Chronic otitis medicine - is there light at the end of the ear canal?

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Preface

While the following options illustrate the various medical means of salvaging chronic otitis in a dog, The ideal option is to prevent acute otitis externa from becoming chronic. This may often be done if one remembers to:

1) Thoroughly examine the ear canal (under sedation if necessary) for any foreign body.
2) Perform cytology from the exudate in the canal, to determine the type of infection.
3). Remember that many recurrent otitis externa cases have an underlying allergic component (atopic dermatitis or food allergy).
4). Show the owner how to flush and administer topical medications !!!!
5). If a bacterial organism is not responding to empiric treatment, culture the ear.

The most common causes for chronic, proliferative otitis externa:
1. Allergic disease – atopy and/or food hypersensitivity
2. Inadequately treated or refractory bacterial and/or Malassezia infections, often leading to otitis media
3. Less commonly: hypothyroidism, idiopathic seborrhea (e.g. Cocker Spaniels)

Therapy
Aggressive attack at medical management - salvage the ear/ears. This usually employs all the modalities of ear therapy commonly employed.
1. Systemic glucocorticoid (e.g. starting at 1-2 mg/kg/day prednisolone/prednisone for two weeks, then .05 - 1 mg/kg for two weeks, then 1 mg/kg every other day for two weeks, then 0.5 mg/kg every other day for two weeks). Systemic glucocorticoid therapy is generally maintained until proliferative changes have been significantly reduced or resolved.
2. Systemic antibiotic (chosen on the basis of cytology initially – cephalaxin for cocci, ciprofloxacin or marbofloxacin for rods; +/- culture and sensitivity testing)
   Doses:
   - Cephalexin 30 mg/kg 12 h
   - Cefpodoxime (Simplicef™) 10 mg/kg q 24 h
   - Enrofloxacin (Baytril®) 15 mg/kg q 24 h
   - Marbofloxacin (Zeniquin®) 6 mg/kg q 24 h
See below for *Pseudomonas* infections

3. If *Malassezia* is present – systemic anti-*Malassezia* therapy ketoconazole (5mg/kg), itraconazole (5mg/kg) or fluconazole (5 mg/kg)

See below for refractory *Malassezia* infections

4. Topical glucocorticoid/antibiotic/antifungal: If the tympanum is intact, all options are acceptable. If the integrity of tympanum is unknown: for bacteria, consider a solution of injectable enrofloxacin (22.7mg/ml): dexamethasone sodium phosphate (4mg/ml) at a ratio of 1:2 or enrofloxacin in TrisEDTA. The gentamicin in Otomax (Schering) provides a broader spectrum gram negative effect (picking up even 50 – 60% of *Pseudomonas*) and is therefore possibly the EMPIRIC antibiotic of choice when rods (usually gram negative organisms) are seen to predominate on an ear cytology.

5. For *Malassezia* consider dexamethasone sodium phosphate: 1% miconazole (1:1); for bacteria and *Malassezia* consider a mix of enrofloxacin:dexamethasone sodium phosphate: 1%miconazole (1:1:2).

6. Topical potent steroid – Synotic (fluocinolone and DMSO; Ft. Dodge) - BID

7. Ear flush: routine cleanser/dryer if tympanum intact; if integrity of tympanum unknown – dilute vinegar and water (1:2) or trisEDTA (TrizEDTA by DermaPet Inc. or T8 or T8 Keto solution by DVM Pharmaceuticals)

8. Intrallesional glucocorticoids: triamcinolone acetonide (2 mg/ml); spinal needle (3.5”, 22 gauge); injected following cleaning; 0.1 ml injections into proliferative lesions or if 360 degree proliferation, administer in a “ring” of 3 points around wall, with each “ring” 1-2 cm apart. The maximum triamcinolone dosage that that Dr. Rosychuk recommends in a 30 – 40 pound dog is 6 mg. Repeat administration may be considered in 3-4 weeks. When intrallesional therapy is used, there is usually a lesser need for very aggressive oral glucocorticoid dosages – i.e. instead of starting at 1-2 mg/kg/day, start at 0.5 – 1 mg/kg/day of presnisone/prednisolone.

9. Once the ears have been somewhat quieted down, an in depth cleaning/examination is often necessary.

10. Laser therapy (CO2 or diode) – for proliferative lesions

11. Oral cyclosporine – 5 mg/kg/day – when one strongly suspects allergy as the underlying source of the problem.

12. Potential primary factors can be further worked up and treated (e.g. document and treat food sensitivity; atopy management etc.).

**Refractory Malassezia infections**

True refractory infections with *Malassezia* appear to be uncommon. Recurrent infections, however, are frequently encountered (especially secondary to allergy). When *Malassezia* appears to be refractory, factors that may affect the efficacy of conventional therapies include:

1. Significant debris within the ear (see above) that may serve as a nidus for continued infection.
2. Hyperplastic changes that prevent access of topical medications to their target areas.
3. Inadequate control of underlying inflammatory disease (primary factors, especially atopy or food sensitivity). Management of these factors to maximize response usually requires glucocorticoid therapy (may require aggressive glucocorticoid therapy).
4. Some individuals appear to be sensitive to even small numbers of *Malassezia*, most likely due to the development of hypersensitivity to *Malassezia* and/or its byproducts. These individuals may require more aggressive, longer term therapy to adequately resolve their *Malassezia*.

**Refractory bacterial infections (emphasis on Pseudomonas)**
Resistance is suspected if:
1. Bacteria persist in the face of appropriate "first line" topical therapies (e.g. Tresaderm, Panalog)
2. Otitis externa has received frequent, periodic therapies with "first line" products
3. Large numbers of rods are seen on cytologic examination (suggesting the possibility of more resistant gram negative organisms such as *Pseudomonas*).

**Current options for managing resistant *Pseudomonas* infections**
*Pseudomonas* infections are quite commonly encountered as complicating factors in chronic otitis externa/media in the dog and, on occasion, may be very resistant to routine anti-microbial therapy. The following are important points to consider in establishing a successful therapeutic protocol for such cases:
1. The presence of a *Pseudomonas* infection is usually heralded by the presence of purulent exudate within the ear. Cytologic examination will reveal "rods" and usually neutrophils on cytologic examination with Diff Quick® or new methylene blue stained slides. The canal may be ulcerated.
2. *Pseudomonas* infections are more likely to be associated with breakdown of the tympanum and the concurrent presence of otitis media. Otitis media is even more common if the canals are hyperplastic and stenotic. These associations warrant early consideration of a thorough "deep" cleaning, direct visualization of the tympanum (when possible) and/or radiographs, CT scanning or MRI to better evaluate for the presence and severity of middle ear involvement.
3. Affected ears are often very inflamed, swollen and painful and may be eroded or ulcerated. Most patients have underlying primary factors (e.g. allergy) responsible for initiating the otitis. Proliferative changes are often present as perpetuators. As such, significant benefit is obtained from concurrent oral glucocorticoid therapy (oral prednisone/prednisolone starting at 1 – 2 mg/kg/day; dose dictated by the severity of inflammation and the degree of proliferative changes). The presence of *Pseudomonas* is not a contraindication to glucocorticoid therapy.
4. Chronic cases, especially with histories of unsuccessful topical antibiotic treatments, are cultured prior to the initiation of topical therapy (samples for cultures should be taken from both the canals and, if involved, the middle ear in that bacterial species and strains may differ from one to the other).
Acute, first time or infrequently recurrent occurrences:

1. The empiric antibiotics we tend to reach for when "rods" predominate on cytologic examination are gentamicin (i.e. Otomax or Mometamax; Schering) or Polymixin B (see later for specifics). The products are used BID. Gentamicin is effective against a significant number of Pseudomonas strains (50 – 60%; polymyxin B 95% - 100%). These antibiotics also work well against other gram negative organisms.

2. Choices of flushes are extensive in this scenario (less resistance expected) and include:
   a. cleanser/dryers (e.g. EpiOtic; Virbac; shown in one study to have efficacy against Pseudomonas when used as the only therapy for Pseudomonas otitis (used twice daily). We tend to most routinely use the product once daily.
   b. Tris-EDTA containing product (e.g. T8 solution, DVM; T8 Keto, DVM; Triz-EDTA, DermaPet). These products are is used to flush the ear twice daily (prior to application of topical antibiotic-containing product)
   c. Acetic acid containing product (e.g. 2% acetic acid, 2% boric acid; Malacetic Otic, DermaPet Inc. or dilute 5% white vinegar and water – 1:2). Acetic acid is noted to have unique anti-Pseudomonal effects. Used once or twice daily (usually once daily).

3. Failure to respond to this therapy would warrant culturing the ear. Should the tympanum be perforated or the integrity of the tympanum is unknown, alternatives to gentamicin should be considered (concern for ototoxicity).

Other products to consider with more chronic, persistent or very recurrent infections or based on culture and testing:

Flush of Preference:

TrisEDTA

Topical Antibiotics:

1. Enrofloxacin in conjunction with Tris-EDTA. Pseudomonas resistance to enrofloxacin is quite commonly encountered. However enrofloxacin is well tolerated within the middle ear (does not appear to be ototoxic). When used in conjunction with tris-EDTA, its in vitro efficacy appears to increase dramatically. When using these products in combination (tris-EDTA and enrofloxacin), Dr. Rosychuk recommends a final concentration of 10 mg/ml of enrofloxacin (i.e. 13 mls of 100 mg/ml injectable enrofloxacin per 118 ml bottle of T8 solution [DVM Pharmaceuticals]). Others have claimed similar success with concentrations of 4 - 5 mg/ml of enrofloxacin. The combination product is used BID to initiate therapy (ear is filled with the combination and massaged in). Dr. Rosychuk has used a combination of enrofloxacin and TrizEDTA (DermaPet Inc.) in middle ears, without apparent ototoxicity. Due to the lack of an anti-fungal component to this product, a flare of Malassezia otitis may occasionally be seen during therapy. However, if the T8 Keto (DVM Pharamceuticals) product is used, this should not be a problem.

2. Baytril Otic (Bayer; 5 mg/ml enrofloxacin, 10 mg/ml sliver sulfadiazine). Silver sulfadiazine is effective against a broad spectrum of gram positive and negative bacteria, including Pseudomonas. In addition, it is a mildly effective therapy for
Malassezia. In ears that have only bacterial infections, silver sulfadiazine helps to reduce the incidence of opportunistic Malassezia infections that may develop when the ears that are treated with topical antibiotics alone. This product can be used with a pre-treatment of Tris-EDTA (see above).

3. Other enrofloxacin mixes utilizing injectable (22.7 mg/ml) enrofloxacin include (products favored by Dr. Rosychuk are highlighted):
   a. 1:2 enrofloxacin: dexamethasone sodium phosphate (for moderate steroid effect)
   b. 1 part enrofloxacin to 1 part dexamethasone phosphate to 2 parts 1% miconazole (Conofite) (for concurrent anti-Malassezia effect)
   c. Saline and enrofloxacin 1:1 to 1:2; used BID
   d. 3–4 cc enrofloxacin to 8 cc Synotic BID (for potent steroid effect)

4. Polymixin B containing products have been shown to be very efficacious based on in vitro sensitivity testing (variably reported as 95%-100% sensitive in the USA, where polymixin B is not used in routine ear preparations). Examples: Cortisporin Otic solution, Glaxo Wellcome - polymixin B, neomycin, 1% hydrocortisone; Colymycin S. Otic , Parke-Davis - colistin or Polymixin E, neomycin, 1% hydrocortisone.

5. Ticarcillin or Ticarcillin and clavulonic acid (Timentin; GlaxoSmithKline). Ticarcillin has proven to be a very beneficial therapy for resistant Pseudomonas in the authors’ experience. We usually use Timentin as 3.1 gm vial; reconstitute with 26 ml (100 mg/ml); freeze in 4 ml aliquots; thaw and use each 4 ml aliquot over 2 days; 1/2 ml in each ear BID. Others have suggested: reconstitute a 6 gram vial of ticarcillin with 12 ml of sterile water. Divide equally into 2-ml portions in syringes and freeze (will remain stable for 3 months); this is the "stock solution". To make up the ear treatment solution, thaw and mix a 2 ml aliquot of concentrate with 40 ml of normal saline. Divide this into four 10-ml aliquots and freeze. Clients should keep these frozen; one aliquot should be thawed at a time, keeping it refrigerated, and used for no longer than 1 week. Anything remaining after 1 week should be discarded and another aliquot thawed. Dr. Sue Paterson in the UK has documented cases of ototoxicity due to Timentin.

6. Silver sulfadiazine 1% cream– very efficacious therapy (although there are resistant cases) – e.g. Kendall Thermazene, the Kendall Company (diluted 1:9 with water) or powder (Spectrum pharmacy; www.spectrumRx.com; make up 1% solution). Ear should be cleaned prior to application to enhance efficacy. May promote re-epithelialization in ulcerated ears.

7. Amikacin injectable (dilute 250 mg/ml to 50 mg/ml) 4-8 drops of 50 mg/ml BID

8. Tobramycin (Tobrex™) is an aminoglycoside that is available as ophthalmic drops. It can be used in the ears but is somewhat expensive (5ml=$4.50) and may be ototoxic in cases of a non-intact tympanic membrane.

Systemic Antibiotics
Systemic antibiotic therapy – There is some evidence supporting the efficacy of systemic antibiotic therapy alone in treating bacterial otitis. Our indications for the use of a systemic antibiotic: canals are hyperplastic or proliferative, erosive or ulcerated and/or there is otitis media or it is difficult for the owners to topically treat the ears. However, it is important to note that the both authors have treated cases of *Pseudomonas* otitis externa +/- media with just a topical antibiotic (e.g. combination of Tris-EDTA and enrofloxacin or combination of ticarcillin and acetic acid flushes) alone.

The authors’ antibiotics of choice are **marbofloxacin (4 – 5.5 mg/kg/day)** and **ciprofloxacin (15 mg/kg BID)**; current therapy of choice based on some data showing potential superior efficacy to other fluoroquinolones; alternative would be enrofloxacin (10 - 20 mg/kg/day).

Appropriate antibiotics are generally chosen on the basis of culture and sensitivity testing. When asking for sensitivity data on suspected cases of *Pseudomonas* infections, one should ask for sensitivities to enrofloxacin, ciprofloxacin, marbofloxacin, ticarcillin and ceftazidime, in addition to those routinely performed. Most laboratories will provide sensitivity data based on the Kirby Bauer disc system. When looking specifically at enrofloxacin, Dr. Rosychuk uses the following guidelines in interpreting sensitivity data.

If the organism is sensitive, then the lower dosage of fluoroquinolone can be used. If resistance is noted on the KB system, then MIC's should be requested. If the MIC is between 2-4 micrograms /ml, then the higher dosages of antibiotic should be used. If the MIC is above 4 micrograms/ml, then the bacteria should be considered resistant to enrofloxacin. Alternative systemic antibiotic considerations for very resistant *Pseudomonas* would include ticarcillin (ticarcillin, 60 - 75 mg/kg BID SQ) or ceftazidime (30 - 50 mg/kg BID SQ) for 2-3 weeks. These injections can be given at home by the owner.