Antimicrobial Therapy in the Real World

Oropharyngeal inflammation: Understanding this enigmatic condition

Many areas of a cat’s mouth can become chronically inflamed, but we’re still not sure of the exact cause. Here’s the best way to help your patients with this painful condition.

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Cats with oral inflammation can be some of the most frustrating patients you manage. Even the terminology for this condition is problematic and confusing. For years, virtually any inflammation of the feline oral cavity was termed stomatitis. This term is still used but only to describe widespread inflammation of the oral cavity as opposed to gingivitis or periodontitis, which involves localized support loss and mucositis. In the past, stomatitis was referred to as lymphocytic-plasmacytic gingivostomatitis as well as plasma cell gingivitis, faucitis, and pharyngitis, though the latter two terms are incorrect in that the fauces and pharynx are normally not involved in stomatitis.

(Figures 1A-1C are included to refresh your knowledge of dental anatomy.)

In August 2009, the American Veterinary Dental College approved the term oropharyngeal inflammation to refer to any type of oral inflammation. This inflammation is then further classified according to location (see boxed text titled “Forms of oral inflammation in cats”). This article will discuss what we currently know about chronic oropharyngeal inflammation in cats. I hope it helps you pinpoint the type of inflammation your patient is experiencing and hone in on the best treatment.

Pathogenesis

Oral tissues are constantly exposed to pathogens and antigenic proteins. In a healthy mouth, a balance exists among disease, the host, and the host’s immune response. The cause of oropharyngeal inflammation has not been definitively determined. Dental plaque intolerance is thought to be involved. Either an inadequate or exaggerated host response occurs in cats with oropharyngeal inflammation, which leads to marked gingival and oral mucosal inflammation.

A multifactorial cause is suspected, including genetic predisposition, environmental stress, diet, and viral (calicivirus, herpesvirus) and bacterial (Bartonella species) infection. Calicivirus has shown significant presence in cats with chronic oropharyngeal inflammation (97%)
**Gingivitis**—Inflammation of gingiva (Figure 1).

**Periodontitis**—Inflammation of the nongingival periodontal tissues, which are the periodontal ligament and alveolar bone (Figures 2-4). Decreased alveolar support is apparent around the mandibular first molar in Figure 4 (arrows).

**Alveolar mucositis**—Inflammation of the alveolar mucosa, which is the mucosa overlying the alveolar process and extending from the mucogingival junction to the vestibular sulcus and the floor of the mouth (Figure 5).

**Sublingual mucositis**—Inflammation of mucosa on the floor of the mouth (Figure 6).

**Labial or buccal mucositis**—Inflammation of lip or cheek mucosa (Figure 7).

**Caudal mucositis**—Inflammation of the mucosa of the caudal oral cavity, bordered medially by the palatoglossal folds and fauces, dorsally by the hard and soft palate, and rostrally by alveolar and buccal mucosa (Figure 8).

**Stomatitis**—Inflammation of the mucous lining of any of the structures in the mouth. The term is reserved to describe widespread oral inflammation (beyond gingivitis and periodontitis) that may also extend into the submucosal tissues (Figures 9A & 9B). Marked caudal mucositis extending into submucosal tissues is termed *caudal stomatitis* (Figures 10A & 10B).

**Palatitis**—Inflammation of the mucosa covering the hard or soft palate.

**Glossitis**—Inflammation of the mucosa of the dorsal or ventral tongue surface (Figure 11).

**Cheilitis**—Inflammation of the lip, including the mucocutaneous junction area and skin of the lip (Figure 12).

**Osteomyelitis**—Inflammation of the bone and bone marrow.

**Tonsillitis**—Inflammation of the palatine tonsil (Figure 13).

**Pharyngitis**—Inflammation of the pharynx.
compared with a control group of cats (25%). When specific pathogen-free (SPF) cats were inoculated with serum from cats with chronic oropharyngeal inflammation, the SPF cats developed oral signs of ulceration, but they did not develop chronic stomatitis.

Cats with oral inflammation also have a higher prevalence of retrovirus infection than the general cat population. In another study of nearly 9,000 cats with oral lesions, greater than 20% of animals with chronic stomatitis had positive test results for feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), or both (Bellows, J.: Unpublished data, 2006). In a study of 60 cats with caudal stomatitis, 7% had positive test results for FeLV, and 8% had positive test results for FIV. None had positive test results for both FeLV and FIV.

Although some cats with stomatitis have positive test results for Bartonella species, a cause-and-effect relationship has not been proved since there is already a high prevalence of antibody-positive cats within the healthy population because of flea exposure. Many cats that have been exposed to the bacteria will have a positive titer even if they are not currently infected. Researchers found both calicivirus and herpesvirus in 87% of 25 cats with chronic oropharyngeal inflammation, while only 21% of cats with periodontal disease were shedding both viruses.

**History and clinical signs**

The median age of cats with oropharyngeal inflammation is 7 years. A patient’s history often includes dysphagia or anorexia causing weight loss, ptalism, bruxism (teeth grinding), and face pawing. The cat may avoid opening its mouth when eating. The cat’s coat is often unkempt secondary to poor self-grooming due to oral pain. Halitosis and bleeding within the oral cavity are common. Glossitis, cheilitis, and mandibular lymphadenopathy may also be evident. Widespread inflammation of the palate and pharynx is usually not present.

In some cats, inflammation is apparent only around the caudal cheek teeth extending from the gingiva beyond the mucogingival junction into alveolar mucosa. Other cats show marked gingivitis and periodontitis 360 degrees around the incisors, premolars, or molars. Caudal stomatitis, incorrectly referred to in the past as faucitis, clinically appears as cobblestone-like, ulcerative, proliferative, hyperemic lesions involving the palatoglossal folds and regions lateral to the folds. Caudal stomatitis is present in 85% of the cats affected by chronic oropharyngeal inflammation. One study found 15% of the cats only had caudal stomatitis without apparent lesions further rostrally. Mandibular lymphadenopathy is common.

**Diagnosis**

Histopathologic examination of the mucosa and submucosa reveals dense infiltrations of plasma cells with lesser numbers of lymphocytes, neutrophils, and macrophages consistent with virtually any inflammation in a cat’s mouth. Unfortunately, the only advantage of histopathology is to rule out neoplasia.

**Treatment**

Supragingival and subgingival plaque appears to be one of the multifactorial initiating sources of oropharyngeal inflammation. The only treatment that has long-term positive results without the need for further medication in most cats with widespread oropharyngeal inflammation is tooth extraction. Removing teeth decreases the plaque burden. The decision of whether to extract all the teeth or only the premolars and molars is based on examination findings. If marked inflammation, periodontal pockets, or tooth resorption are noted around the canines or incisors, the affected teeth are also extracted.

To evaluate the response to extraction in cases of chronic caudal stomatitis, a retrospective study of dental extractions in 30 cats with calicivirus was conducted. In that study, 24 of the 30 cats (80%) were significantly improved or clinically cured at the time of follow-up, which was 11 to 24 months after treatment.

For anorectic patients that present in poor condition, nutritional support through a pharyngostomy or
gastrostomy tube is indicated before or after surgery, or both, until eating returns to normal. Pain management in surgical patients is accomplished with preanesthetic opioid administration (buprenorphine at 0.006 to 0.02 mg/kg SC, IM, or IV), intraoperative local anesthetics (bupivacaine at 1 mg/kg), and postoperative opioids given orally for five to seven days (buprenorphine at 0.006 to 0.02 mg/kg).

Pulsed monitoring radiographs are important to evaluate root anatomy and pathology. Teeth with resorption lesions are often undergoing root replacement resorption, making luxation and elevation difficult. These teeth should be treated by amputating the crown and suturing the gingiva. Pulverizing or atomizing the root within the alveolus with a water-cooled high-speed handpiece and dental bur may result in removing excess support ing bone, removing too little tooth, or causing trauma to adjacent anatomy and should be avoided. If any teeth remain after the procedure, apply a plaque preventive (OraVet—Merial) while the patient is anesthetized.

**Monitoring**

Postoperative examination is performed two weeks after surgery. It is important to show the client how to control plaque on any remaining teeth by using cotton-tipped applicators and 0.12% chlorhexidine gluconate irrigation daily and OraVet application weekly.

In cases in which oropharyngeal inflammation persists for months despite extractions, extraction of all remaining teeth and root fragments is indicated. If lesions persist and the patient has been affected for months to years, the condition is termed refractory oropharyngeal inflammation. Removing multiple teeth and root fragments together with periodic laser thermoablation and medication (prednisone at 0.5 mg/kg every two to three days) may be helpful in these cases.

**ACKNOWLEDGMENT**

Figures 1A–1C and Figure 6 courtesy of Dr. Alexander Reiter, University of Pennsylvania.

**REFERENCES**


**SUGGESTED READING**

Successful treatment of bacterial pneumonia

Properly chosen antimicrobial drugs—in conjunction with other concurrent therapies in selected cases—can effectively penetrate sometimes difficult-to-access airway and pulmonary regions in which pathogenic bacteria can hide.

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Infections can occur in any component of the respiratory system, from the nose to the upper or lower airways, the pulmonary parenchyma, or even the pleural space. Infections in these regions present unique challenges. For instance, not all antimicrobials will gain equal access to the lumenal secretions of the airways. Only those that achieve good airway penetration (e.g. enrofloxacin, doxycycline) are likely to be effective in the treatment of tracheobronchitis. This article focuses on the treatment of pulmonary parenchymal infection, and, more specifically, the treatment of bacterial lung infection (i.e. bacterial pneumonia).

EVALUATION AND DIAGNOSIS

Bacterial pneumonia may be an acute or chronic, unilobar or multilobar, clinically silent infection that can lead to fatal infection. Most bacteria that cause pneumonia are secondary pathogens and cause disease only when allowed the opportunity (e.g. aspiration or immune suppression). Bacterial pneumonia is often the result of mixed flora infections, with obligate anaerobes accounting for as many as a quarter of pathogens involved. The bacteria most commonly implicated include enteric pathogens (e.g. Escherichia coli, Klebsiella species); Pasteurella, coagulase-positive Staphylococcus, Streptococcus, and Mycoplasma species; and Bordetella bronchiseptica (see boxed text). It is unusual for healthy adult pets, and especially cats, to develop bacterial pneumonia. With the exception of infections caused by primary bacterial respiratory pathogens (e.g. B. bronchiseptica), most pets with bacterial pneumonia have some predisposing cause, such as extreme age, debilitation, immunocompromise, or pre-existing respiratory disease.

The clinical presentation of bacterial pneumonia varies widely. Occasionally, bacterial pneumonia is accompanied by only minor clinical signs or physical abnormalities. Common signs include a soft, productive cough; nasal discharge; exercise intolerance; or respiratory distress; as well as anorexia and lethargy. Fever is an inconsistent finding. Loss of body condition, tachypnea, increased (or when consolidation is present, decreased) bronchovesicular lung sounds, inspiratory crackles, sinus arrhythmia, and cyanosis may be identified. Neutrophilia (with or without a left shift), lymphopenia, and mild anemia are inconsis-
Hypoxemia development depends on the severity of functional lung impairment. Bacterial pneumonia often results in an alveolar pulmonary pattern with a predominantly ventral distribution. Sometimes only a single lung lobe is involved (particularly after foreign body inhalation or aspiration). Dorsal caudal involvement may predominate after hematogenous bacterial exposure, and all lung fields may be involved in severe pneumonia. In less severe pneumonia or early in the disease course, only an interstitial pattern may be identified.

Identification of pulmonary sepsis confirms the diagnosis of bacterial pneumonia. Airway lavage provides material for cytologic examination as well as for bacterial culture and sensitivity testing. Bacterial culture is strongly advised before you initiate antimicrobial therapy, but antimicrobials are not withheld pending culture results. Treatment is likely to be prolonged, and culture and sensitivity allow for the identification of the safest, most economical and also correctly targeted antimicrobial drugs. Prior antibiotic therapy, incorrect sample handling, or infection with fastidious organisms may result in negative culture results even in the face of bacterial pneumonia. Since bacterial pneumonia often results in a productive cough, lavage of the large airways (e.g. transtracheal or transoral wash) can be safe, inexpensive, and useful. Bronchoalveolar lavage can also be used to derive samples for cytology and culture. The airways are not sterile even in healthy animals, and noninfectious respiratory disease may be associated with secondary bacterial infection. Therefore, a diagnosis of bacterial pneumonia must be based on integration of all clinical and radiographic findings, ideally in conjunction with demonstrated neutrophilic airway inflammation and intracellular bacteria, in addition to positive bacterial culture.

**TREATMENT**

Bacterial pneumonia should be treated with antimicrobial drugs. Adjust initial treatment based on the results of bacterial culture and susceptibility testing. Initial therapy can be guided in part by cytologic morphology and staining characteristics of microbes recovered from airway lavage. For severely affected or unstable pets, initial therapy must include antimicrobials with gram-positive, gram-negative, and anaerobic efficacy. Most often this involves combination therapy administered parenterally (Table 1); I often begin with a combination of enrofloxacin and ampicillin. Dogs and cats with mild to moderate disease may be treated initially with orally administered antimicrobials with a more limited spectrum of activity. Although many antimicrobials (including beta-lactam antimicrobials) do not readily penetrate the airway’s blood bronchus barrier, pneumonia is a parenchymal tissue infection rather than an airway infection. Although aerosolized administration of antimicrobials may benefit some patients with bacterial pneumonia, no studies support its use. Thus, aerosol delivery should only be considered as an adjuvant therapy and never as a replacement for systemic antimicrobials. Antimicrobial therapy should be continued at least one week past radiographic resolution, typically a minimum of three to four weeks.

**Dogs with severe bacterial pneumonia are often hypoxemic.** Ideally, PaO2 is determined via arterial blood gas analysis, but SpO2 determined through pulse oximetry can be used as a rough correlate of blood oxygen content. In pets with acute hypoxemia, oxygen supplementation should be provided when PaO2 is < 80 mm Hg or SpO2 is < 94%. The most practical means of delivery include an oxygen cage or the placement of a nasal cannula. Oxygen should be humidified before delivery to prevent drying of the airways with resultant impaired mucociliary clearance. Persistent hypoxemia or continued marked respiratory ef-

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### Table 1

**Empirical Antimicrobial Choices for the Initial Treatment of Bacterial Pneumonia***

<table>
<thead>
<tr>
<th>Severe, Unstable Disease</th>
<th>Combination therapy</th>
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<tbody>
<tr>
<td>Monotherapy</td>
<td>Meropenem, imipenem-cilastatin, or ticarcillin</td>
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<tr>
<td></td>
<td>Fluoroquinolone (e.g. enrofloxacin, marbofloxacin, orbifloxacin) or aminoglycoside (e.g. amikacin, gentamicin) plus beta-lactam antibiotic (e.g. ampicillin, amoxicillin-clavulanate, second- or third- generation cephalosporin)</td>
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<tr>
<th>Moderate, Stable Disease</th>
<th>Combination therapy</th>
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<tbody>
<tr>
<td>Monotherapy</td>
<td>Amoxicillin-clavulanate or trimethoprim-sulfonamide</td>
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<tr>
<td></td>
<td>Fluoroquinolone and beta-lactam antibiotic</td>
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<table>
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<tr>
<th>Mild, Stable Disease</th>
<th>Combination therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monotherapy</td>
<td>Fluoroquinolone, amoxicillin-clavulanate, or trimethoprim-sulfonamide</td>
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*Initial, empirical choice of antimicrobials should be adjusted based on results of microbial culture and sensitivity testing. The more severe the initial disease, the more important it is to initiate broad-spectrum therapy.
Bacterial Pneumonia Pathogens Worthy of Specific Mention

*Bordetella bronchiseptica*. *Bordetella bronchiseptica* is a contagious, primary respiratory pathogen. While infection usually results in tracheobronchitis it can cause severe pneumonia in immunocompromised or young cats and dogs. The author has recognized severe pneumonia in *Bordetella*-infected puppies treated with amoxicillin or amoxicillin-clavulanate despite in vitro susceptibility of the organism. I have often used enrofloxacin to treat severe pneumonia due to *B. bronchiseptica* in puppies without any subsequent problems, such as lameness. The addition of nebulized aminoglycosides to systemic antimicrobials may be useful.

*Streptococcus equi subspecies zooepidemicus*. *Streptococcus equi* subspecies *zooepidemicus* can cause necrotizing hemorrhagic pneumonia in dogs. Recently, this pathogen has gained attention as a cause of contagious canine infectious respiratory disease complex. The pathogen is particularly likely to cause severe and even fatal hemorrhagic pneumonia in kenneled dogs, including those in shelters and research colonies. The problem relates more to the extremely rapid disease course of this contagious infection in shelter settings than to inherent resistance of the pathogen to antimicrobial drugs. Although culture and susceptibility testing from airway lavage samples should guide treatment of these gram-positive cocci, empiric antimicrobial choices including beta lactam antibiotics (e.g. procaine penicillin G) should be effective.

*Mycoplasma*. *Mycoplasma* species, fastidious microbes that lack a cell wall, include pathogenic and commensal organisms. Many different species have been isolated from dogs and cats. *Mycoplasma* species are found commonly in the upper airways and occasionally in the lower airways of healthy dogs and cats. Experimental inoculation of some *Mycoplasma* species causes pneumonia, and naturally occurring pneumonia in both dogs and cats has occasionally been attributed to *Mycoplasma* infection (especially *Mycoplasma cynos*). However, in Jameson and colleagues’ study of 93 dogs with bacterial pneumonia specifically tested for mycoplasma, *Mycoplasma* species were recovered from only 7 dogs as the sole bacteria and from 58 dogs with additional nonmycoplasma bacteria.1 *Mycoplasma* infections usually respond well to standard dosages of fluoroquinolone, macrolide, tetracycline, and chloramphenicol antimicrobials but do not respond to those that interfere with cell-wall synthesis (e.g. beta-lactam antibiotics).

*Mycobacteria*. Cats and dogs are occasionally diagnosed with mycobacterial pneumonia. Both tuberculosis (i.e. *Mycobacterium tuberculosis*, *Mycobacterium bovis*, *Mycobacterium microti*) and nontuberculosis type (e.g. *Mycobacterium avium* complex, *Mycobacterium fortuitum*) mycobacterial infections cause pneumonia in pets. Mycobacterial pneumonia is often granulomatous and radiographs may demonstrate lymphadenomegaly and pleural effusion in addition to interstitial to alveolar pulmonary infiltrates. Acid-fast organisms are found in low numbers, if at all, in samples retrieved by bronchoalveolar lavage or fine-needle aspiration of lungs, or aspirate of lymph nodes. Mycobacteria are notoriously slow growing but polymerase chain reaction can confirm their presence. *M. tuberculosis* is primarily a human pathogen. The local health department should be contacted and owners of infected pets should contact their physician when tuberculosis-type infections are identified. Mycobacterial infections require prolonged, multiple drug treatment regimens to achieve control; readers are referred to textbooks such as *Infectious Diseases of the Dog and Cat* (Craig Greene, editor).

*Yersinia pestis* (plague). Practitioners in the mid- and far-western United States, especially in New Mexico and Colorado, must consider plague (*Yersinia pestis* infection) as a differential diagnosis in any cat with pneumonia. Although infection is rare, it is a zoonotic pathogen that can be spread to people through contact or inhalation of aerosolized droplets. Untreated, pneumonic plague is uniformly fatal. In endemic regions any cat with pneumonia should be isolated and handled with extreme caution. Cytologic examination of exudate or lymph node aspirates typically reveals bipolar gram-negative rods. The Centers for Disease Control and Prevention should be contacted if the diagnosis is suspected. Pending diagnosis, cats should be treated for fleas and antimicrobial therapy begun immediately. Aminoglycosides, fluoroquinolones, chloramphenicol, and tetracyclines have all been used at standard dosages for the treatment of *Y. pestis* infection.

REFERENCE


Fort despite oxygen supplementation indicates the need for mechanical ventilation. Fluid therapy is indicated for the treatment of dogs and cats with severe bacterial pneumonia. In addition to the systemic effects of hypovolemia, dehydration impairs mucociliary respiratory defenses. Crystalloid fluids should be provided at a rate to attain and maintain hydration. Overly aggressive fluid therapy can lead to pulmonary edema and worsen respiratory compromise. Although unproven, nebulization of sterile saline may facilitate mucus fluidity and more effective mucociliary function. In the author’s opinion, saline nebulization is beneficial for many patients. Cough is encouraged in patients with bacterial...
pneumonia, and cough suppressants are contraindicated. Coupage is a simple technique of thoracic percussion that aids mobilization of airway secretions and encourages cough. Coupage should follow saline nebulization when both are used. Encourage patients to move, if possible, and reposition recumbent pets frequently to help mobilize respiratory secretions.

Additional therapeutic considerations for dogs and cats with pneumonia include bronchodilators, mucolytics, and nutritional and supportive care. Although bronchodilators are not used routinely to treat bacterial pneumonia, inhaled albuterol or oral methylxanthine bronchodilators (e.g. theophylline) should be considered in patients that remain hypoxemic despite supplemental oxygen administration, when there is concurrent bronchoconstriction (likely in cats), or before administering inhalant drug therapy. Bacterial pneumonia may result in the production of thick, tenacious mucus. Theoretically, liquefaction of mucus may result in more effective mucociliary clearance. Simple maintenance of systemic hydration and airway humidification are usually adequate, but mucolytic drugs are sometimes advocated. The mucolytic N-acetyl cysteine reduces viscosity by breaking mucin disulfide bonds, but unfortunately nebulizing it causes bronchoconstriction. Oral administration of N-acetyl cysteine has not been investigated in pets with naturally occurring pneumonia, but in other species has demonstrated some utility in treating both infectious and noninfectious airway disease associated with excessive mucus secretion. I have used oral N-acetyl cysteine (available through health food stores) in pets with excessive mucus accumulation due to pneumonia at a dose of 125 mg up to 600 mg orally b.i.d. to t.i.d. with good results. Finally, pets with pneumonia may be reluctant to eat, but nutritional support is important and should not be neglected. Enticing foods, appetite stimulants (e.g. mirtazapine), or even feeding tubes may be required during the period of recuperation.

Lung lobectomy is occasionally indicated for treatment when pneumonia fails to resolve with appropriate antimicrobial therapy. Residual infection in a single lobe may be related to an underlying physical problem (such as bronchial foreign body, abscess, or tumor) and removal of the lobe can be curative. Occasionally, failure to respond to appropriate antimicrobial therapy is the result of an incorrect diagnosis, so lung tissue removed surgically should be submitted both for tissue culture and histopathology.

**SUGGESTED READING**

Challenges in dermatology: Resistant pyoderma and otitis

Gain insight from the management of these two challenging cases that involve battling recurrent bacterial infections.

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Relapsing bacterial pyoderma and otitis are two of the most common reasons dogs are presented for veterinary examinations. Up until recently, the main frustration with resolving relapsing pyodermas was determining and controlling the underlying reason for these infections. Now practitioners are also encountering staphylococcal infections that are multidrug-resistant and, therefore, more difficult to clear. This is also an important concern with relapsing otitis. The unique design of the ear canal provides an ideal environment for antibiotic-resistant organisms such as *Pseudomonas aeruginosa*.

As the prevalence of resistant bacterial infections of the skin and ear increases, practitioners are challenged to develop clear strategies for long-term management of these pesky infections. The goal of this discussion is to provide an update on the staphylococcal organisms that cause most skin infections and to describe the role *P. aeruginosa* plays in relapsing or recurrent otitis. Additionally, I will cover specific strategies for resolving these stubborn infections.

A challenging case of pyoderma

**History**

Duncan, a 5-year-old neutered male West Highland White terrier, was presented for evaluation of pruritus and relapsing infections of the skin and ears. The signs had first started at 1.5 years of age and had been nonseasonal from the beginning. Skin infections had been treated repeatedly with cephalexin. The owner reported that the response to cephalexin was not as complete as it once had been. Serum allergy testing had been performed about one year ago, and it was determined that Duncan was reactive to multiple pollen allergens and house dust mites.

Duncan had been receiving allergen-specific immunotherapy for about one year with minimal response. He had also been consuming a sensitive skin formula dog food for several years. He received a monthly topical flea adulticide and an oral heartworm preventive. Recently, a thyroid panel had been performed, and the results had been normal. Trial treatment for sarcoptic mange with 1% ivermectin had not led to any improvement.

**Presentation**

On physical examination, Duncan had a generalized, papular, pustular dermatitis with collarettes and crusts on...
the interdigital spaces revealed six to 10 yeast/hpf. The results of the pustule culture were still pending at the time of treatment initiation.

Management and outcome
The initial focus was on treating the current bacterial and yeast dermatitis. Clindamycin (11 mg/kg orally twice a day) was initiated while culture results were pending. Duncan was also prescribed ketoconazole (5 to 10 mg/kg orally once a day) for yeast pododermaatitis. The owners were advised to bathe Duncan with a ketoconazole-chlorhexidine shampoo twice weekly for two weeks and then once weekly. A strict diet trial using a novel protein diet (venison and potato) was initiated to rule out adverse food reactions. Because of frequent bathing, the owners were advised to apply the flea adulticide product every two weeks. Allergen-specific immunotherapy was continued at 0.5 ml administered subcutaneously once a week.

Culture and sensitivity results received about five days later showed a methicillin-resistant *Staphylococcus pseudintermedius* that was sensitive only to gentamicin and chloramphenicol. Chloramphenicol therapy was initiated (50 mg/kg orally three times a day). Clindamycin was discontinued based on culture and sensitivity results. Because of concerns about liver toxicity, the ketoconazole was discontinued at this time. The owner was advised to continue bathing Duncan with the ketoconazole-chlorhexidine shampoo twice weekly. Antibiotic therapy was continued for six weeks, at which time no evidence of bacterial or yeast dermaatitis was present. After 10 weeks of receiving the venison and potato diet, Duncan showed no signs of infection or pruritus. Because of the difficulty in clearing the most recent infection, the owners elected not to have Duncan undergo a provocative challenge to confirm the presence of food allergy.

Discussion
As a practitioner, I have two primary goals as I begin working with a dog with relapsing bacterial pyoderma: 1) resolve the current infection, and 2) diagnose and control the underlying reason for the infection whenever possible.

Resolving infection. Resolving the current pyoderma involves determining whether systemic antibiotics are indicated and, if so, choosing the appropriate medication. Virtually all cases of superficial and deep bacterial pyoderma require systemic antibiotics. Table 1 shows common antibiotics used for treating pyoderma.

Many practitioners recommend choosing a narrow-spectrum antibiotic, such as erythromycin or lincomycin, as the first choice when pyoderma initially occurs. These antibiotics are often effective for the first or second infection, but resistance develops quickly with repeated use.

The cephalosporins have been widely used to treat recurrent pyoderma in dogs. In one study, 97% of *Staphylococcus intermedius* strains were sensitive to cephalexin as recently as 2003. However, in the past several years, an increase in the frequency of methicillin-resistant strains of *Staphylococcus* species has occurred. Empirical treatment with the cephalosporins is still reasonable, but once this class of antibiotic is not working in a particular case, further diagnostic tests are indicated.

Skin culture should be considered whenever one or more commonly effective antibiotics do not resolve the infection. In the case of a superficial pyoderma, culture of an intact pustule is ideal. If a pustule is not available, careful gathering of purulent material from beneath a crust or...
from the margin of a collarette lesion may be useful. Swabbing the surface of the skin often results in culture of insignificant contaminant organisms. In cases of deep pyoderma, the culture should be obtained by taking a sterile biopsy sample for macerated tissue culture. Samples should be submitted to a laboratory for aerobic culture and sensitivity testing, rather than performing in-house testing.

Once the appropriate antibiotic is determined, the infection should be treated aggressively. The length of therapy depends on the type of infection and the clinical aspects of the case. As a general rule, superficial pyoderma should be treated for a minimum of three weeks. Ideally, treatment should extend for seven days past clinical resolution of the infection. For deep pyoderma, longer treatment is indicated. It is not uncommon for treatment to last six to sixteen weeks for some dogs with deep pyoderma. The end point of therapy should be based on physical examination and palpation of previously affected areas, since the visible aspects of deep pyoderma resolve long before the deeper infection.

With superficial and deep pyoderma, topical treatment should be prescribed along with systemic antibiotics. Benzoyl peroxide products have excellent activity against S. intermedius. Chlorhexidine- and ethyl lactate-based products are also effective and may be gentler to the skin. Bathing one or two times weekly is sufficient in most cases. Mupirocin, a topical antibiotic ointment, has excellent activity against Staphylococcus species and is useful for localized areas of infection.

Follow-up is critical with recurrent cases of pyoderma. Clients are

<table>
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<tr>
<th>Class</th>
<th>Drug and Dosage</th>
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| Macrolides          | • Erythromycin: 15 mg/kg orally three times a day, with food  
• Lincomycin: 22 mg/kg orally twice a day  
• Clindamycin: 5.5–11 mg/kg twice a day | • Relatively narrow spectrum  
• Erythromycin often causes vomiting.  
• Resistance develops quickly with erythromycin and lincomycin. |
| Penicillins with clavulanic acid | • Amoxicillin-clavulanic acid: 22 mg/kg twice a day | • Broad spectrum  
• Dermatologic dose is higher than label dose  
• Diarrhea is occasionally seen |
| Potentiated sulfonamide | • Trimethoprim-sulfadiazine and trimethoprim-sulfamethoxazole: 25–30 mg/kg orally twice a day  
• Sulfadimethoxine-ormetoprim: 55 mg/kg orally first day, then 27.5 mg/kg once a day | • Broad spectrum  
• Activity against some gram-negative organisms  
• Numerous potential side effects (sulfamethoxazole-trimethoprim)  
• Long-term therapy contraindicated  
• Contraindicated in Doberman pinschers |
| Cephalosporins      | • Cephalexin: 22–33 mg/kg orally twice a day  
• Cefpodoxime proxetil: 5-10 mg/kg orally once a day  
• Cefovecin sodium: 8 mg/kg subcutaneous injection (provides two weeks of treatment) | • Resistance is uncommon.*  
• GI upset can occur.  
• Convenience of once-daily dosing with cefpodoxime  
• Rare GI upset with cefpodoxime  
• Cefovecin may need to be redosed to provide sufficient treatment for difficult pyodermas. |
| Fluoroquinolones    | • Enrofloxacin: 5–20 mg/kg orally once a day  
• Orbifloxacin: 2.5 mg/kg orally once a day  
• Difloxacin: 5 mg/kg orally once a day  
• Marbofloxacin: 2.75 mg/kg orally once a day | • Broad spectrum  
• Excellent tissue penetration  
• Contraindicated in young dogs |
| Chloramphenicol     | • 40–50 mg/kg orally three times a day | • Bacteriostatic antibiotic  
• Good activity against Staphylococcus intermedius, but resistance may develop quickly.  
• Not recommended for patients with impaired renal or hepatic function.  
• Side effects include reversible bone marrow suppression, and hepatotoxicosis. Muscle weakness, especially of the hind legs, is seen in some dogs. In people, a peripheral neuropathy may be present, which could be the case in the dog; this side effect is reversible upon withdrawal of drug. |

often unable to determine whether all lesions have resolved at the end of a course of antibiotics. Patients should be rechecked every two or three weeks until the infection has resolved to ensure that undertreatment does not occur.

Managing the underlying cause. The second major focus of managing recurrent pyoderma is diagnosing and controlling the underlying cause of the infection. Table 2 lists both common and uncommon causes of recurrent pyoderma in dogs. The search for an underlying cause can be initiated simultaneously with the beginning of antibiotic treatment. Some underlying causes can be ruled out quickly (demodicosis, dermatophytosis), while others may require more aggressive diagnostic tests (adverse food reactions, atopy). A thorough history, including age of onset and determination of concurrent signs, will often shorten the list of potential underlying causes. Idiopathic, recurrent pyoderma is always a diagnosis of exclusion.

In Duncan’s case, he most likely has a combination of atopy and adverse food reaction (food allergy). While he had plenty of positive reactions on serum allergy testing, he did not respond to allergy immunotherapy alone. Once the food component of his allergies was addressed, we were able to better control his signs. The prevalence of adverse food reactions in dogs is not known. In our practice, about 10% to 20% of our allergic patients are food allergic. In addition, about half of the patients that respond to dietary manipulation have a component of atopy. In dogs with nonseasonal signs, it is always better to address possible adverse food reactions before performing allergy testing (intradermal testing is the gold standard).

A challenging case of Pseudomonas otitis

History

Lewis, a 5-year-old neutered male Labrador retriever, had a four-year history of recurrent otitis. Signs had initially been intermittent but nonseasonal. Infection in the left ear had been responsive to topical therapy but relapsed almost immediately upon withdrawal of treatment.

Infection within the right ear continued to relapse about every three to four months and cleared easily with topical treatment (Otomax—Schering-Plough Animal Health), typically used twice daily for 10 days.

Presentation

Physical examination findings revealed a severe, erosive to ulcerative otitis with marked purulent discharge in the left ear (Figure 3). We were unable to assess the condition of the left tympanic membrane because of the purulent discharge within the left horizontal ear canal. Pain and discomfort were significant on examination.

The right ear canal had moderate erythema with a brown, waxy discharge. The right tympanic membrane was intact and appeared normal. No other skin signs were noted on physical examination.

The main differential diagnosis was resistant bacterial otitis in the left ear. Because of the frequent relapse within the left ear, otitis media was suspected. The main differential diagnosis for the right ear was relapsing otitis externa due to bacteria or yeast. Recurrent otitis is typically secondary to an underlying primary cause. In this case, the differential diagnoses included atopy and adverse food reactions. Hypothyroidism could be considered at this age but would be an unlikely cause of recurrent otitis in a dog with signs starting at 1 year of age.

Ear cytologies revealed 10 to 12 yeast/hpf in the right ear and neutrophils with 4+ intracellular rod-shaped bacteria in the left ear (Figure 4). Lewis was anesthetized for a thorough otic...
examination. The right ear canal was flushed with a tromethamine–EDTA solution. Because minimal inflammation was present within the ear canal and the tympanic membrane appeared to be intact and normal, a myringotomy was not performed on the right side. A culture swab was taken of the left ear canal. The left ear was then flushed with copious amounts of tromethamine–EDTA solution. The ear canal was ulcerated throughout. A small portion of the tympanic membrane was visible but appeared opaque and thickened. A myringotomy was performed to obtain a culture sample, followed by lavage of the left tympanic bulla. A swab from the middle ear was submitted for culture and sensitivity testing. Butorphanol was administered at the time of the ear flush for analgesia.

Management and outcome

Malassezia otitis externa was diagnosed in the right ear, while bacterial otitis externa and media were diagnosed in the left ear. Because of the severity of the inflammation and the presence of intracellular rods, Pseudomonas otitis was suspected, and empirical treatment was initiated.

Enrofloxacin (20 mg/kg orally once a day) was prescribed. Lewis also received prednisone at a dosage of 1 mg/kg orally once a day tapered after seven days to 0.5 mg/kg once a day for seven days and then 0.5 mg/kg every other day. Tramadol (2.2 mg/kg orally twice daily for five days) was prescribed for pain management.

The owner was instructed to flush the left ear with a tromethamine–EDTA solution twice daily for the first two weeks. The solution was instilled into the ear canal and gently massaged. The owner was instructed to allow two to three minutes contact time before wiping out visible excess and discharge. The owner was also instructed to deposit 0.5 ml of neomycin–polymyxin B-1% hydrocortisone solution into the left ear twice daily after the tromethamine–EDTA flush. Miconazole solution was prescribed for use in the right ear twice daily until recheck.

Culture and sensitivity results were obtained about five days after the ear flush. Pseudomonas aeruginosa was cultured and was determined to be sensitive to enrofloxacin, marbofloxacin, amikacin, and polymyxin B. The owner was instructed to continue all treatments as directed and bring Lewis in for a recheck two weeks after the ear flush.

On recheck, there was mild erythema of the left ear canal with minimal discharge. The left tympanic membrane appeared to be intact but opaque (Figure 5). The right ear canal had minimal inflammation and discharge. Ear cytology was negative in both ears. The owner was instructed to continue enrofloxacin as before. Prednisone was continued every other day. Flushing of the left ear canal with tromethamine–EDTA was decreased to every other day to avoid maceration of the ear canal. The neomycin–polymyxin B-1% hydrocortisone solution was continued twice daily. No further treatment was recommended for the right ear. The owner was instructed to bring Lewis in for a recheck every two weeks for a total of six weeks.

Four weeks after flushing, ear cytology results continued to be negative, and minimal inflammation was present. The neomycin–polymyxin B-1% hydrocortisone solution was discontinued at that time. Flushing with tromethamine–EDTA solution was continued twice weekly. Enrofloxacin and prednisone were continued as before. A novel protein diet containing venison and potato was initiated to begin ruling out food allergy.

Six weeks after flushing, ear cytologies continued to be negative for bacteria and yeast, and minimal inflammation was present. The left tympanic membrane was intact and appeared normal. Enrofloxacin and prednisone were discontinued. The owner was instructed to continue flushing the left ear with tromethamine–EDTA solution twice weekly as well as to maintain the strict diet trial with venison and potato.

Eight weeks after the diet trial was started (and 12 weeks after ear flushing), Lewis developed a bilateral yeast otitis. At this time, food allergy seemed less likely (the relapse of otitis was similar to before the diet trial). Intradermal testing was performed, and Lewis began receiving allergen-specific immunotherapy for atopy. After clearance of the yeast otitis, the owner was instructed to flush both ears with a tromethamine–EDTA solution containing ketoconazole twice weekly. Ear drops containing fluocinolone, a synthetic corticosteroid, were prescribed for twice-weekly use to minimize allergic inflammation within the ear canals.
Did you know? New information regarding canine pyoderma

What organism causes canine pyoderma?
The nomenclature for the staphylococcal species most commonly causing pyoderma in dogs has recently changed. The *Staphylococcus intermedius* group is now composed of three distinct species: *Staphylococcus intermedius*, *Staphylococcus pseudintermedius*, and *Staphylococcus delphini*. *Staphylococcus intermedius* has long been considered the most common cause of pyoderma in dogs. This pathogen is now known as *S. pseudintermedius*. This species is not a new organism but simply a new name for the organism that has always been the cause of these infections.

*Staphylococcus schleiferi* has recently been recognized as a cause of canine pyoderma. It has been isolated most frequently from dogs with prior antibiotic use. Two subspecies of this organism exist: *S. schleiferi* subspecies *coagulans* and *S. schleiferi* subspecies *schleiferi*. Both variants have been identified in dogs, and both may be methicillin-resistant.

*Staphylococcus aureus* (both methicillin-sensitive and methicillin-resistant) is rarely seen as a cutaneous pathogen in dogs. However, both methicillin-sensitive and methicillin-resistant strains of *S. aureus* were isolated from normal dogs and dogs with inflammatory skin disease. The predominant evidence shows that infections due to methicillin-resistant *S. aureus* (MRSA) in dogs and cats have been transmitted from people to pet animals. These infected (or carrier) pets may serve as a reservoir for reinfection of people with whom they are in contact.

What is the significance of methicillin resistance?
There is now published evidence that the prevalence of oxacillin-resistant strains of *S. intermedius* has increased in the past several years. From a clinical perspective, methicillin and oxacillin resistance are equivalent.

Methicillin resistance in staphylococcus species is mediated by the penicillin-binding protein 2a (PBP2a), which has reduced affinity for the penicillinase-resistant penicillins such as methicillin and oxacillin. The mecA gene encodes this protein. By definition, methicillin-resistant strains are resistant to all other beta-lactam antibiotics (amoxicillin-clavulanic acid, cephalaxin). Of further concern, methicillin-resistant strains of *S. pseudintermedius* are often resistant to other classes of antibiotics, such as fluoroquinolones and the sulfonamides. In one study, methicillin-resistant *S. intermedius* strains were sensitive to enrofloxacin only 55% of the time, and marbofloxacin 57% of the time. In the same study, methicillin-sensitive strains were susceptible to both enrofloxacin and marbofloxacin 98.5% of the time, indicating the need to identify resistant strains.

REFERENCEs

Discussion
The two goals of treating recurrent otitis are similar to those of managing recurrent pyoderma: 1) resolve the current infection, and 2) diagnose and manage the underlying cause.

Resolution of otitis media due to *P. aeruginosa* poses some unique challenges compared with other organisms. *Pseudomonas aeruginosa* is an aerobic, non-spore-forming, gram-negative, rod-shaped bacterium. This organism is relatively ubiquitous in the environment, being found in water and soil and on plants. *Pseudomonas aeruginosa* is rarely isolated from normal ears but may be cultured in 20% to 36% of patients with chronic otitis. It is an opportunistic invader. Changes within the ear canal that occur with chronic inflammation (stenosis, ceruminous gland hyperplasia) and repeated treatment may provide a biological niche that allows this organism to thrive.

*Pseudomonas aeruginosa* is often a highly resistant organism and will develop resistance quickly upon exposure to antibiotics.

Otitis media is a common cause of recurrent otitis externa and frequently goes unrecognized because the tympanic membrane is often intact. Numerous diagnostic techniques can be used to diagnose otitis media. Skull radiographs may indicate changes within the bullae that are compatible with infection or inflammation but can appear normal in about 25% of otitis media cases. Computed tomography or magnetic resonance imaging may have increased sensitivity in diagnosing otitis media but are not readily available to many practitioners. In one study, myringoto-
my was the most accurate diagnostic test for otitis media when the tympanic membrane was intact. Myringotomy can be accomplished by passing a micro-tipped culturette through the caudoventral portion of the eardrum into the tympanic bulla. This technique is indicated in cases of chronic recurrent otitis that do not respond to appropriate therapy.

In my opinion, myringotomy and deep ear flush are the most important procedures when *Pseudomonas* otitis is suspected. Exudates, foreign materials (e.g. hairs), old medications, and ceruminous debris can accumulate within the external and middle ear. Purulent debris may inhibit the activity of some antibiotics. In addition, foreign materials may serve as a nidus for future infections. Successful treatment of otitis media depends on thoroughly cleaning the middle ear cavity.

Exercise caution when flushing the middle ear. Many antiseptic products and antibiotics can be ototoxic, leading to deafness or neurologic deficits if they gain entry into the inner ear structures. We generally flush the ear only with saline or tromethamine-EDTA solution. Flushing with tromethamine-EDTA is ideal when *Pseudomonas* species infection is suspected since it potentiates the activity of antibiotics against gram-negative organisms.

### Systemic treatment of *Pseudomonas* otitis

Interestingly, few well-controlled clinical trials have evaluated the efficacy of various treatments for *Pseudomonas* otitis. For that reason, most treatment recommendations are based more on anecdotal reports and personal experience.

The fluoroquinolone antibiotics are generally effective systemic antibiotics against *Pseudomonas* species. Enrofloxacin and marbofloxacin have been shown to have in *vitro* efficacy against this organism. A recent study has shown that ear tissue concentrations of enrofloxacin and its metabolite ciprofloxacin are significantly higher than plasma concentrations after intravenous infusion. A dosage of enrofloxacin at 20 mg/kg given intravenously resulted in the highest tissue concentrations. Tissue concentrations were not high enough to be effective against strains that had intermediate sensitivity or were resistant to enrofloxacin. In general, when enrofloxacin and marbofloxacin are used, we recommend using each drug at the highest recommended dose. Difloxacin and orbifloxacin have poor activity against *Pseudomonas* species and should not be used.

### Corticosteroids and otitis

Corticosteroids decrease pruritus and inflammation, making the dog more comfortable and the ears easier to treat. In addition, they decrease exudate formation, glandular secretions, and stenosis and may reduce some of the chronic changes within the ear canal that promote recurrence. I almost always treat otitis media patients with systemic corticosteroids for the first one to three weeks. By decreasing pain and discomfort, compliance with home treatments is improved. Once the ear is looking better and the patient is more comfortable, systemic corticosteroids are tapered and discontinued. Topical corticosteroids may be useful at this time, depending on the underlying cause of the otitis and the extent of the chronic changes within the ear canals.

### Topical treatment for *Pseudomonas* otitis

Numerous topical medications have been advocated over the years to treat *Pseudomonas* otitis. When otitis media is present, topical therapy alone is generally not effective because therapeutic concentrations may not be achieved within the tympanic bulla.

Tromethamine-EDTA products should be a part of all treatment plans in patients with *Pseudomonas* otitis. Tromethamine-EDTA is a chelating agent that binds metal ions important for cell wall integrity. Additionally, tromethamine-EDTA products used in conjunction with systemic or topical antibiotics may have a synergistic effect. These combination products appear to be more effective for gram-negative organisms than for gram-positive organisms. There are several commercially available tromethamine-EDTA products that I have had good success with.

Enrofloxacin is available as a veterinary-approved otic product in combination with silver sulfadiazine. Both antibiotics have good activity against sensitive organisms.

Polymyxin B is a topical antibiotic with excellent efficacy against *Pseudomonas* species. In some studies, this antibiotic was effective against 95% to 100% of *Pseudomonas* species strains. This antibiotic is not available as a veterinary product. We use a human product containing neomycin, polymyxin B, and 1% hydrocortisone in a solution.

Ticarcillin (systemically and topically) has been shown to be effective against *Pseudomonas* otitis. In one study, 11 of 12 dogs responded to treatment with intravenous ticarcillin (15 to 25 mg/kg three times daily) and topically applied ticarcillin. Long-term intravenous treatment is not realistic in many clinical situations. We have used this antibiotic topically for some patients with success. Once reconstituted, ticarcillin must be used immediately or refrigerated or frozen to maintain stability for future use.

The aminoglycoside antibiotics (gentamicin, neomycin, tobramycin, and amikacin) have been reported to be
Effective against *Pseudomonas* species. From a referral standpoint, I don’t see many strains of *Pseudomonas* species that are still sensitive to gentamicin and neomycin. Anecdotally, tobramycin ophthalmic and amikacin injectable (as a topical) have both been used successfully in many instances by the author and others. Keep in mind that aminoglycosides are potentially ototoxic.

**Monitoring therapy**

These problematic cases require that you recheck the patient every two weeks. Owners should see steady improvement during the course of therapy. An increase in discomfort, redness, or amount of discharge should prompt a call from the owner. Possible reasons for a worsening of signs during treatment include a resistant organism, a new organism, or contact hypersensitivity to ear medications (*i.e.* neomycin). Here are a few helpful tips:

- If an excessive amount of exudate remains within the ear canal at recheck, repeat anesthesia and deep ear flush. Purulent debris within the ear canal can inactivate antibiotics and may serve as a nidus for relapse.
- Continue systemic antibiotics for six to eight weeks, even if the ear looks great at the two-week recheck.
- Continue the topical therapy for two weeks past negative ear cytology.

**Once the infection is resolved, what do I do?**

This question is one of the most important parts of retaining a client. If you are lucky enough to have a dedicated owner who follows your recommendations and the infection resolves, you need to have a plan to keep the infection from returning.

In most cases, otitis media results from direct extension of otitis externa. So, start working through your differentials for recurrent otitis externa. Maintenance home cleaning by the owner is usually required while you work to identify the underlying reason for the otitis. The product I use depends on the predominant organism that caused otitis.

If the underlying cause is most likely allergic, continuing with a topical corticosteroid may be useful to minimize inflammation within the ear canal. Initially, a potent, fluorinated corticosteroid product such as fluocinolone may be indicated. As the signs lessen, changing to a less potent corticosteroid such as hydrocortisone is recommended.

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Antimicrobial Therapy in the Real World

Managing difficult urinary tract infections

The judicious use of appropriate antimicrobials, owner compliance with prescribed medications, and periodic urine cultures to monitor for urine sterility are necessary to successfully manage UTIs in dogs and cats.

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Uncomplicated, community-acquired urinary tract infections (UTIs) in dogs generally occur in healthy dogs, and the most common urinary pathogen has been reported to be strains of *Escherichia coli*, accounting for approximately 45% of all pathogens isolated in one study. When added together, *Staphylococcus*, *Proteus*, *Klebsiella*, and *Enterococcus* species accounted for approximately 40% of all isolates in that same study. A similar bacterial spectrum has been reported in cats with UTIs. It is reported that most cats with UTIs are generally older and have concurrent diseases such as hyperthyroidism or chronic kidney disease.

There are two hypotheses as to why *E. coli* UTIs occur so commonly. The first is titled the special pathogenicity hypothesis, which implies that *E. coli* putative virulence genes contribute to host infection. The second hypothesis, the prevalence hypothesis, states that certain strains of *E. coli* have the ability to persist and predominate in the intestine, allowing these prevalent strains more opportunity to colonize the urinary bladder. Research indicates that in dogs, the special pathogenicity hypothesis seems more plausible, but further research is needed.

Treatment and management of uncomplicated and recurrent UTIs

Before treating a dog or cat for a bacterial UTI, clinicians should first ask themselves whether the patient is likely to benefit from treatment for bacterial cystitis. When a dog or cat exhibits clinical signs such as stranguria, pollakiuria, hematuria, or urinary incontinence, treatment with proper antimicrobials is clearly warranted. Treating dogs or cats with “asymptomatic bacteriuria,” however, has recently become more controversial. Overzealous use of antimicrobials can lead to resistant pathogens and may not improve the patient’s outcome.

The Infectious Diseases Society of America (IDSA) has published guidelines for treating asymptomatic bacteriuria in adult humans. According to these guidelines, people with positive cultures but no clinical signs should be treated only when certain surgical procedures or interventional procedures such as cystoscopy are scheduled. People whose asymptomatic bacteriuria is associated with diabetes mellitus or spinal cord injuries or who may be elderly residents of retirement communities, are rarely treated, however, because such treatment does not appear to affect the outcome, and again, can lead to developing resistant strains of bacteria. (For a complete list of the IDSA’s recommendations for humans, see Refer-
To the author’s knowledge, available methods for treating incidental UTIs in dogs and cats have not been formally investigated. So therapeutic plans for these patients vary by clinician. The author treats dogs and cats with incidental preoperative UTIs, as well as those with a positive urine culture that will be undergoing laser lithotripsy or voiding urohydropropulsion. Theoretically, bacteria could ascend to the upper urinary tract during these latter two procedures, so treatment seems justified. In contrast, the author does not routinely treat bacterial cystitis in dogs and cats with tube cystostomies or indwelling urinary catheters, and, similarly, does not always treat chronic UTIs in patients with micturition problems (e.g., an upper motor neuron bladder) unless the patient develops clinical signs or there is concern that the patient’s infection could spread to sites such as the kidney or prostate. While we have reported that the status of diabetic control in cats appears to be unrelated to a positive or negative urine culture, these animals are oftentimes treated for UTIs, regardless of clinical signs.3 Prospective studies are needed to see whether treatment, particularly for the latter disorders, affects clinical outcome or leads to bacterial resistance. When a UTI is treated, antimicrobial selection should ideally be based on susceptibility testing results.

Urine culture and susceptibility testing
Once a decision is made to treat a cat or dog for a bacterial UTI, administering appropriate antimicrobial therapy and performing periodic urine cultures are ideal. Therapy should be based on the results of urine cultures and susceptibility testing. Although empirical therapy is started in many cases, bacterial identification and susceptibility testing is imperative if the infection recurs. Although some laboratories still offer susceptibility testing based on the Kirby-Bauer disk diffusion method, minimal inhibitory concentration (MIC) values based on an automated dilution method are preferable.

Current in vitro susceptibility testing is based on utilizing a bacterial inoculum of 10^5 CFUs/ml. Discriminatory antimicrobial concentrations are used to interpret the results of susceptibility testing by defining isolates as either sensitive (S), intermediate (I) or resistant (R). Clinical, pharmacological, and microbiological considerations are used to set these

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Figure 1

An algorithm for evaluating cats and dogs with bacterial urinary tract infections.

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[Reference: 4]
levels. MIC values are expressed in μg/ml. The average urine concentration of an antimicrobial must exceed the growth-inhibiting concentration (MIC value) for the infecting bacteria by at least four-fold. If the average urine concentration is greater than or equal to that of the MIC value times four, the drug will be at least 90% effective.

Some commercial laboratories use Kirby Bauer plates or only run trays set up with attainable serum levels of antibiotics. However, attainable urine concentrations of some antimicrobials can be 100 times the attainable serum concentration. For example, enrofloxacin (and its active metabolite, ciprofloxacin) can achieve concentrations of 200 μg/ml in the urine, which is 100 times the attainable serum concentration after a standard oral dose of 5 mg/kg in healthy dogs. However, this is true only if the patient’s kidneys are functioning properly. Clinicians should consult the laboratory to determine whether serum concentrations or urine concentrations of the antimicrobials are used in susceptibility testing for urinary bacterial isolates. If the infection is in the kidneys or prostate, or if kidney disease is diagnosed, serum MIC concentrations should be obtained to treat the patient properly.

Uncomplicated infections
Many patients will have uncomplicated UTIs. In such cases, the urine is sterilized during treatment and remains sterile after cessation of treatment. Although there are no studies to determine duration of therapy for simple, uncomplicated UTIs in dogs and cats, by convention, these patients usually are treated for 10 to 14 days. Studies currently are under way to evaluate dosing strategies for uncomplicated UTIs in dogs. Proper dosing and administration is essential in such cases to prevent misusing antibiotics in ways that could promote resistance. (See Figure 1 for managing bacterial UTIs in dogs and cats.)

Complicated infections
If a patient’s urine is sterile during therapy but the infection recurs weeks or months later, a reinfection or relapsing infection has occurred. Reinfections imply that a new organism or strain of bacteria has invaded the host, while relapsing infections imply that the same pathogen is present. Although antibiograms were thought to be helpful in determining different strains of bacteria, molecular probes using pulse gel electrophoresis appear to be superior in their ability to determine whether persistent infections are due to acquisition of new isolates or failure to eradicate existing isolates. Pulse gel electrophoresis can be requested from certain laboratories. Before pursuing an extensive diagnostic work-up, the clinician should question the client to be certain correct medications were given and no doses were missed. If medications were given as prescribed and reinfection or relapsing infection is diagnosed, the clinician should search for predisposing causes for the infection.

Predisposing factors
For recurrent (> three per year) or persistent infections, other diagnostics such as contrast radiography or ultrasonography should be performed to evaluate for mass lesions or nonradiopaque stones. Cystoscopy with mucosal biopsy (Figure 2) should be considered to evaluate the patient for deep-seated infections. In dogs, even when urine cultures are negative, bladder mucosa or uroliths (if present) can yield positive growth. In mouse models, E. coli has developed within the superficial epithelial cells of the mouse bladder, forming intracellular bacterial communities. These pathogens can emerge once antimicrobial therapy has been discontinued. A similar hypothesis has been proposed in small animal patients. If pyelonephritis, prostatitis, or a deep-seated bacterial infection is suspected, antimicrobials that achieve good tissue concentrations are warranted and the dog or cat should be treated for a longer period of time (one to two months).

Recurrent infections can occur secondary to other predisposing factors. These include metabolic diseases such as hyperadrenocorticism or diabetes mellitus. For this reason, a CBC and biochemical profile should be evaluated in all dogs and cats that have multiple or persistent infections. Other differentials for recurrent infections include a multitude of abnormalities that can occur within the urinary system. For example, a recessed vulva (Figure 3) can predispose to UTIs; performing an episiotomy can prevent perivulvar pyoderma and improve anatomic defenses against uropathogens. Antibiotics should be continued for at least two to three weeks after surgery. Micturition disorders, such as urinary incontinence or urine retention, should
be addressed. If polypoid cystitis or urachal diverticuli are noted with imaging studies, removal of these structures can help remove the nidus for infections. Some bacteria such as *Corynebacterium urealyticum* can lead to pronounced struvite plaque formation that can cover the urothelium. This plaque needs to be debrided either surgically or cystoscopically in order for the antibiotic to have good contact with the urothelium (*Figure 4*). In older dogs or cats that present with recurrent UTIs, a search for urinary tract neoplasms should be performed.

**Uroliths:** Uroliths can predispose to UTIs by acting as a nidus for infection. The most common uroliths in cats and dogs are calcium oxalate and struvite. If an infection is found in a patient with a calcium oxalate stone, the infection likely occurred secondary to the urolith being present. However, struvite stones in dogs usually are formed by urease-producing bacteria, such as *Staphylococcus intermedius* and *Proteus* species. Dissolution of these stones can be attempted with diet and antimicrobial therapy. Penicillins and fluoroquinolones are good choices for these pathogens. All antibiotics must be given throughout the dissolution protocol.

The key to successful management of both uncomplicated and complicated UTIs in dogs and cats is the evaluation of urine culture throughout therapy. Ideally, urine should be collected by cystocentesis, cultured seven days after antimicrobial therapy has started, and again seven to 10 days after cessation of the antimicrobial. This will allow the clinician to distinguish persistent infections from reinfections and decide if further workups are needed.

**Bacterial prostatitis:** Bacterial prostatitis is a chronic or acute condition in sexually intact male dogs. Dogs with benign prostatic hypertrophy or squamous metaplasia may be at risk for bacterial infections in the prostate. Acute prostatitis can have serious systemic ramifications, including depression, dehydration, and leukocytosis. Vomiting, diarrhea, and septic shock may also occur. In addition, chronic prostatitis can occur with vague clinical signs. In chronic cases, the prostate is usually symmetrical and nonpainful upon palpation. Many dogs with chronic prostatitis will present with chronic UTIs, weight loss, or prepuce discharge. Prostatic abscesses can occur after acute or chronic prostatitis, and may cause life-threatening peritonitis if such abscesses are allowed to rupture.

Most dogs with bacterial prostatitis also have a bacterial cystitis. The pathogens commonly isolated are very similar to isolates obtained from the bladder. Although urine cultures will suffice for most dogs, prostate cultures are indicated when there is a negative urine culture or when the animal has clinical signs despite appropriate treatment. Prostatic fluid can be obtained by ejaculation, prostatic massage, and most commonly by ultrasound-guided fine needle aspirate of the prostate. The fluid should be analyzed for cytologic abnormalities and cultured for pathogens. Diagnostic imaging, such as abdominal ultrasonography or retrograde contrast study (*Figure 5*), should be performed to evaluate the prostate for size, cysts, and abscesses, as well to evaluate for neoplasia. While the prostate can be mineralized in intact dogs with bacterial prostatitis, when seen in neutered dogs, prostatic mineralization is highly suggestive of prostatic neoplasia.

Treatment of prostatitis involves appropriate antimicrobial therapy and castration. Castration should be performed as soon as the patient is stable enough to undergo anesthesia. If castration is not an option for a breeding animal, the 5-alpha-reductase inhibitor, finasteride (0.1 to 0.5 mg/kg once daily), can be used to help decrease the size of, and secretions from, the prostate. Surgical removal of the prostate is rarely performed because high mor-
bidity associated with that procedure. However, prostatic abscesses often need to be surgically addressed, and omentalization of the prostatic abscess is performed to prevent fluid and purulent material from accumulating in the area.

Antimicrobial treatment for acute prostatitis should be continued for at least four weeks. For chronic prostatitis, longer treatment regimens are often warranted. Due to the blood-prostate barrier, it can be difficult to achieve antibiotic levels above the desired MIC for the bacterial pathogen. Although the blood-prostate barrier is often broken in acute prostatitis, antibiotics capable of penetrating the blood-prostate barrier should be used to ensure that they are present as the infection resolves. For example, due to this barrier, antibiotics with high lipid solubility, low protein binding, and an appropriate pKa should be used. While non-ionized forms of antibiotics pass through lipid membranes, ionized forms do not. For gram-negative prostate infections, trimethoprim-sulfonamides, chloramphenicol, and the fluoroquinolones are most appropriate. Enrofloxacin (10 mg/kg orally once daily; higher doses may be needed) is the drug of choice for canine bacterial prostatitis due to its high lipid solubility, low protein binding, low MIC profile, and broad spectrum of activity against many uropathogens. Furthermore, unlike the other two antibiotics, side effects with enrofloxacin are rare. Oral enrofloxacin is readily absorbed from the GI tract and approximately 20% to 40% is metabolized to its active metabolite, ciprofloxacin. Similar fractions of metabolized enrofloxacin have been reported after either intravenous or oral administrations of the drug.

Oral ciprofloxacin should not be used as a substitute for enrofloxacin because the bioavailability of ciprofloxacin varies widely and is approximately only 40% in dogs. The routine dose of enrofloxacin for prostatitis is usually 10 mg/kg once daily. Higher doses may be needed for certain strains of Pseudomonas species. Once-daily dosing is preferred because it achieves higher maximum concentrations of the antibiotic.

**Summary**

While diagnosing and treating UTIs in dogs and cats can be rewarding, it requires owner compliance with prescribed medications, periodic urine cultures to monitor for urine sterility, and judicious use of appropriate antimicrobials. In complicated UTIs, searching for and eradicating underlying causes often prevents future infections. When infections are present in a patient’s kidney or prostate, longer courses of therapy should be implemented using appropriate antimicrobials and performing subsequent cultures to confirm effectiveness. New therapies for recurrent infections, particularly those related to *E. coli*, are being investigated in mouse models. Further research is warranted in dogs and cats with both uncomplicated and complicated UTIs in order to provide data for better treatment regimens and monitoring protocols.

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