

Otitis Externa Series: Part 2

Topical Therapy for
OTITIS EXTERNA

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In Part 1 of this series—*Diagnosis of Otitis Externa*—the factors and causes of this disease, diagnostic testing and imaging, and ear cleaning and flushing were discussed. Visit tvjournal.com to read this article, which was published in the September/October 2014 issue of Today's Veterinary Practice.

Ear disease accounts for up to 15% of all canine veterinary case presentations.^{1,2} Regardless of the primary cause of otitis externa, secondary infection treatment is usually the focus of therapy.

Otic preparations that address bacterial and/or yeast infections are usually combinations of antimicrobials and corticosteroids. The large number of commercial topical otic preparations reflects the demand for these products.

It is important to understand the underlying causes of otitis, as well as factors that contribute to the condition, in order to provide targeted therapy and effective treatment (Table 1).

TABLE 1. Common Factors & Causes of Otitis Externa

PREDISPOSING FACTORS	<ul style="list-style-type: none"> Abnormal external ear canal and pinna conformation, such as congenital stenosis Excessive moisture within ear canal Adverse effects from previous treatments, such as topical reactions
PRIMARY CAUSES	<ul style="list-style-type: none"> Atopic dermatitis Food allergy Epithelialization disorders, such as seborrhea Metabolic disorders, such as hypothyroidism Neoplasia
SECONDARY CAUSES	<ul style="list-style-type: none"> Yeast overgrowth Bacterial overgrowth
PERPETUATING FACTORS	<ul style="list-style-type: none"> Ear canal/pinna fibrosis and stenosis Calcification of tissues Neoplasia (polyps, tumors, cysts) Excessive cleaning and/or inappropriate use of cleaning products²⁻⁵

OTIC CYTOLOGY

Otic cytology is an integral part of:

- Diagnosing otic disease
- Determining best treatment approach and maintenance protocol
- Assessing treatment success.

Otic cytology is inexpensive, highly informative, and easily self-taught. With practice, the practitioner can quickly become familiar with samples from inflammatory lesions, including recognition of:

- Bacteria
- Yeast (**Figure 1**)
- Dermatophyte spores and hyphae (**Figure 2**)
- Other fungal conditions, such as aspergillosis or cryptococcosis
- Parasites (**Figure 3**)
- Foreign material (**Figure 4**).

Cytology is an integral part of therapy and needs to be performed throughout the treatment process to monitor and adjust your treatment. Part 1 of this article series provides more in-depth discussion of otic cytology.

OTIC FORMULATIONS

General properties of topical otic formulations include 2 important components—the vehicle and the active ingredient.

Vehicle

Otic product vehicles have different properties that determine their efficacy in practice, and their functions include (Table 2):

- Promoting delivery of active ingredients
- Stabilizing active ingredients
- Determining drying or occlusive properties
- Modifying pH
- Adding factors, such as texture and fragrance, to enhance product pleasance.

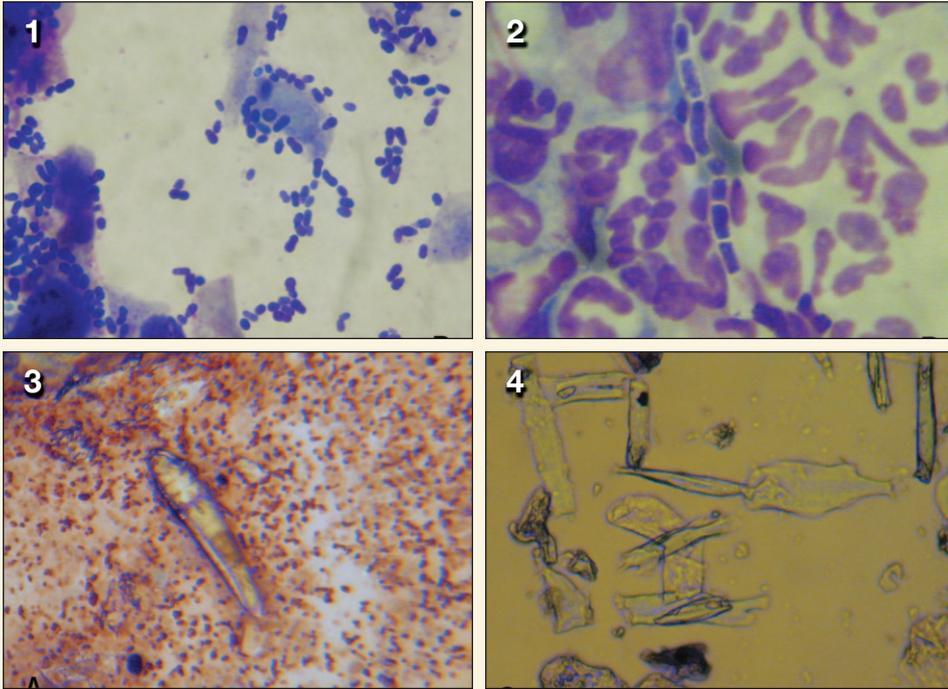


Figure 1. Yeast organisms revealed on cytology of purulent otic exudate (Diff Quik; 1000x).

Figure 2. Fungal hyphae revealed on cytology of purulent debris from a patient with severe unilateral otitis (Diff Quik; 1000x).

Figure 3. Demodex mite identified on otic cytology (Diff Quik; 100x).

Figure 4. Accumulation of medication crystals revealed on cytology from a patient exhibiting signs of otic irritation during treatment with otic product. Oscopic examination revealed white exudate in ear canal; cytology indicated contact irritation from medication crystals despite resolution of infection (Diff Quik, 1000x).

However, product vehicles can have irritant properties, which must be taken into consideration.

Active Ingredient

When a practitioner chooses a topical otic product, appropriate treatment for the patient’s specific condition, as well as the practitioner’s familiarity with the product, must be taken into consideration. Active ingredients of topical otic preparations are often combined to reach a desired effect (Table 3).

EAR CLEANING

As described in Part 1 of this article series, ear cleaning is imperative for successful otitis therapy. In many cases, the ears should be thoroughly cleaned by the veterinarian, followed by owner administration of medications at home.

Excessive cleaning by clients can be a perpetuating factor in chronic recurrent otitis. Most cleansers should be used no more than 2 to 3

times weekly, and sometimes not at all. Frequency of cleaning is based on the amount of inflammation and degree of exudate, wax, or debris that is being produced, which depends on the primary condition and perpetuating factors.

When regular cleaning is imperative, consider the patient and type and amount of exudate. For example:

- In cases of chronic ceruminous otitis—most commonly seen in idiopathic seborrhea in cocker spaniels—regular ear cleaning and maintenance by the client is extremely important.
- In dogs with increased ceruminous (waxy) debris build-up, ceruminolytic action is desired (Table 4, page 26-27).^{3,6,7}
- Drying cleansers can be used to prevent infection in “allergic” ears that tend to develop infections but are not severely exudative.

TABLE 2. Otic Formulation Vehicles

VEHICLE	INDICATIONS & CONTRAINDICATIONS
Rinse solutions	<ul style="list-style-type: none"> • Can be poured into the ear canal in large amounts • Most appropriate for cleansing and disinfecting
Lotions	<ul style="list-style-type: none"> • Soothing lotions or solutions usually do <i>not</i> contain alcohol • Cooling lotions or solutions generally contain alcohol • Alcohol or propylene glycol tends to be drying; drying agents are often used in maintenance protocols • However, alcohol can be irritating, particularly in erosive and ulcerative ears
Creams Emulsions Ointments	<ul style="list-style-type: none"> • Occlusive properties prevent contact with the environment • Creams are least occlusive, ointments are most occlusive • May be contraindicated in exudative otitis cases, when increased water loss and drying are desirable^{3,6}

TABLE 3. Otic Formulation Active Ingredients

Acidifying agents	Ceruminolytic agents
Alkalinizing agents	Disinfectants
Antibiotics	Keratolytic agents
Antifungals	Keratoplastic agents
Anti-inflammatories	Parasiticides
Astringents	Soothing agents

TABLE 4. Veterinary Otic Formulations

AGENT	BRAND NAME	ACTIVITY & INDICATIONS
CLEANSERS & RINSES		
<i>Ceruminolytics</i>		
Phytosphingosine	Douxo Micellar Solution (ceva.us)	<ul style="list-style-type: none"> • Anti-inflammatory/antimicrobial properties • Removes cellular debris and excess sebum (wax) • Can be used for soothing, seborrheic conditions, and maintenance
Squalene	Cerumene (vetoquinolusa.com) KlearOtic (dechra-us.com)	<ul style="list-style-type: none"> • Softens and removes exudate • <i>Not</i> generally used for maintenance because it may overly strip ears affected by chronic allergic otitis
<i>Maintenance Products</i>		
Phytosphingosine	Douxo Micellar Solution (ceva.us)	See above
Spherulites (lactic acid and salicylic acid)	Epi-Otic <i>Advanced</i> (virbacvet.com)	<ul style="list-style-type: none"> • Variety of acidic solutions • Used for mild and chronic recurrent cases of allergic and infectious otitis • Maintain pH of ear canals • Prevent bacterial adherence and overgrowth • Deodorizes ears • Spherulites and zinc help maintain healing of ear canal • Disinfectant, cleansing, and drying activities promote wound healing
Zinc (boric acid)	Maxi/Guard Zn4.5 Otic (addisonlabs.com)	
Disinfectant Cleansing agents Drying agents	Clean N Dry (pinnaclifeanimalhealth.com) Epi-Otic (virbacvet.com) MalAcetic Otic (dechra-us.com) OtiClens (zoetis.com)	
Enzymes	Zymox Otic (petkingbrands.com)	
ANTIBACTERIAL PRODUCTS		
<i>Fluoroquinolones</i>		
Enrofloxacin	Baytril Otic (bayerdvm.com)	<ul style="list-style-type: none"> • Bactericidal for gram negative and gram positive bacteria • Some products can be irritating
Orbifloxacin	Posatex (merck-animal-health-usa.com)	
<i>Aminoglycosides</i>		
Gentamicin	Mometamax (merck-animal-health-usa.com) Otomax (merck-animal-health-usa.com) Easotic (virbacvet.com) Generic formulas: Betagen Otic (medpharmex.com)	<ul style="list-style-type: none"> • Bactericidal for gram negative bacteria • Bactericidal for staphylococci • Reported ototoxicity
Neomycin	Dermalone (vedco.com) Tresaderm (us.merial.com) Generic formulas	
<i>Other</i>		
Polymyxin	Surolan (elanco.com)	<ul style="list-style-type: none"> • Contains miconazole for synergistic effect against <i>Staphylococcus</i> and yeast • Effective for gram negative rods, including <i>Pseudomonas</i> and <i>Escherichia coli</i> infections
Silver sulfadiazine	Baytril Otic (bayerdvm.com) Silvadene Cream (pfizer.com)	<ul style="list-style-type: none"> • Bacterial cell disruption • Broad spectrum antibacterial • Some antiyeast activity
Tromethamine (Tris) EDTA	Keto-Tris Flush (ceva.us) Keto-Tris Flush PS (ceva.us) Tris Flush (ceva.us) Triz EDTA (dechra-us.com) Triz EDTA Plus (dechra-us.com) Triz Ultra + KETO (dechra-us.com) T8 Keto (bayerdvm.com)	<ul style="list-style-type: none"> • Alkalinizing chelating agent • Effective for gram negative infections • Can be used synergistically with antibiotics, such as an aminoglycoside or fluoroquinolone

TABLE 4. Veterinary Otic Formulations

AGENT	BRAND NAME	ACTIVITY & INDICATIONS
ANTIFUNGAL PRODUCTS		
Clotrimazole	Otomax (merck-animal-health-usa.com) Generic formulas	<ul style="list-style-type: none"> Moderate potency against <i>Malassezia pachydermatis</i>
Ketoconazole	Keto-Tris Flush (ceva.us) Keto-Tris Flush PS (ceva.us) Triz Ultra + KETO (dechra-us.com) T8 Keto (bayerdvm.com)	<ul style="list-style-type: none"> High potency against <i>M pachydermatis</i>
Miconazole	Surolan (elanco.com) Generic formulas	<ul style="list-style-type: none"> Surolan is the only remaining veterinary labeled product (2.3% concentration) Numerous generic companies make a 1% lotion
Nystatin	Dermalone (vedco.com) Generic formulas	<ul style="list-style-type: none"> Polyene antifungal Relatively weak against <i>M pachydermatis</i>
Posaconazole	Posatex (merck-animal-health-usa.com)	<ul style="list-style-type: none"> Newer generation triazole Potent antifungal
Thiabendazole	Tresaderm (us.merial.com)	<ul style="list-style-type: none"> Benzimidazole antifungal
ANTI-INFLAMMATORY PRODUCTS		
Betamethasone	Otomax (merck-animal-health-usa.com) Generic formula: Betagen Otic (medpharmex.com)	<ul style="list-style-type: none"> Potent steroid 25× more potent than hydrocortisone Even short term use can result in suppression of the adrenal axis and systemic effects
Dexamethasone	Tresaderm (us.merial.com)	
Dimethyl sulfoxide (DMSO)	Synotic (zoetis.com)	<ul style="list-style-type: none"> Nonsteroidal anti-inflammatory Possible antifibrotic activity
Fluocinolone acetonide	Synotic (zoetis.com)	<ul style="list-style-type: none"> Potent steroid 100× more potent than hydrocortisone
Hydrocortisone	Malacetic HC (dechra-us.com) Medicated Ear Hydrogel (pinnaclifeanimalhealth.com) Zymox Otic (petkingbrands.com)	<ul style="list-style-type: none"> Hydrocortisone based products are safest Generally only effective in mild allergic otitis conditions Best used as maintenance product
Hydrocortisone aceponate	Easotic (virbacvet.com)	<ul style="list-style-type: none"> Potent steroid Minimal systemic absorption
Mometasone	Mometamax (merck-animal-health-usa.com) Posatex (merck-animal-health-usa.com)	
Triamcinolone	Generic formulas	<ul style="list-style-type: none"> Moderately potent steroid Capable of creating systemic effects

ANTIMICROBIAL THERAPY

Topical antimicrobial therapy for active infections is imperative to success. The antimicrobial agent best utilized is initially often chosen empirically based on:

- Cytologic examination of ear canal exudate
- Otosopic evaluation of the ear canal.

Antibacterial Therapy

Several veterinary topical otic formulations contain antibacterial agents (Table 4).

The use of bacterial culture and sensitivity (C/S) of otic exudate to determine antibiotic selection is controversial.

The concentration of antibiotics in topical otic preparations is much higher than those tested at the laboratory to determine the minimum inhibitory concentration (MIC) of any bacteria. Thus, some bacteria with a low MIC (that would usually be considered resistant) may actually prove

to be sensitive to topical otic preparations. However, when the MIC is 0, complete bacterial resistance is likely, and use of an antimicrobial at any concentration against the resistant organism will not be helpful.

In general, C/S tends to be more useful when there is:

- Persistence of bacteria despite antibiotic therapy
 - Middle ear involvement.^{2,3}
- When treating with antimicrobials:
- Use fluoroquinolones with caution against *Staphylococcus* species; reports demonstrate an increased likelihood of oxacillin-resistant bacteria development.⁸
 - Consider pretreating the ear canal with a product containing tromethamine ethylenediaminetetraacetate (Tris EDTA) prior to administration of a topical antibiotic when addressing resistant bacterial infections, especially gram negative infections, such as *Pseudomonas aeruginosa*.

OTOTOXICITY

Although a large percentage of products that are commercially available contain potentially ototoxic agents, they rarely create any complications; however, the client should be informed of the risks and benefits of any topical therapy.² Clients should be made aware of signs of ototoxicity, which usually present as hearing loss. If such signs develop, the patient should be immediately brought into the clinic for flushing and irrigation to remove the product from the ear.

Patients with otitis can present with ruptured tympanic membranes. When a ruptured tympanum is present, certain otic formulations are contraindicated because they often contain aminoglycosides, which can be ototoxic. In addition, products that are not ototoxic, but are irritating, such as acetic acid, can also be of concern.

Remember that ototoxicity can occur even if the tympanic membrane is intact.

- Tris EDTA has both antibacterial properties and synergistic bactericidal activity with aminoglycosides and fluoroquinolones.

Silver sulfadiazine may be used instead of other antibiotics for treatment of some bacterial infections, although accumulation of medication debris in the ear canal may limit its long-term use. Newer generation colloidal silver-based products are now becoming available.

Antifungal Therapy

Malassezia pachydermatis is the most common isolate from diseased ears.^{2,4} Numerous products are available to address yeast otitis (Table 4). In many cases of mild allergic yeast otitis, decreasing otic inflammation with a topical glucocorticoid alone can resolve the infection.

- Thiabendazole, clotrimazole, and miconazole are used alone or, more commonly, in combination with a corticosteroid and antibiotic.
- Ketoconazole is available in combination with Tris EDTA.^{2,3,9}

In chronic recurrent yeast otitis, the use of products that contain boric or acetic acid can be effective in preventing recurrence of infection.⁹

- Boric acid solutions are:
 - » Generally effective at managing chronic recurrent yeast otitis
 - » Effective in treating mild to moderate acute yeast otitis⁹
 - » Not apparently effective against bacterial organisms.
- Acetic acid solutions may markedly irritate the ear canal, especially at concentrations of 2% or higher.

ANTI-INFLAMMATORY THERAPY

The majority of antimicrobial topical formulations contain anti-inflammatory agents (Table 4), which aid in decreasing inflammation of the ear canal associated with:

- Primary ear disease

- Secondary infections.

Topical use of corticosteroids as anti-inflammatory agents is necessary to decrease inflammation and pain in the ear canal when treating otitis. Topical use is less likely to result in adverse clinical signs compared with systemic use; however, many commonly used corticosteroids, such as betamethasone and dexamethasone, have shown systemic absorption to some extent.¹⁰

Mometasone is a potent glucocorticoid that has minimal systemic absorption, making it potentially less of a concern for adrenal axis suppression; it also has longer residual effects, allowing for once daily therapy.

Hydrocortisone aceponate is converted to HC17 propionate, a highly active anti-inflammatory with potency equivalent to that of dexamethasone. Further, absorption through the skin and ear causes the drug to become deactivated, allowing it to be excreted without causing systemic effects.¹

Hydrocortisone can potentially be used for chronic recurrent allergic otitis, but is not usually beneficial in acute, exudative, or proliferative otitis.^{2,3} Maintenance products containing hydrocortisone need to be selected on a case-by-case basis, depending on their efficacy in controlling inflammation.

MAINTENANCE THERAPY

Cases of chronic recurrent otitis are usually secondary to an inadequately controlled primary condition, which can result in damage to the ear canal lining and the normal physiologic mechanism for ear cleaning, further complicating the chronicity. Also, undiagnosed and/or uncontrolled otitis media can cause chronic otitis externa.

Preparations designed for long-term control are combinations of:

- Mild cleansers
- Drying agents or disinfectants
- Sometimes antimicrobial agents.

See **Goals of Maintenance Therapy** for further information. ■

C/S = culture and sensitivity; MIC = minimum inhibitory concentration; Tris EDTA = tromethamine ethylenediaminetetraacetate

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Goals of Maintenance Therapy

1. **Keep the ear clean** and free of excess wax and ceruminous debris by:
 - Cleaning at a frequency determined by the veterinarian (see text)
 - Using corticosteroids (sometimes) to decrease excessive wax/cerumen production.
2. **Decrease inflammation and pruritus**, avoiding self-trauma and discomfort, by:
 - Addressing primary disease
 - Providing anti-inflammatory therapy.
3. **Decrease the number of infectious organisms** in the canal and maintain an environment that slows or prevents their growth by:
 - Decreasing the canal pH
 - Using disinfectants or other products that interfere with microorganism metabolism and growth.
4. **Provide therapy** that promotes regulation or normalization of epithelialization and wound healing by using products containing zinc or phytosphingosine.

ear rinse containing tromethamine, EDTA, benzyl alcohol and 0.1% ketoconazole on *Malassezia* organisms from dogs with otitis externa. *Vet Dermatol* 2007; 18(2):115-119.

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