

Topical Therapy of Otitis Externa

Canine ear disease is a prevalent and persistent problem and accounts for up to 15% of all canine veterinary case presentations. The large variety and quantity of veterinary topical otic preparations available demonstrate the demand for a wide range of therapeutics for this condition. Primary causes of otitis externa include hypersensitivity disorders (e.g., atopy, food allergy), parasitic diseases, and metabolic disorders (e.g., primary keratinization defects, hypothyroidism, hyperadrenocorticism).

Perpetuating and predisposing factors such as proliferative changes, excessive cleaning, or the use of inappropriate cleaning products also contribute to the prevalence of ear problems. Otitis externa can also be secondary to an infection of the ear canal. *Malassezia pachydermatis* is the most common isolate from diseased ears. Identifying and managing the primary disease(s) are the goals of treating most cases of canine otitis externa and are often sufficient to prevent recurrence if no perpetuating factors are present. However, even when the primary cause is identified and addressed, cases occasionally require continuous topical and/or systemic therapy. On the other hand, in some cases of allergic otitis, as well as other chronic primary conditions, controlling secondary infections is sufficient to alleviate clinical signs. Otic preparations are designed to either address an immediate infection/infestation or prevent recurrence in chronic disease. Otic preparations that address bacterial and/or yeast infections are usually combinations of corticosteroids and antimicrobials. Preparations designed for long-term control are combinations of mild cleansers, drying agents, or disinfectants and may contain antimicrobial agents. Overall the therapeutic approach to chronic ear disease is truly an art, and there is no “blanket” approach for treating this condition. Each case represents varying levels of proliferation and exudate with a different degree of infection versus inflammation. Therapy needs to be targeted at each aspect of the condition. Becoming familiar with the products available and their effects is essential to formulating the best therapeutic plan for each patient. Since new products are introduced into the market each month, it is important to have a good relationship with the various industry representatives who can keep the practitioner updated on what is newly available and the advantages the products may provide.

General Properties of Topical Formulations

The Vehicle

As with all forms of topical therapy, multiple formulations and vehicles are used in otic products. Each has specific properties that need to be considered when selecting an appropriate product. The various vehicles have different mechanisms for delivery of the active ingredients, as well as therapeutic, irritant, or cosmetic properties that determine their efficacy in practice. Various vehicles encountered in veterinary topical otic therapy include solutions/rinses, lotions, creams, emulsions, and ointments. Rinses generally are formulated by diluting concentrated solutions or powders with water. These can be poured into the ear in large amounts and therefore are the most appropriate vehicle for cleansers. Lotions are liquids in which the active ingredient has been dissolved or suspended. Thus, when the liquid dries, a thin layer of powder is left in the ear. Lotions tend to be drying because of their alcohol or

propylene glycol content. Generally a “cooling” lotion or solution tends to contain alcohol, whereas a “soothing” one does not. Creams, emulsions, and ointments are occlusive and prevent contact with the environment. Creams are least occlusive, and ointments are the most occlusive; emulsions have characteristics of both. In exudative cases, use of an ointment may be contraindicated since increased water loss and drying are desired.

Active Ingredients

Astringents, soothing agents, acidifiers, alkalinizing agents, keratolytic agents, keratoplastic agents, antibiotics, antifungals, and antiinflammatory and antiparasitocidal products all can be found in the enormous milieu of topical otic preparations. Often these products are combined. When a practitioner is choosing a topical otic product, the patient’s specific condition, as well as the practitioner’s familiarity with the product, must be taken into consideration. Practitioners and dermatologists occasionally prepare “in-house” otic remedies from injectable antibiotics or antifungal agents or mix a variety of available otic products to create a single mixture that targets their specific patient’s need. This practice is a controversial and extralabel use of these drugs and is a topic beyond the scope of this chapter. However, if this approach is taken, it is important to remember that the stability and efficacy of the active ingredients may be affected, and the client must be clearly informed of the off-label formulation.

Treatment of Infections

Initial Approach

Cytology: Cytology is an inexpensive procedure that can be performed easily in house, allowing the practitioner to make immediate decisions regarding treatments or further diagnostics; it should be performed with every reevaluation of the ear. Often the character of the infection or the degree of inflammation will change. Repeating cytology may reveal a change in the infectious organisms that indicates that a change in the topical antimicrobial is in order. In addition, the presence of various inflammatory cells could be a sign that an irritant or allergic/immune-mediated reaction might be present. If a practitioner is not comfortable making decisions based on his or her abilities, duplicate slides can be submitted to a commercial laboratory for corroboration.

Cleaning

Cleaning and removing purulent, ceruminous, or foreign debris from an ear canal before initiating therapy is imperative for effective management of otitis. In addition to being therapeutic, cleaning removes exudates that can not only prevent a thorough examination of the ear canal but also interfere (chemically and physically) with the therapeutic agents. Ceruminolytic agents used in the clinic can aid greatly in removing debris; however, use of the more potent ceruminolytic formulations is not generally recommended for home care by the client. Table 95-1 lists a variety of different cleansers that can be selected based on severity of debris in the ear canal and whether the product is to be used in the practice or at home by the owner. Numerous cleaning techniques are described in the literature

Cleaning is imperative for successful therapy; however, excessive cleaning by clients is often a perpetuating factor in chronic recurrent otitis. It is generally found that the initial cleaning is best left to the clinician during the initial acute phase of therapy. Once the acute episode is resolved, clients can be given products and instructions to keep the ears from relapsing. Most cleansers should be used no more than two to three times weekly. In some cases of mild otitis secondary to mild seasonal allergies, regular cleaning should only be recommended during the offending season or not recommended at all. One of the exceptions to this rule is in cases of chronic ceruminous otitis (e.g., cocker seborrhea). In this case regular ear cleaning and maintenance by the client are extremely important if any kind of therapeutic success is to be achieved.

Antibacterial Therapy

Topical therapy of active infections is imperative to success.

Systemic (oral or injectable) therapy is sometimes necessary but is unlikely to achieve therapeutic concentrations within the ear as a sole treatment modality. The antimicrobial agent best used is often chosen empirically based on cytologic examination of ear canal exudate and otoscopic evaluation of the ear canal.

Bacterial culture and sensitivity results can be of value, especially when dealing with gram-negative organisms (e.g., *Pseudomonas* spp.) from the middle ear. However, sensitivity results of bacterial cultures may be misleading since topical antimicrobial concentrations are much higher than serum concentrations. Occasionally cultures need to be repeated because infected ear canals often contain numerous bacteria colonies with different resistant patterns that are not all represented with one single culture.

Several veterinary topical otic formulations contain antibacterial agents (Table 95-2). It is important to consider previous therapies the patient may have received for the infection, the type of bacteria encountered, and the degree of inflammation and amount of exudate in the ear canal. If the canals are severely inflamed, the patient will likely need to return on a weekly basis for cleaning and reevaluation until the bulk of the infection and inflammation is resolved. For more resistant bacterial infections, especially gram-negative infections such as *Pseudomonas aeruginosa*, pretreatment of the canal with a tromethamine ethylenediaminetetraacetic (Tris EDTA)-containing product before administration of a topical antibiotic is recommended. Tris EDTA has antibacterial properties but also acts synergistically with aminoglycosides and fluoroquinolones to increase their bactericidal activity. A product (T8 Keto) is available that contains both Tris EDTA and ketoconazole to help control mixed bacterial and yeast infections.

Antiyeast Therapy

Numerous products are available to address yeast otitis. Many of these products contain potent, broad-spectrum antibiotics; however, the antifungal included is sometimes less potent against the commonly encountered yeast organism *M. pachydermatis*. On the other hand, in cases of mild allergic yeast otitis, decreasing the otic inflammation with a topical glucocorticoid alone can aid in the elimination of a yeast

infection or overgrowth by controlling many of the inflammatory by-products on which yeast survive. In chronic recurrent yeast otitis the use of boric acid or acetic acid-containing products is often effective in preventing recurrence of infection. Acetic acid may be markedly irritating to the ear canal, especially at concentrations of 2% or higher (white vinegar has a concentration of 5%). It has generally been found that boric acid solution, without the presence of acetic acid (Zinc Otic) is effective at managing chronic recurrent yeast otitis and has been demonstrated effective in treatment of mild-to-moderate acute yeast otitis.

Anti inflammatory Therapy

The majority of antimicrobial topical formulations contain antiinflammatory agents (Table 95-4). These aid in decreasing inflammation of the canal associated with the primary ear disease and also reduce inflammation from secondary infections. In some situations products used to clean and treat the ear can have irritant effects, and the addition of glucocorticoids may counteract some of these effects. It is important to remember that the use of products containing more potent steroids such as dexamethasone or betamethasone can suppress the adrenal axis and that animals may exhibit systemic side effects when these are used on a long-term basis. A recently released formulation is a mixture of gentamicin, clotrimazole, and mometasone (Mometamax). Mometasone is a potent topical glucocorticoid, with minimal systemic effects in normal and laboratory animals. It also has longer residual effects, thus allowing for once-daily therapy, and is potentially less of a concern for adrenal axis suppression. Products containing hydrocortisone can potentially be used for chronic recurrent otitis secondary to mild allergies.

However several of these products contain ingredients that are irritating, which can negate the mild antiinflammatory effect of hydrocortisone. Maintenance hydrocortisone products need to be selected on a case-by-case basis, depending on how effective they are in controlling the inflammation from the primary disease, usually allergic. They are not very beneficial in acute, exudative, or proliferative otitis.

Topical Ototoxicity

Patients with otitis commonly present with ruptured tympanic membranes. Certain formulations contain ingredients that have been shown to be ototoxic and are contraindicated when a ruptured tympanum is present.

Ototoxicity is defined as the tendency of certain therapeutic agents to cause functional impairment and cellular degeneration of the inner ear and the eighth cranial nerve. It may be reversible or irreversible. Ototoxicity is differentiated from neurotoxicity, in which the site of action is central to the eighth cranial nerve. Most notable of the ototoxic drugs are the aminoglycoside antibiotics (especially gentamicin), but other numerous known ototoxic agents are listed below (Box 95-1). Products such as acetic acid that are not ototoxic but are irritating can also be a concern. At times culture and sensitivity testing directs clinicians to use ototoxic antibiotics if other options are not available. Dermatologists may recommend these products in resistant cases; however, the client must be informed of the risks and benefits of pursuing this therapy.

Maintenance of Chronic Recurrent Conditions

Cases of chronic, recurrent otitis are usually secondary to an inadequately controlled primary condition, permanent damage to the ear canal, or undiagnosed/uncontrolled otitis media. Changes to the canal from chronic recurrent disease can destroy the physical and immunologic mechanisms of the ear canal that keep it free of pathogens and debris. This makes the ear even more susceptible to recurrent infections. Table 95-1 gives a list of products frequently used by veterinarians; however, scores of products are available over the counter through pet stores and on the Internet. It is important to know which products are being applied into the patient's ears and to understand their possible effects.

Maintenance therapy has the following goals:

1. To keep the ear clean and free of excess wax and ceruminous debris. This is achieved with cleaning and sometimes antiinflammatory agents that decrease excessive wax and cerumen production.
2. To decrease inflammation and pruritus, thus avoiding self-trauma and discomfort. This is achieved by addressing the primary disease and providing antiinflammatory therapy and/or by achieving the other goals listed and thus decreasing the inflammation.
3. To decrease the number of infectious organisms in the canal and maintain an "unfriendly" environment or their growth, by either decreasing the canal pH or adding detergents or other products that interfere with microorganism metabolism and growth.
4. To provide therapy that promotes regulation of epithelialization and wound healing. For example, products such as Alocetic or Otirise contain aloe to help soothe and maintain the moisture barrier of the ear canal. Another product, Duoxo micellar solution contains phytosphingosine and other products to decrease excessive buildup in seborrheic conditions. In addition, Zinc Otic contains zinc gluconate with the goal of promoting normalization of canal epithelium and wound healing.