82% for 4 weeks after application.

Canine Eosinophilic Furunculosis of the Face
In some reported cases of this syndrome, which causes severe inflammation on the face and dorsal muzzle, possible insect or arthropod exposure was suspected. Lesions typically develop within 24 hours and are first seen on the dorsal aspect of the dog’s muzzle. Initially, these lesions may be papular but rapidly progress to crusted nodules, erosion to ulceration, and serous to hemorrhagic crusts.

Differential diagnoses include bacterial folliculitis/furunculosis and dermatophytosis, both of which have a slower onset. In eosinophilic furunculosis, however, cytologic examination of skin samples from affected areas will usually show a predominance of eosinophils with occasional evidence of secondary bacterial infection. Histopathology findings will usually demonstrate marked eosinophilic folliculitis and furunculosis.

Systemic glucocorticoid therapy is the treatment of choice. Oral prednisone (1–2 mg/kg Q 24 H) often leads to rapid improvement, with complete resolution over a 10- to 14-day period. Steroids can be tapered quickly as the lesions resolve. Many practitioners treat concurrently with systemic antibiotics in case of secondary bacterial dermatitis. Most reported cases in the literature have not relapsed.

Myiasis
Considered a disease of neglect, myiasis is the infestation of the skin or other body tissues by fly larvae. Attracted by wounds or skin that is macerated by moisture, feces, or urine, adult flies lay eggs on the skin of older, weak, or debilitated animals. The larvae hatch and invade susceptible areas of skin. As infestation progresses, the skin breaks down and becomes more susceptible to other species of flies.
Treatment of myiasis should begin immediately by clipping and cleaning the affected areas to manually remove all visible larvae.

The larvae can cause significant tissue destruction, sometimes moving beneath the skin and into other tissue planes. Affected animals may develop secondary infection, shock, and collapse. Commonly affected areas include the perineal region, nose, eyes, and mouth, but myiasis can occur anywhere on the body where neglected wounds are present.

Diagnosis of myiasis is made by observation of larvae or maggots in the affected areas. Treatment should begin immediately by clipping and cleaning the affected areas to manually remove all visible larvae. Supportive care is often necessary, including intravenous fluids, antibiotics, and treatment for shock. Ivermectin (0.2–0.4 mg/kg) and nitenpyram (Capstar®; capstar.novartis.us) have anecdotally been reported to be effective for treating any remaining maggots. After the patient is stable, surgical debridement of affected tissues should be performed to speed the healing process. Antibiotic therapy is necessary until secondary infections are resolved and lesions have healed. Any predisposing factors, including poor management practices, should be corrected to prevent recurrence.

**CUTEREBRA INFESTATION**

A rarer cause of local irritation in dogs and cats, Cuterebra infestation begins when pets come into direct contact with eggs that adult Cuterebra deposit in and around burrows or nests of rabbits and rodents. These eggs stick to the hair coat and penetrate the skin, or the animal ingests them during grooming. Most cases occur on or around the head and neck in dogs and cats. The initial clinical signs may be fever of unknown origin, localized swelling, pruritus, and erythema. As the larva enlarges, a small fistula will develop (Figure 5). Treatment involves carefully opening this fistula and removing the Cuterebra larva completely intact. Local flushing of the lesion followed by systemic antibiotic therapy may be useful in speeding resolution.

**REFERENCES**

At its 23rd annual meeting in Bled, Slovenia, the European Society and Congress of Veterinary Dermatology (ESVD-ECVD) commemorated the 25th anniversary of the European College of Veterinary Dermatology. Contributors to this year’s meeting presented the latest research in the fields of dermatopathology and immunology, clinical pharmacology, canine pyoderma and pruritus, equine dermatology, immune-mediated diseases, and comparative epidemiology of human atopic dermatitis and human nail diseases. The following are selected topics from presentations thought to have valuable clinical relevance.

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### CANINE PYODERMA

**Microbial Overgrowth—Lloyd**

Microbiologists and clinicians continue to disagree on the distinguishing features of bacterial overgrowth and surface pyoderma. For this presentation, bacterial overgrowth (> 5 bacteria/oil-immersion field [oif]) was defined as a newly described canine skin condition characterized by a substantially increased population of bacteria. True overgrowth, however, does not contain the inflammatory cells or proteinaceous debris that would be more typical of a true pyoderma. Bacterial overgrowth occurs in response to a breakdown of defense mechanisms that allows bacteria to adhere to keratinocytes and proliferate (*Staphylococcus pseudintermedius* thrives in this type of supportive microenvironment). When high numbers of bacteria are present, they produce toxins that irritate and damage the skin. Conditions that can lead to this include atopic dermatitis, excess moisture, self-trauma, seborrheic changes, and depressed immune response (Figure 1).

*Malassezia* overgrowth (> 2 yeasts/oif) can also occur, with greater quantities found over the lips, anus, and interdigital areas than in the ears of healthy dogs (Figure 2). Similar to the case with bacteria, this overgrowth results from weakened defense mechanisms; chronic use of antibiotics and glucocorticoids may also have a role.

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**Figure 1A**
Dog with atopic dermatitis and bacterial overgrowth

**Figure 1B**
Cytology sample from this dog has bacteria and epithelial cells but no inflammatory cells or protein debris.

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**Figure 2**
*Malassezia* overgrowth in the ear (A) and cytology sample from a healthy dog (B).
Hypersensitivities to *Malassezia* exist, and some breeds, such as basset hounds and West Highland white terriers, are predisposed to *Malassezia* overgrowth. Both bacterial and yeast overgrowth can be controlled with use of chlorhexidine shampoo and sprays. Systemic antibiotics should be avoided when possible to prevent resistance.

**Methicillin-Resistant *Staphylococcus pseudintermedius*—De Lucia et al**

Researchers in a private practice in Padua, Italy, reported on the incidence of multiresistant, *mecA*-positive *S pseudintermedius* among canine diagnostic samples.² A total of 48 samples were obtained from skin (N=28), ear (N=10), urinary tract (N=7), and peritoneum (N=3). Kirby-Bauer disk diffusion was used to determine sensitivity, and resistance was defined by breakpoints from the Clinical and Laboratory Standards Institute (CLSI). Ten species demonstrated multiresistance to three or more classes of antibiotics, including beta-lactams, macrolides, lincosamides, and fluoroquinolones. Of these ten, nine were identified as *S pseudintermedius* (Figure 3).

**Conjunctival Microflora in Canine Atopic Dermatitis—Furiani et al**

This study compared the prevalence of bacterial isolation from the conjunctiva of dogs with atopic dermatitis (AD) (N=21) with that obtained from normal dogs (N=21).³ Bacterial culture and cytologic evaluation were performed on specimens obtained from the conjunctival sac. Cultures showed a significant difference in prevalence of bacteria isolated from AD dogs (57.1%) versus that of healthy dogs (14.2%); cytology studies showed bacteria in 85.7% of the AD dogs and 42.9% of the normal dogs. Although *S pseudintermedius* dominated the isolates from AD dogs (58.3%), researchers could not determine any qualitative variations in bacteria isolated from the two groups.

**Clindamycin Pharmacokinetics in Canine Skin—Saridomichelakis et al**

This study compared serum and tissue levels of clindamycin in normal canine skin at two dosages: 5.5 mg/kg Q 12 H and 11 mg/kg Q 24
H. Serum and tissue levels correlated closely and differed significantly between the two dosages: Maximal concentration (Cmax), elimination half-life (T1/2), and area under the curve (AUC) were higher at the 11 mg/kg Q 24 H dosage. In fact, the Cmax and AUC were more than double at this dosage. Therefore a better antibacterial profile can be expected when clindamycin is administered at a higher dose once daily.

Effects of Staphylococcus Lysates on Gene Expression—Deboer et al
Staphylococcal lysates have been advocated as immunomodulatory treatments for canine recurrent pyoderma for many years, but their mode of action remains largely unknown. In this study, canine peripheral blood mononuclear cells (PBMCs) from healthy dogs were cultured with and without Staphage Lysate (Delmont Laboratories; delmont.com) or an investigational Staphylococcus intermedius phage lysate (SIL). At 18 and 72 hours after incubation, several genes demonstrated altered expression. Immunity genes with the greatest changes included interferon gamma, CCL20, IL-2 and IL-2R, CD40L, TNF-alpha, and CCL13. These results indicate that staphylococcal lysates have demonstrable in vitro effects on gene expression, including the expression of genes that code for certain immunoregulatory molecules. SIL may be more potent than Staphage Lysate, which could translate into a future product that would treat canine recurrent pyoderma more effectively (Figures 4 and 5).

Strategies to Reduce Antibiotic Resistance
- Frequent hand-washing
- Use of gloves when handling animals with suspected infection
- Use of proper disinfectants for cleaning cages, doors, counters, and instruments
- Proper antibiotic selection, dosing, and duration

Strategies to Manage Antibiotic-Resistant Infections—Papich
Using methicillin-resistant S. pseudintermedius as an example, this presentation reinforced the importance of adhering to treatment guidelines to minimize antibiotic resistance. Methicillin resistance results from the presence of the mecA gene in a bacterial strain. The mecA gene can be transferred horizontally between staphylococci of the same species or to other species. This particular gene codes for production of penicillin-binding protein 2a (PBP2a), which confers complete resistance to all beta-lactam antibiotics, including penicillins, cephalosporins, cefamycins, carbapenems (including imipenem), and monobactams. Oxacillin is used as a marker of this type of resistance; when oxacillin resistance is confirmed, no beta-lactams should be used.

The 2007 CLSI guidelines state that the Staphylococcus aureus interpretive criteria should be used for all other veterinary isolates of coagulase-positive staphylococci. Under these guidelines, a minimum inhibitory concentration (MIC) value of ≥ 0.4 mcg/mL is regarded as resistant. Newer research, however, supports use of an MIC of ≥ 0.5 mcg/mL as the cutoff for coagulase-positive staphylococci, and the updated CLSI standards will reflect this new evidence. Because this change may lead to misidentification of resistant staphylococci, diagnostic labs should regard any non-aureus, coagulase-positive Staphylococcus as resistant to all beta-lactam antibiotics if it has an MIC value of ≥ 0.5 mcg/mL.
Treatment of toxic epidermal necrolysis must focus on compensating for fluid, electrolyte, and colloid losses, and managing secondary infections to guard against sepsis.

AUTOIMMUNE DISEASE UPDATES
Erythema Multiforme and Toxic Epidermal Necrolysis—Yager and Rosenkrantz
Two separate presentations addressed the importance of using both clinical and histopathologic features to distinguish these conditions.7,8 A new histopathologic pattern referred to as “cytolytic dermatitis” (instead of interface dermatitis) may be useful for distinction. Erythema multiforme is often of unknown etiology; drugs have been implicated, but bacterial and viral infections, neoplasia, and connective tissue diseases are also possible causes.7 In older dogs, an idiopathic erythema multiforme has been described. The pathogenesis of erythema multiforme is not fully understood, but triggering of aberrant keratinocyte apoptosis is a key feature. An immunologic pathogenesis is possible, given the condition’s similarities to graft-versus-host disease and the T lymphocyte–induced apoptosis of keratinocytes.

In general, erythema multiforme lesions may be flat or raised, and target-shaped or polycyclic; unlike in humans, the typical, regular target lesion is extremely rare in the dog. Less than 50% of the body is affected by an erythematous or purpuric macular eruption. The condition is further differentiated into major and minor forms, primarily based on the degree of mucosal involvement. In the minor form, only one mucosal surface (if any) is involved (Figure 6), whereas two or more mucosal surfaces are affected in the major form. If more than one mucosal surface is involved and lesions are present over more than 50% of the body surface area, toxic epidermal necrolysis should be suspected (Figure 7).

Toxic epidermal necrolysis is a rare vesiculobullous and ulcerative disorder that is generally more extensive and painful than erythema multiforme.8 Although the pathologic mechanisms of toxic epidermal necrolysis are unknown, immunopathologic mechanisms are most often suggested. Research in humans has suggested that high levels of toxic cytokines, particularly tumor necrosis factor–alpha, interferon gamma, and soluble Fas ligand, play a role in this disease, but other factors may contribute. The source for these cytokines is likely a combination of macrophages, keratinocytes, dendritic cells, and, to a lesser extent, T cells.

The prognosis for toxic epidermal necrolysis is generally poorer than that for erythema multiforme, although cases of the latter may be challenging to treat if mucosal involvement is extensive. In epidermal necrolysis, a thorough drug history should be obtained and all possible drug exposure should be avoided. Treatment must focus on compensating for fluid, electrolyte, and colloid losses, and managing secondary infections to guard against sepsis. The use of systemic glucocorticoids is controversial, but pentoxifylline and cyclosporine have been shown to be helpful. Trials of intravenous immunoglobulin therapy have been promising, but availability is limited.
Pemphigus Foliaceus and Discoid Lupus Erythematosus—Rosenkrantz

Pemphigus foliaceus and discoid lupus erythematosus (DLE) are the two most common autoimmune skin diseases seen in dogs. The etiology of pemphigus foliaceus still remains largely unknown, but autoantibodies most likely develop as a result of abnormal immune regulation or abnormal antigen stimulation. The Akita and the chow chow appear to be genetically predisposed (Figure 8). Viruses have been suspected in certain regionalized outbreaks, and canine lesions show interesting similarities to those of a South American form of the human disease that has been linked to black flies, viruses, local heat and humidity, and tannin decomposition. Ultraviolet light irradiation may also exacerbate acantholysis.

One interesting area of research involves the density of certain cell adhesion molecules in sites where lesions typically occur. These adhesion molecules, particularly the desmogleins, are the targets that are destroyed in pemphigus foliaceus. Multiple site samples in dogs and cats have shown no differences in intensity of desmoglein antigen, suggesting that factors other than the distribution of desmogleins may be responsible for the localization of primary clinical lesions.

The exact mechanism underlying acantholysis is not completely understood. The patient’s autoantibodies bind to one of two members of the cadherin group (cell-to-cell adhesion molecules). Recent studies have shown that canine desmoglein-1 is involved in only a limited number of pemphigus foliaceus cases, and no autoantibodies against the extracellular domain of desmoglein-1 are involved; another cell surface molecule may be involved. More recent studies have shown variability of indirect immunofluorescence patterns seen with four main IgG intercellular epidermal patterns, suggesting that canine pemphigus foliaceus is a heterogeneous immunologic disease.

More than a third of pemphigus foliaceus cases are controlled only with glucocorticoid therapy. Combination therapy with glucocorticoids and azathioprine may be particularly useful for resistant cases.

Most common in the long-nose breeds, DLE is a disease of young to middle-aged dogs. Clinical signs are usually limited to the face and most commonly involve depigmentation and ulceration of the nasal planum, the lips, the periorcular area, membrane nictitans, and oral cavity. Well-circumscribed areas of gray or silver scaling may be seen on the inner pinnae. In general, DLE lesions are more likely to be depigmented and less likely to be encrusted.
With the advent of new therapies such as cyclosporine better control of refractory atopic dermatitis can be achieved.

Indications for Glucocorticoid Therapy in Atopic Dermatitis

- Initial management of severe pruritus
- Management of flares
- Long-term therapy when financial limitations preclude other treatments
- As adjunctive therapy in cases that do not respond to other modalities
- In conjunction with early phases of ASIT

ALLERGIC SKIN DISEASE
Medical Management of Atopic Dermatitis—Hill

In this overview of medical management of pruritus and atopic dermatitis the author shares his experiences from the United Kingdom and Australia. Of particular interest are reports of success with allergen-specific immunotherapy (ASIT). As many as two thirds of patients may have noticeable improvement in their clinical signs with this form of therapy, yet oral prednisolone or prednisone remain the treatment of choice for atopic dermatitis in Dr. Hill’s experience. When using long-term glucocorticoid therapy, the goal is to achieve the minimal effective dose with alternate-day therapy. Maintaining an optimal quality of life should remain the single most important consideration when managing chronic atopic dermatitis. Monitoring for side effects is very important with glucocorticoids.

Other options presented included cyclosporine therapy. Before beginning cyclosporine therapy, the diagnosis of atopic dermatitis should be confirmed on the basis of age of onset, breed affected, clinical distribution of lesions, and exclusion of other major differentials (eg, food allergy or parasites). Any secondary pyoderma and Malassezia infections should be controlled. The recommended starting dose of cyclosporine is 5 mg/kg Q 24 H, or slightly higher if the pill size doesn’t allow for exact dosing. Ideally, the drug should be given at night on an empty stomach; if vomiting occurs, try administering with food until the vomiting subsides, then increase the interval between meals and dosing. If vomiting continues, metoclopramide may be given before the cyclosporine capsules. Approximately 70% of patients will require daily dosing; 25% can be tapered to alternate-day dosing, and 5% will require only twice-weekly dosing (Figures 10 and 11). In addition to vomiting, less common side effects are gingival hyperplasia, hypertrichosis, papillomatosis, and lymphoplasmacytoid dermatitis. No renal side effects have been seen, but some dogs may have mild increases in renal enzyme activity.
Fexofenadine versus Methylprednisolone for Canine Atopic Dermatitis—Plevnik Kapun et al

The safety and efficacy of oral fexofenadine were evaluated in 15 dogs with atopic dermatitis during a 6-week period. A second group of 15 dogs was treated with antipruritic dosages of methylprednisolone. Canine atopic dermatitis extent and severity indexes (CADESI) and pruritus scores were measured on days 0, 21, and 42. Both groups had statistical improvement in CADESI scores at days 21 and 42; pruritus scores were lower in both groups by day 42, but only the methylprednisolone group had lower pruritus scores at day 21. Serum biochemistry profiles and electrocardiograms showed no significant side effects. The results show efficacy and safety of fexofenadine after 6 weeks of treatment in atopic dogs.

REFERENCES

In addition to displaying numerous primary skin diseases, the skin can also serve as a marker for systemic disease. In some instances, the visual appearance of a lesion can be distinct enough to point directly to a diagnosis. In other cases, the clinical lesions are not specific but provide evidence to look for an underlying systemic cause.

**SUPERFICIAL NECROLYTIC DERMATITIS**

A rare disease in dogs, superficial necrolytic dermatitis (SND) goes by many names, including metabolic epidermal necrosis, hepatocutaneous syndrome, necrolytic migratory erythema, diabetic dermatopathy, glucagonoma syndrome, and metabolic dermatosis.

Most commonly seen in middle-aged to older dogs, SND is characterized by very specific skin lesions (Figure 1) in conjunction with several possible systemic disorders. Most references indicate no sex or breed predilection, but one study reported 75% of patients were male. Glucagonomas, the most common cause of SND-like disease in humans (ie, necrolytic migratory erythema), have been reported to cause SND in dogs; however, most canine cases are associated with advanced liver disease. The cause of the liver disease is often undetermined, but mycotoxins or chronic administration of liver-toxic drugs (such as phenobarbital) may be to blame. Concurrent hyperadrenocorticism (HAC) or diabetes mellitus may also be associated with SND. Fewer than 10% of canine cases are associated with pancreatic neoplasia. Although hypoaminoacidemia is not considered a cause of SND, case studies have shown that plasma amino acid levels are often significantly decreased.

**Clinical Signs**

The footpads are involved in almost all cases, with affected pads demonstrating severe hyperkeratosis, fissure formation, and ulceration with concurrent erythema of the interdigital spaces (Figure 2). Pododermatitis is common. Skin lesions are fre-
Cumulatively seen on the face, distal paws, mucocutaneous junctions, inguinal regions, and over pressure points. These lesions begin as erythematous macules or papules but progress to erosive to ulcerative lesions with crusting, scaling, and associated alopecia. Pruritus is variable and is most often associated with secondary infections. The skin and footpad lesions often precede signs of systemic disease.

Systemic signs are variable, depending on the underlying disease. Lethargy, weight loss, and pain with walking are common, especially if pododermatitis is severe. Polyuria and polydipsia may also be reported.

**Diagnosis**

The diagnosis of SND should be suspected in middle-aged to older dogs with compatible cutaneous signs that have not responded to therapy. Cutaneous cytologic evaluation often reveals significant secondary bacterial and Malassezia infection. Histopathology findings can be pathognomonic, but samples should be sent to a dermatopathologist to maximize the chances of getting a definitive diagnosis.

When compatible cutaneous lesions are present, abdominal ultrasound may show a characteristic “honeycomb” appearance (Figure 3) that results from parenchymal collapse surrounding nodules of normal liver tissue. The pancreas and adrenal glands should also be evaluated thoroughly.

**Treatment**

The prognosis for dogs with SND is generally considered to be poor, so therapy is often palliative. Skin lesions may resolve if glucagon-secreting tumors are excised, phenobarbital doses are tapered or eliminated, or mycotoxin exposure can be identified and eliminated. For dogs with advanced liver disease, average survival is less than 6 months.

Treating secondary bacterial and yeast dermatitis usually improves patient comfort, but clinicians should exercise extreme caution when using antibiotics or antifungal therapies that are metabolized by the liver. In our practice, we try to clear Malassezia dermatitis and pododermatitis with aggressive topical therapy before considering systemic treatments. Corticosteroids should also be used very cautiously in dogs with SND. Although skin lesions may improve immediately with corticosteroid therapy, these agents frequently promote the onset of diabetes mellitus.

Recently, the somatostatin analog octreotide was used as palliative therapy in a dog with metastatic pancreatic glucagonoma-associated SND. Skin lesions improved with daily subcutaneous injections (2–3.2 mcg/kg Q 12 H) and recurred after treatment was discontinued.

Nutritional supplements are often useful in managing the skin lesions. Use of some or all of these supplements may help resolve or lessen the severity of the lesions, making the patient more comfortable (see Table).

**Calcinosis Cutis**

Calcinosis cutis, the abnormal deposition of calcium within the skin, may be related to several clin-
In time, virtually all dogs affected with nodular dermatofibrosis will be found to have polycystic kidneys, renal cystadenomas, or renal cystadenocarcinomas. "Figure 4" Close up of calcinosis cutis, showing erythematous papules with visible calcium deposits

Calcinosis cutis lesions usually begin to improve after corticosteroid levels normalize, but complete resolution usually takes several months. Once- or twice-daily application of topical dimethylsulfoxide (DMSO) gel may speed healing. If lesions are widespread, I usually recommend treating only one quarter of the lesions daily to prevent absorption of excessive calcium from the skin.

**NODULAR DERMATOFIBROSIS**

Seen primarily in German shepherd dogs, nodular dermatofibrosis is a syndrome in which firm, haired nevi develop over the head, neck, ventral trunk, and limbs. Typically, these collagenous nodules measure 0.5 to 5 cm in diameter and displace hair follicles and other adnexal structures. The mean age of onset is reported to be 6.4 years, and no sex predilection has been determined. Individually, the nevi are benign, but the presence of multiple lesions warrants additional workup, including serum biochemical profile, urinalysis, and abdominal radiography and ultrasound. In time, virtually all affected dogs will be found to have polycystic kidneys, renal cystadenomas, or renal cystadenocarcinomas. Some dogs have palpably enlarged kidneys at the time skin lesions are diagnosed, but renal disease often does not develop for several years.

If renal lesions are not detected at initial diagnosis, abdominal ultrasound should be repeated approximately every 6 months. Uterine leiomyomas often develop in intact female dogs, so ovariohysterectomy is recommended. Multiple, benign intestinal polyps may also be seen in some cases. Rarely, nodular dermatofibrosis can be seen in breeds other than German shepherd dogs, so a complete internal medicine workup should be initiated in any dog found to have multiple collagenous nevi.

**PARANEoplastIC ALOPECIA IN CATS**

This is a rare syndrome in older cats in which alopecia develops in association with internal neoplasia. On examination, alopecia is often observed along the ventral abdomen, medial aspects of the limbs, and ventral neck (Figure 5), and less commonly over the pinnae and periorbital regions.

In time, virtually all dogs affected with nodular dermatofibrosis will be found to have polycystic kidneys, renal cystadenomas, or renal cystadenocarcinomas.
Skins lesions of feline thymoma-associated exfoliative dermatitis typically begin over the head and neck but can become generalized with time. The skin in the affected areas can develop a smooth, glistening appearance. Hair in unaffected areas may epilate easily. Footpad involvement may occur, and cases of Malassezia dermatitis have been reported. In addition to alopecia, affected cats may also have such nonspecific signs as lethargy, poor appetite, and weight loss.

Results of serum studies are often normal or show nonspecific changes. Skin biopsies reveal epidermal hyperplasia with alternating ortho- and parakeratosis with focal areas of hypokeratosis. Marked follicular atrophy may also be present.

In the reported cases in the literature, most cats had pancreatic carcinoma, but two cats had bile duct adenocarcinoma. Overall, the prognosis is typically poor because metastasis typically occurs before a diagnosis can be confirmed, and most cats die or are euthanized within weeks. In two case reports, the tumors were excised and the alopecia resolved; in one cat, alopecia recurred about 4 months later and evidence of metastasis was confirmed at that time.

**FELINE THYMOMA-ASSOCIATED EXFOLIATIVE DERMATITIS**

In this rare skin condition affecting older cats, a nonpruritic, exfoliative dermatitis develops in association with a thymoma. Skin lesions typically begin over the head and neck (Figure 6) but can become generalized with time. Erythema with moderate to severe scaling are the primary signs, with alopecia or hypotrichosis also occurring in some affected areas. The lesions are inherently nonpruritic, but the onset of secondary bacterial and Malassezia infections can cause pruritus. Treatment of the secondary infections may decrease pruritus but does little to control the scaling. Most affected cats appear healthy except for the skin lesions.

Skin biopsies reveal a cell-poor, hydropic interface dermatitis of the surface and follicular epithelium. Orthokeratosis is prominent, but focal areas of parakeratosis may also be noted. Apoptotic cells are prominent in the basal layer of the epidermis. The biopsy findings are highly specific for this syndrome.

In cats with compatible clinical and histopathology findings, thoracic radiographs should be taken. Most thymomas are benign, and cutaneous signs generally resolve after the tumor is removed.

**FELINE ACQUIRED SKIN FRAGILITY SYNDROME**

In this condition in which the cat’s skin becomes very thin and easily traumatized, underlying systemic diseases are common. Although exogenous administration of corticosteroids (eg, methylprednisolone acetate and triamcinolone) has also been associated with this condition, diabetes mellitus and HAC are the most common causes. Cats with naturally occurring HAC are typically middle-aged to older, and females may be slightly more at risk. Approximately 50% of cats with HAC will present with cutaneous atrophy or skin fragility, and the diagnosis may be suspected when tearing of the skin occurs with routine handling during the physical examination. Because signs of HAC are often subtle and nonspecific in...
The diagnosis of skin fragility syndrome is based primarily on the physical signs at presentation. Many cases have progressed before a diagnosis is confirmed. A poor response to insulin in the diabetic patient should prompt a search for HAC. The diagnosis of naturally occurring HAC is difficult, but approximately 80% of cases are pituitary-dependent.

The diagnosis of skin fragility syndrome is based primarily on the physical signs at presentation, the most obvious of which is very thin skin that has the consistency of tissue paper. Focal or generalized alopecia may also be present, depending on progression of the underlying disease. The skin is thin, easily bruised, and blood vessels are easily seen.

Skin biopsies are unreliable in skin fragility syndrome; some specimens show significant cutaneous and adnexal atrophy whereas others do not. Decreased dermal collagen content may be the most reliable finding. Ehlers-Danlos syndrome, an inherited collagen deficiency, has similar clinical signs and biopsy findings but typically presents earlier in life.

The prognosis for cats with skin fragility syndrome is relatively poor. Affected cats should be kept in a low-stress environment where they will not be subjected to trauma from other cats or playmates. In iatrogenic cases, signs may improve with discontinuation of corticosteroid therapy. For cats with underlying pituitary-dependent HAC, trials of mitotane and trilostane therapy have not yet produced any conclusive data. Surgical excision of adrenal neoplasms is difficult but may be curative.

The diagnosis of skin fragility syndrome is based primarily on the physical signs at presentation.

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