ALLERGIC OTITIS EXTERNA IN THE DOG AND CAT

Rod A.W. Rosychuk DVM, DACVIM
Colorado State University, Ft. Collins, Colorado

Atopy and, to a lesser degree, food sensitivity are without question the most common primary factors noted to initiate inflammation within the ears of the dog. While they are less commonly encountered in the cat, they tend to be an underdiagnosed reason for chronic otitis externa in the cat.

Atopy history and physical findings:
1. At least 80% -85% of canine atopics have otitis externa. In one study (Muse R. et al, Proc. AAVD/ACVD, 1996) otitis was the initial sign of allergic disease in 25% of atopics. Only 3-5% of atopics will manifest as an otitis externa only (without other cutaneous signs of atopy eventually being present – although it may take many months to see those first signs of more generalized skin involvement).
2. Primary area of the ear affected: proximal pinna, proximal vertical canal with rest of canals relatively less involved. Horizontal canal is more likely to be involved with chronicity and/or secondary infections.
3. It is very common to see dilatation of the pars flaccida of the tympanum in affected dogs (not cats).
4. The most common secondary colonization and infection problems encountered in atopic individuals are with Malassezia. Secondary bacterial infections are less common, but when present, are usually with Staphylococcus intermedius and with more chronic cases or those that have been intermittently treated in the past, gram negative bacterial such as Pseudomonas, E. coli, klebsiella etc. It is important to note that individuals may develop hypersensitivity to Malassezia and its by-products, and as such, relatively few organisms may contribute significantly to inflammation and pruritus.
5. Atopy is one of the more common underlying associations with aural hematomas.
6. Atopic otitis is generally glucocorticoid responsive.
7. Atopic otitis externa is usually bilateral, but the signs may predominate in one ear (without secondary infections explaining the asymmetry).
8. Atopic otitis externa appears is less commonly encountered in the cat but it may be the only manifestation of atopy in the cat and may predominantly affect just one ear.
9. Diagnosis: Rule out; response to therapy (e.g. glucocorticoids, antihistamines), ID skin test or in vitro serologic testing.

Food sensitivity – history and physical findings
1. Otitis externa is commonly associated with food sensitivities in the dog (present in 60 – 80% of cases?).
2. It has been suggested that as many as 20% of food allergic dogs may manifest as only a bilateral otitis externa (suggesting that if you are dealing with a patient who has had a chronic persistent or recurrent otitis externa which has lasted for 2-3 years, but no other signs of pruritus are noted, then food sensitivity would be a more likely etiology for the problem than atopy in this patient).
3. Distribution of changes in the ear is as for atopy.
4. Food sensitivities appear to be a relatively uncommon cause of otitis externa in the cat.
5. Diagnosis: Assessing response to a restrictive diet trial. Whenever possible, secondary ear infections should be resolved prior to or during the early stages of the trial restrictive diet. Clinical/otoscopic/cytologic examinations should be repeated every 3 weeks during the diet trial.

Flea bite hypersensitivity: uncommon to see otitis as a manifestation of FBH. In one recent study (Muse R, Proc. AAVD/ACVD, 1996) 4 of 17 dogs had a concurrent otitis externa.
Routine Treatment of Acute and Infrequently Recurrent Allergic Otitis Externa

In many cases seen in clinical practice, such cases are often readily managed with topical products that contain a combination of an antibiotic, anti-fungal and glucocorticoid. The neomycin in products such as Tresaderm and Panalog provide reasonable gram positive and gram negative coverage; the thiabendazole in Tresaderm and the nystatin in Panalog provide reasonable anti-Malassezia therapy; and the dexamethasone in Tresaderm and triamcinolone acetonide in Panalog provide a relatively potent anti-inflammatory effect. When rods predominate in our Diff-Quick stained cytology, we often reach for the gentamicin in Otomax or if large numbers of Malassezia are noted, we may look for the superior antifungal effect of clotrimazole in Otomax. The betamethasone in an ointment base (Otomax) also appears to give us a more potent anti-inflammatory effect.

For ears that are severely inflamed, a short course of oral glucocorticoid is readily rationalized to more quickly reduce the inflammation and pain, open up the canals to facilitate medication getting to where it needs to get in the ear and to allow the owners to more readily medicate the ears. Dosages used to initiate therapy are anti-inflammatory – i.e. 0.5 – 1.0 mg/kg/day of prednisone or prensisone in the dog and 1.0 – 2.0 mg/kg/day prednisolone in the cat.

Long Term Management of Allergic Otitis Externa

1. Resolve secondary bacterial/yeast infections with a broad spectrum product such as noted above.
2. Consider long term maintenance therapy with a topical glucocorticoid product devoid of an antibiotic. More severely inflamed ears - Synotic (Syntex; fluocinolone acetonide and DMSO) every 48 to 72 hours maintenance. Because this is a very potent steroid there is a concern for creating iatrogenic Cushigoid signs with more frequent, long term therapy. Less severely inflamed ears - e.g. Bur-Otic HC (Virbac; Burrow’s solution, acetic acid, 1% hydrocortisone, polyethylene glycol; once every 24-72 hours long term) or if prone to recurrent Malassezia, 1:2 or 1:1 mix of dexamethasone sodium phosphate and 1% miconazole (Conofite) or if prone to recurrent Malassezia and bacterial infection, 1:1:2 mix of injectable enrofloxacin, dexamethasone sodium phosphate and 1% miconazole. Another option would be long term use of Otomax used twice weekly.
3. Combine these long term topical glucocorticoids with routine flushes using a combination cleanser/dryer 1-2 times per week.
4. Flares of allergic otitis are often most rapidly put in to remission with a course of oral glucocorticoid.
5. Overall control of the otitis will be much easier if the patients underlying allergic problem is well controlled (e.g. hypoallergenic diet for food sensitivities or hyposensitization, antihistamines, fatty acids, glucocorticoids, oral cyclosporine etc. for atopy).

Refractory Malassezia pachydermatis infections

True refractory infections with Malassezia appear to be rare. Recurrent infections, however, are common (i.e. secondary to atopy).
1. Before considering a Malassezia infection refractory, should look for and control underlying inflammatory (usually allergic) conditions.
2. Otomax (Schering Animal Health; clotrimazole, gentamicin, betamethasone)
3. Conofite lotion (Schering; 1% miconazole; use every 12 hr; antiinflammatory component can be added to this by mixing 7.5 mg dexamethasone phosphate (4 mg/ml) to a 10 ml bottle of Conofite). Conofite may prove irritating in some ears
4. A 2% acetic acid/ 2% boric acid solution (DermaPet) has proven to be a good flush for this problem and is used as a long term, routine therapy to minimize recurrence.
5. Oral ketoconazole has proved to be an excellent systemic therapy for Malassezia otitis; 5 - 10 mg/kg q 12 - 24hr for 2-4 weeks. Others have used 10mg/kg q 24 hrs. Long term maintenance therapy has
been achieved with 5-10 mg/kg given for 2-3 consecutive days of the week. In the author's experience, the major complication of ketoconazole therapy has been anorexia. Hepatotoxicity is uncommonly encountered but should be evaluated if anorexia/vomition is noted. The anorexia is often transient, or can be minimized by starting at _ dosages for the first 2-3 days, then going up to full dosages.

6. Oral itraconazole (5 - 10 mg/kg/day for 2-4 weeks). Likely shorter duration of therapy required than for ketoconazole because of prolonged tissue half life for itraconazole. Likely a better choice for "pulse" therapy for chronic maintenance therapy (two days of each week). Best choice for treating cats (less toxic than ketoconazole)

**What to do with the Chronic, Proliferative Otitis Case**

1. Aggressive attack at medical management - salvage the ear/ears. This usually employs all the modalities of ear therapy commonly employed.
   a. 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.
   b. Systemic antibiotic (chosen on the basis of cytology, +/- culture and sensitivity testing)
      a. Topical glucocorticoid/antibiotic/antifungal
      b. Cleanser/dryer
      c. +/- systemic anti-malassezia therapy
   d. Consider intralesional 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, in “ring” of 3 points around wall, with each “ring” 1-2 cm apart. The maximum triamcinolone dosage that this author usually uses in a 30 – 40 pound dog is 6 mg. Repeat administration may be considered in 3-4 weeks. When intralesional 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.

Once the ears have been somewhat quieted down, an in depth cleaning/examination is in order. Once secondary bacterial infections have been controlled and proliferative changes have been significantly improved, then potential primary factors can be further worked up and treated (e.g. document and treat food sensitivity; atopy management etc.).

Note: As part of our aggressive initial management of those chronic/proliferative ears - we will often start a restrictive diet at the outset of topical/systemic otic therapy. We prefer a commercial, balanced restrictive diet because it will likely be fed long term (several months) before a more definitive decision can be made about the actual role dietary hypersensitivity may be playing in the pathogenesis of the disease. Once more intensive topical/systemic therapy is completed and the ears doing well, see if diet alone is able to keep the otitis from recurring. To prove the benefit of restrictive diet, challenge with the previous diet to see if problem exacerbated and to document the future need of feeding special diets.

**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*).

Examples: Gentocin-Otic (gentamicin, betamethasone ) or Otomax (gentamicin, betamethasone, clotrimazole). If these products fail to resolve the bacterial component of the problem, then further treatment is dictated by culture and sensitivity testing (usually stop the gentamicin containing product for 3-5 days prior to culturing).
Pseudomonas Infections

Pseudomonas infections are quite commonly encountered as complicating factors in chronic allergic otitis externa/media in the dog. The development of more resistant strains of Pseudomonas pose a continual challenge. The following is a compilation of thoughts regarding the treatment of Pseudomonas infections:

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.

2. The "shoot from the hip" antibiotic that we tend to reach for first when "rods" predominate on cytologic examination is gentamicin (i.e. Otomax, Gentocin Otic). This antibiotic does pick up a significant number of Pseudomonas strains and also works well against other gram negative organisms. Failure to respond to this therapy would warrant culturing the ear.

3. 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 findings warrant early consideration for culturing exudates, thorough "deep" cleaning, direct visualization of the tympanum (when possible) and/or radiographs, MRI or CT scanning to better evaluate for middle ear involvement.

4. 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.

5. Other antibiotics available for topical use that have greater efficacy in treating Pseudomonas infections and are used based on culture and sensitivity testing or while awaiting C and S data include:

   a. Polymixin B containing products have been shown to be very efficacious based on in vitro sensitivity testing (95%-100% efficacy in one study). Examples: Cortisporin Otic solution, Burroughs Wellcome - polymixin B, neomycin, 1% hydrocortisone; Colymycin S. Otic, Parke-Davis - colistin or Polymixin E, neomycin, 1% hydrocortisone. Contraindicated if a perforated tympanum.

   b. Baytril Otic (Bayer; 5 mg/ml enrofloxacin, 10 mg/ml sliver sulfadiazine). Enrofloxacin is bactericidal, with activity against a broad spectrum of gram positive and gram negative bacteria, including Pseudomonas. Silver sulfadiazine is also effective against a broad spectrum of gram positive and negative bacteria. It also has reasonable efficacy in treating Pseudomonas infections. In addition, it is a moderately 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 preparation should not be routinely used for more acute, first time or infrequently recurring otitis externa with "rods" seen on cytologic examination, for fear of developing resistance to enrofloxacin.

   c. Formulations with injectable (22.7 mg/ml) enrofloxacin
      i. 1:2 (saline to enrofloxacin), 1:1 enrofloxacin - BID
      ii. 3-4 cc enrofloxacin to 8 cc Synotic
      iii. 1:2 or 1:1 enrofloxacin: dexamethasone sodium phosphate
      iv. 4 ml injectable enrofloxacin to one bottle of EpiOtic
      v. 1 part enrofloxacin to 1 part Dexamethasone phosphate to 2 parts 1% miconazole (Conofite)
      vi. 600 mg enrofloxacin to 4 oz TrizEDTA (DermaPet) or 12 mls TrisEDTA to 4 mls enrofloxacin (22.7 mg/ml).

   d. Amikacin injectable (dilute 250 mg/ml to 50 mg/ml) 4-6 drops of 50 mg/ml BID
e. Ticarcillin and clavulonic acid (Timentin) - the author uses a 3.1 gm vial; reconstitute with 26 ml (100 mg/ml); freeze in 2 ml aliquots; thaw and use each 2 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. 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. Ticarcillin has proven to be a very beneficial therapy for resistant *Pseudomonas* in the author's experience.

6. Tris-EDTA - presoaking the ear (e.g. filling the ear with Tris-EDTA 10 minutes before the topical application of antibiotic, this repeated twice daily) has been shown to enhance the effectiveness of gentamicin and several other antibiotics (enrofloxacin, cephaloridine, kanamycin). It also has inherent anti-malassezia and anti-bacterial effects. Tris EDTA can be formulated for you by one of the several pharmacies that now formulate for Veterinarians. It is also available as T8 solution from DVM pharmaceuticals or Triz-EDTA from DermaPet Inc., PO Box 59713, Potomac, MD, 20859. The T8 product also has surfactants in it that facilitate debris removal, and, as such, in our clinic, it is used to replace the use of a flush in the ears, prior to treating with a topical antibiotic. Tris-EDTA by itself may be an effective chronic maintenance therapy for patients with recurrent *Pseudomonas* infections (i.e. 2-3 times per week).

7. We do routinely recommend flushing affected ears. Because of its unique anti-pseudomonal effects, we tend to favor acetic acid flushes (i.e. acetic acid 5% - white vinegar- diluted 1:2; DermaPet - 2% acetic acid, 2% boric acid). Flush once daily. It should be noted that the Tris-EDTA noted above can replace these flushes (as noted above).

8. What is safe as a topical therapy in the face of a perforated eardrum? If the integrity of the eardrum is in serious question, products that, to date, been used with minimal concern for ototoxicity include enrofloxacin +/- dexamethasone sodium phosphate mixes, ticarcillin and tris-edta.

9. If the ear canals are hyperplastic/proliferative - treat with a 2-4 week course of glucocorticoid (prednisone or prednisolone, starting at 1-2 mg/kg/day) – see above for proliferative changes.

10. Systemic antibiotic therapy - If the cytology has neutrophils, the canals are hyperplastic or proliferative and/or there is otitis media, start on systemic antibiotic therapy. Antibiotics of choice include marbofloxacin (2.5 – 5.5 mg/kg/day; current therapy of choice); enrofloxacin (10 - 20 mg/kg/day), or ciprofloxacin 15 - 20 mg/kg/day. Appropriate antibiotics are generally chosen on the basis of culture and sensitivity testing. Most laboratories will provide sensitivity data based on the Kirby Bauer disc system. When asking for sensitivity data on suspected cases of *Pseudomonas* infections, one should always ask for enrofloxacin, ciprofloxacin, marbofloxacin, ticarcillin and ceftazidime. 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 for the fluoroquinolones. 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 the fluoroquinolones. In these instances, ticarcillin or ceftazidime remain viable options but require parenteral administration. Consideration should be given to using ticarcillin, 60 - 75 mg/kg BID SubQ or ceftazidime 30 - 50 mg/kg BID SubQ for 2-3 weeks. These injections can be given at home by the owner.

11. Because of the relatively high incidence of underlying allergies that predispose to *Pseudomonas* infections, the author routinely starts a work-up and therapy for these problems as soon as possible (e.g. start restrictive diet to rule out food sensitivity).