

## SA228 & SA229

### TREATMENT OF OTITIS EXTERNA & MEDIA I & II

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#### Overview of the Issue

Topical therapy is very important in the management of otitis externa and otitis media. Topical therapies include ceruminolytic agents, cleaning and drying agents, antiseptics, antimicrobial agents, and glucocorticoids. There are several situations involving otitis externa that require special attention in management. These include: *Pseudomonas* infections, *Malassezia* infections, hyperplastic changes and maintenance therapy for allergic animals. First there are some general principles that should be considered in the management of infectious otitis externa and media in dogs. We will first discuss a few general principles then we will detail treatment options for some of the more difficult scenarios.

#### General Principles:

- All cases presenting for evaluation of ear disease must have cytologies performed.
- Owners should be informed that management of chronic ear infections cannot be done thru the telephone or by the “smell” test. It is important to monitor patients treated for bacteria and/or yeast, preferably 2-3 weeks after initiating therapy. At that time, otic examination and microscopic examination of the ear exudate should be repeated. If there has been no improvement and compliance has been good, a change in medications is indicated. The therapy should be continued until cytology and examination of the ears are that of what is considered normal.
- Routine (I prefer weekly) ear cleaning at home by the owners is an essential component in the management of chronic otitis. It is also important that the veterinarian or technician spend time with the owner showing the proper method of cleaning. Most cleaning products contain various types of acids often with a ceruminolytic or alcohol added.
- Corticosteroids are important to use in the treatment of otitis externa to relieve the inflammation present (and its concurrent discomfort), especially if treating obstructive ear disease due to progressive pathologic change. Systemic steroids are usually indicated in severely stenotic, hyperplastic or erosive ear canals. This will be discussed in detail later.
- It is important to remember that otitis should be thought of as a symptom of an underlying disease and not a disease entity itself.

#### Ceruminolytic Agents

See Table 1 for a list of agents. These agents are detergents and surfactants that dissolve ear wax and facilitate its removal by flushing. They should be instilled into the ear at least 5 minutes before each flushing procedure, repeatedly. Use caution in dispensing for home use, as ceruminolytics left in the ear without subsequent adequate flushing can be irritating. Ototoxicity is a concern when it is questionable if the tympanum is intact.

## Otitis externa

### Management of *Malassezia* otitis:

See Table 2 for a complete list of agents. Topical antifungal agents include nystatin, thiabendazole, clotrimazole, miconazole, and ketoconazole. Clotrimazole is available as a single agent (Clotrimazole Solution 1%, VET Solutions) and in combination with gentamicin and betamethasone valerate or mometasone (DVMax, DVM; Otomax, Schering-Plough & Mometamax® Schering-Plough) for mixed infections. Miconazole is most commonly used in the lotion formulation (Conofite Lotion, Schering-Plough). Many self-formulated mixes are being used, especially for cases of *Malassezia* with concurrent hypersensitivity reactions in the ear canal. These types of patients usually have a primary allergy with secondary yeast otitis. These combinations include 1% clotrimazole solution and dexamethasone (2 mg/ml) mixed 1:1 and miconazole lotion and dexamethasone (2 mg/ml) mixed 1:1 and applied q12h. For otitis media and chronic cases, I routinely prescribe Ketoconazole (10mg/kg PO daily) for a minimum of 30 days.

### Management of Staphylococcal otitis:

See Table 2 for a complete list of agents. For most cases of cocci (seen on microscopic examination of ear exudates), the following topicals are effective: Tresaderm® [neomycin, thiabendazole and dexamethasone ] Merial; Otomax® [gentamicin, betamethasone, and clotrimazole ] Schering-Plough; Mometamax® [gentamicin, mometasone, and clotrimazole ] Schering-Plough; Ear/Skin Cleanser® [boric acid, acetic acid] DermaPet.

### Glucocorticoids in Otitis

See Table 3 for list of agents. Glucocorticoids are antipruritic, anti-inflammatory, antiproliferative, and decrease sebaceous and apocrine secretions. They are beneficial in decreasing the pain, pruritus, stenosis, and hyperplasia associated with otitis. Glucocorticoids are usually found in combination with other agents but may be beneficial when used alone in allergic causes of otitis and some ceruminous otitis cases.

Fluocinolone acetonide 0.01% in 60% DMSO (Synotic, Fort Dodge) is very effective in the initial resolution of edema, stenosis, and hyperplastic otitis. With chronic usage, it is important to use the lowest potency glucocorticoid at the lowest frequency needed to control the otitis. This is usually accomplished with 1% hydrocortisone (Cort/Astrin, Vedco; CortiSpray, DVM Pharmaceuticals; Bur-Otic HC, Allerderm/Virbac).

### Cyclosporine Therapy

Cyclosporine is becoming increasingly popular for the treatment of a variety of skin and system diseases in both dogs and cats. In a pilot study by Hall, five client-owned dogs were treated with oral cyclosporine at 5 mg/kg twice daily for a minimum period of 12 weeks. All dogs were re-evaluated clinically every four weeks to monitor progress. All five cases showed significant clinical improvement based on owner and clinical assessments. Individual owners also commented on improved disposition, hearing and quality of life. Although bacterial colonization was noted on ear cytology, adjunctive ear medications were not required. Therefore Cyclosporine may be another option for the treatment of severe hyperplastic ear disease in the Cocker Spaniel.

### **Management of Gram-negative Otitis:**

Gram-negative bacteria that are associated with purulent otitis include the following: *Pseudomonas aeruginosa*, *Proteus mirabilis*, *E. coli* and *Klebsiella* spp. Gram-negative bacteria have a thick cell wall that consists of an outer and inner cell membranes composed of a phospholipid bilayer. The outer membrane contains porin proteins and lipopolysaccharide molecules with attached O antigens, which are important in the serotyping of the organism. The porins are important in the passage of molecules into the cell. The periplasmic space contains a small amount of peptidoglycan compared with gram-positive organisms. This thick cell wall plays an important role in the development of resistant and treatment failures. Gram-negative infections are associated with chronic and persistent infections due to multiple antibiotic resistances. The most common gram-negative bacteria associated with chronic otitis externa, media and persistent infection is *Pseudomonas aeruginosa*. Otitis media is highly probably when gram negative organisms are present. Topical antibiotic treatment of otitis media has gained recent favor in veterinary medicine. The use of topicals is based on the high levels of antibiotic that can be placed into the bulla coupled with the poor drainage of the tympanic bulla. Infused antibiotics can remain in contact with the inflamed, granulating middle ear mucosa much longer because the fluid filling the bulla cannot readily escape. Probably the most important technique for treating otitis media is flushing the bulla. Topical otic medications cannot penetrate through the thick exudate that fills the middle ear during otitis media, so this exudate and secretory material must be removed. Additionally, many destructive enzymes that are trapped in the mucoid secretions in the bullae remain in contact with the mucoperiosteum, which prolongs the disease. Hydrating the mucus with the water in flushing solutions makes it less dense and easier to suction.

- **Tris-EDTA for treatment of gram-negative otitis**

- Cell surfaces of gram-negative bacteria are damaged by exposure of cells to Ethylenediaminetetraacetic acid (EDTA). Tris buffer enhances the effects of EDTA. Gram-negative bacteria exposed to Tris- EDTA have increased permeability to extracellular solutes and leakage of intracellular solutes; are more sensitive to lyozyme, bactericides and antibiotics.
- Two commercial veterinary preparations have been marketed (T8 Solution, DVM; TrizEDTA, DermaPet).
- Tris EDTA in combination with benzoyl alcohol (T 8 solution<sup>®</sup>, DVM pharm.) is effective against both gram positive and gram negative bacteria.

**TREATMENT:**

- 2-4 weeks of prednisone at 1-2mg/kg.
- Deep ear flush preferably with a video-otoscope
- Infusing drugs into the bulla is an effective method of providing long acting high concentration effects.
- Aqueous solutions of non-ototoxic antibiotics can be placed directly onto the infected mucoperiosteum.
- Antibiotic sensitivity patterns are important for treating otitis media when systemic antibiotics alone are used to get levels within the bulla. Unlike topical antibiotics, which can achieve many times the blood MIC, systemic antibacterial therapy for otitis media relies on lower levels of antibiotics arriving in the middle ear hematogenously or through inflammatory cells. Due to the poor blood supply in the external ear canal and middle ear, there is limited diffusion of antibiotic from the serum into the lumen of the ear canal or tympanic bulla.
- Twice daily flush with Tris-EDTA followed 15 minutes later with Baytril Otic or polymixin-containing ear drop. I prefer to use an "all in one product of a Trisedta product (4oz bottle) with 12ml of LA Baytril = 10mg/ml
- Recheck every 7 days for 6 to 8 weeks for patency of ear canal, presence of exudate and cytological evaluation of status of infection. During this period it would be good to evaluate for signs of allergy or other potential underlying cause of the severe otitis as well, as so that the work-up can begin in a timely fashion.

**Table 1 - Ceruminolytic agents**

| <b>Ingredients</b>                    | <b>Trade Name</b>  |
|---------------------------------------|--|
| Cerumene®-Evsco                       | Squalene 25% in isopropyl myristate, liquid petrolatum   |
| (MalAcetic Otic ®,<br>Dermapet, Inc.) | 2% acetic acid, 2% boric acid  |
| (Nolvacleanse®, Fort<br>Dodge)        | Propylene glycol, surfactants,<br>fragrance and water  |
| (Clear X®-DVM<br>pharmaceuticals)     | Diocetyl sodium sulfosuccinate, carbamide peroxide   |
| (Epiotic®)                            | Lactic acid, salicylic acid, Parachlorometaxylenol (PCMX),<br>propylene glycol Diocetyl sodium sulfosuccinate, spherulites |

**Table 2 -Topical Antimicrobial Otic Preparations**

| <b>Trade Name</b>          | <b>Ingredients</b>  |
|----------------------------|---|
| Conofite Lotion            | Miconazole  |
| Derma 4 Ointment           | Nystatin, neomycin sulfate, thiostrepton, triamcinolone acetonide                             |
| Dermagen Ointment          | Nystatin, neomycin sulfate, thiostrepton, triamcinolone acetonide                             |
| Dermalone Ointment         | Nystatin, neomycin sulfate, thiostrepton, triamcinolone acetonide                             |
| Forte-Topical              | Hydrocortisone, neomycin sulfate, penicillin G procaine, polymyxin B, chlorobutanol anhydrous |
| Gentocin Ophthalmic        | Gentamicin sulfate  |
| Gentocin Otic Solution     | Gentamicin sulfate, betamethasone valerate  |
| Liquichlor                 | Chloramphenicol, prednisolone, tetracaine, squalene   |
| Otomax, DVMax              | Gentamicin sulfate, betamethasone valerate, clotrimazole                                      |
| Panolog Cream and Ointment | Nystatin, neomycin sulfate, thiostrepton, triamcinolone acetonide                             |
| Mometamax Ointment         | gentamicin, mometasone, and clotrimazole  |
| Quadritop Ointment         | Nystatin, neomycin sulfate, thiostrepton, triamcinolone acetonide                             |
| Topagen Ointment           | Gentamicin sulfate, betamethasone valerate  |
| Tresaderm                  | Thiabendazole, dexamethasone, neomycin sulfate  |
| Tritop                     | Neomycin sulfate, isoflupredone acetate, tetracaine hydrochloride                             |
| Veltrim                    | Clotrimazole  |

**Table 3 –Topical Glucocorticoid preparations**

| Trade Name             | Ingredients   |
|------------------------|---|
| Bur-Otic HC            | 1% hydrocortisone, propylene glycol, water, burrow's solution, acetic acid, benzalkonium chloride |
| ClearX Drying Solution | Acetic acid, colloidal sulfur, hydrocortisone   |
| Cort/Astrin Solution   | Burrow's solution, 1% hydrocortisone  |
| CortiSpray             | 1% hydrocortisone   |
| Synotic Otic Solution  | 0.01% fluocinolone acetonide, 60% DMSO  |

**Table 4 Topical Treatment for Pseudomonas otitis**

| DRUG                                  | DOSE  | FORMULATION   |
|---------------------------------------|---|---|
| 5% acetic acid.                       | Clean ears q 12-24 hours  | Prepared  |
| Ciprofloxacin                         | Small Amount q 12 hours   | Prepared  |
| Enrofloxacin injectable               | Fill canal completely q 12 hours  | Dilute 12ml (100 mg/ml) in 4 oz of TrisEdta   |
| Iodine complex solution               | Apply small amount q 12-24 hours  | Dilute 1:5, diluted solution should be used within two hours                                      |
| Polymyxin B or C containing solutions | Apply drops q 12 hours after cleaning and drying  | Prepared  |
| Silver sulfadiazine - 1%              | Apply small amount q 24 hours   | Mix 1:1 with sterile water  |
| Tobramycin                            | Small Amount q 12 hours   | prepared  |
| Tris -EDTA solution                   | Rinse ears out q 12 hours; 15 minutes prior to application of antibiotic-containing solutions | Tris-EDTA (q L distilled water, 1.2 g EDTA, 6.05 g trisaminomethane and 1 ml glacial acetic acid) |

## **Summary**

- Recurrent otitis is typically secondary to an underlying etiology, with allergic disease being most common.
- Recurrent otitis may be the only clinical signs of allergic disease, which can be unilateral or bilateral.
- Evaluation of otitis externa should be based on otoscopic examination and cytology from the external ear canal.
- Culture of the external ear canal is typically not necessary unless gram negative rods are present on cytology.
- In cases of chronic otitis externa (> 8 weeks), especially with gram negative rods, otitis media should be suspected.
- An intact tympanic membrane does not rule out otitis media.
- Otitis media can be confirmed with bullae imaging (radiographs, CT, MRI) and/or myringotomy and culture from the middle ear.
- Otitis externa should be treated topically based on results of cytology and/or culture from the external ear canal.
- Topical therapy of otitis externa should be continued until results of cytology/culture are negative.

## **References/Suggested Reading**

1. Hall, JA. Oral cyclosporine in the treatment of end state ear disease: A pilot study. Proceedings of the 18<sup>th</sup> Annual Meeting of the American Academy of Veterinary Dermatology and American College of Veterinary Dermatology. Monterey, California 2003: 217.