

# Diagnosis and Treatment of Otitis Externa in the Real World (or What they Don't Teach you in Veterinary School)

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It is important to understand that ear disease is only a symptom (no more specific than “pruritus”). As Dr Flemming Kristensen stated “A patient showing ear problems is a dermatology case until proven otherwise”. It is appropriate therefore to approach the diagnosis of ear disease just as you would for any other skin disease.

Obtaining a detailed history is an important first step in trying to identify the underlying cause of the ear disease. Specific questions that should be asked include:

1. When did the symptoms first occur? This is an important question, because many owners will only tell you when this current episode of symptoms occurred, not the very first time it occurred;
2. Other than the problem the owner presents the patient for, you must ask all owners if the dog has EVER had problems with excessive licking, scratching, chewing, biting or rubbing. Has the dog ever had ear problems before this episode? If so, when, with what medication and what was the response to treatment;
3. Where does the dog live- indoor, outdoors, both? Describe the environment, especially the outdoor environment;
4. Is the dog on heartworm and flea preventative? If so, what product, how often is it administered and is it year round or seasonal?
5. Are there any other pets in the household? If so, what kind and are they symptomatic. If they are cats, do they go outside? ;
6. Are any of the humans in the household showing “new” skin problems? If so, what kind;
7. Do they board the dog, take him to obedience school, training or to the groomers? If so, when was the last time? ;
8. Do they know if the parents of the dog or any siblings have ear or pruritic skin problems? If so, what was done and what was the response? ;
9. What does the dog eat?
10. How do the ears seem today- is today's presentation the best, worse or average since the problem began?
11. Do you notice if the symptoms were better, worse or no different or not sure between the different seasons.

After reviewing signalment and thoroughly questioning the owner, the next step is to do a complete physical examination – be sure to note any constitutional signs that may be present that could explain the ear problem (eg fever associated with pemphigus, lethargy associated with vasculitis, etc)

This is followed by a complete dermatologic examination. Because ears are really just skin attached to the skull many diseases that affect the ears frequently will be affect the rest of the skin and vice versa. Therefore even when a dog is presented only for otic pruritus you still need to examine the rest of the body. And the opposite also holds true, when a dog is presented for truncal pruritus be sure to do an otic examination. .

In order not to miss an abnormality, an otic exam should be done in a systematic manner beginning with the pinna. You should note any alopecia, erythema, ulceration, crusting, scaling or swelling. Then palpate the canals for pain, calcification or thickening. This is followed by an otoscopic examination of the ear canals. Due to the curve in the external ear canal, the ear canal must be straightened in order to see the horizontal canal and the tympanic membrane. This is accomplished by placing the tip of the cone of the otoscope in the opening of the external ear canal. As you advance the cone is proximally you need to pull the pinna laterally (outward). By “stretching” the pinna laterally into a straight line horizontally the ear canal becomes straight and allows examination of the horizontal canal and the tympanic membrane

The presence, degree and location of inflammation, ulceration & proliferative changes should be noted (i.e. cobblestone hyperplasia). Describing the size of both the vertical and horizontal canals along with the type, location and quantity of debris or exudate should also be included in the medical record. Next it should be documented whether the tympanic membrane is visualized. If it is not, then note why the membrane is not seen- is it due to swelling in the ear canal, the presence of a ceruminolith or is there debris in the proximal horizontal canal obstructing the view? Sometimes it is because the animal is too painful to allow deep examination of the ear canal. If you can visualize the tympanic membrane (TM) you need describe if it is normal in appearance or not. Changes that may be noted include discoloration or bulging.

It is important to then evaluate for concurrent middle or inner ear disease. This is because dogs with chronic recurrent otitis externa (OE) may have concurrent otitis media (OM). This step may require heavy sedation or general anesthesia. Evidence of middle ear involvement include a ruptured TM or an abnormal appearing TM (i.e. thickened, change in lucency (opaque), bulging or discolored).

Horner's syndrome (damage to sympathetic innervation); keratoconjunctivitis sicca (damage to the parasympathetic component of the facial nerve) and facial nerve paralysis may be present in cases of OM due to the close association of the respective nerves to the middle ear. Deafness may also be present with OM.

Some veterinarians will have their staff collect ear cytology samples prior to examining the ear (as a time saver) but this makes it more difficult to evaluate the true appearance of the ear canal. Debris may be pushed into the horizontal canal thereby limiting visualization of the tympanic membrane due to the compacting of debris in the canal.

Now diagnostics and treatment needs to be pursued. The first step is to identify and treat the primary (underlying) cause(s) of the ear disease. These would include:

1. Parasitic (including Demodex, Otodectes, Sarcoptes);
2. Foreign bodies;
3. Hypersensitivities (atopy- NOTE OE may be the ONLY symptom in 3-5% of the environmentally triggered atopic dermatitis cases and it may be UNILATERAL!!; it may be seen in cutaneous adverse food reactions where it too may be the ONLY symptom in up to 20% of the cases and also may be unilateral or flea allergy dermatitis. In cases of FAD there should be involvement of the posterior 1/3 of the body in addition to the OE;
4. Allergic or irritant contact dermatitis;
5. Endocrinopathies, keratinization or sebaceous gland disorders leading to an altered lipid layer in the epidermis, alteration in normal keratinization or glandular function; idiopathic seborrhea (is there such a disease?);
6. Autoimmune or immune mediated diseases (eg pemphigus complex, vasculitis- note these diseases involve the pinna >>> canals);
7. Zinc responsive dermatosis (will involve more than the pinna);
8. Juvenile cellulitis;
9. Immunosuppressive diseases (distemper, FeLV, FIV, parvo virus);
10. Neoplasia (adenoma, adenocarcinoma) ;
11. Dermatophytosis (affects the pinna rather than the ear canal).

In addition to identifying the primary cause, secondary factors must be addressed if possible. Secondary factors don't cause ear disease but increases the risk of developing ear disease and may make successful treatment more difficult. Secondary factors are: anatomical factors (eg- long pendulous ears in the Basset Hound or stenotic ear canals in Shar Peis); excessive moisture in ears (swimming); and iatrogenic trauma (plucking hairs from the ear canals, cleaning ear canals with cotton tip applicators).

Lastly perpetuating factors must be identified and treated. These factors don't initiate the problem, but will cause the disease to continue, even with the elimination of the primary factor, once it has been established until these factors have also been addressed. Perpetuating factors include:

1. Bacteria (cocci most commonly *Staphylococcus intermedius* (acute infections), beta hemolytic streptococci and rods most commonly *E. coli*, *Pseudomonas* spp (chronic infections); *Proteus* spp, *Klebsiella* spp and *Corynebacterium* spp);
2. Fungi (*Malassezia pachydermatis* (which may cause a hypersensitivity reaction so that small numbers may be significant) ;
3. Progressive pathological changes;
4. Otitis media;
5. Contact hypersensitivity/irritant;
6. Treatment errors (most commonly due to under treating the infection).

Laboratory tests are a necessary component to the proper workup of a case of canine ear disease. CBC, serum chemistry profile, urinalysis, skin scrapings, fungal culture, endocrine testing and skin biopsies may be necessary depending on what the differential diagnoses are for that patient.

Cytologic examination of a roll swab sample should be performed on any exudate. The numbers & type of bacteria, yeast and inflammatory cells should be quantitated. In cases of OE the question of what is an abnormal number of organisms, per oil field, has not been settled. Depending on the study, cutoff numbers, per oil immersion field, that differentiates between normal and abnormal ears ranges from >1 *Malassezia* to >4 *Malassezia* and from >1 bacteria to >10 bacteria. It is the author's opinion that the number of organisms present to be considered significant is not just a "number". The author doesn't perform cytology on normal ears – it is only done if the ears that are inflamed or have exudate. Therefore ANY organism seen will be considered significant and will be treated as part of the therapy regardless of the number present. As for follow-up cytologies, the only time cytology is performed during therapy is when the ear is not clinically improving OR if the initial cytology had rods. If there is a mixed population of organisms present at the initial examination without rods and the ear is clinically normal at the recheck examination, follow-up cytology is not performed.

Bacterial culture and susceptibility (c/s) should only be rarely, if ever, performed in cases of OE. If a c/s is performed, it should be done in conjunction with cytology. One reason that the author doesn't perform cultures in OE cases is that with a culture the

susceptibility is based on systemically achieved antibiotic levels (measured in microgram/ml) not topically. Since topical medication has a 1000 fold higher concentration (milligrams/ml) the resistance reported on the culture can't be extrapolated to topical therapy.

Other concerns include poor reproducibility of c/s results when culturing the ear. In a study where two samples were taken for bacterial c/s from the same location in the external ear canal of dogs who had otitis externa, there were different bacterial isolates identified 20% of the time and the same isolate with different susceptibility patterns another 20% of the time. Eleven percent of the *P. aeruginosa* isolates had different susceptibility patterns. A second study took triplicate samples and sent the samples to 3 different laboratories. There were 18 samples that had *Pseudomonas spp.* Identified. All three laboratories only agreed on the presence of *Pseudomonas* in 15 (83.35) of the ears while 2 agreed on 2 (11.1%) of the samples and on one occasion (5.5%) only 1 laboratory identified *Pseudomonas* but none of the samples had identical patterns of antibiotic susceptibility. A 3<sup>rd</sup> study was performed in which duplicate samples were sent to the same lab<sup>1</sup>. Seventy percent of the *Pseudomonas aeruginosa* had different susceptibility profiles.

There are a few possible reasons for these discrepancies. These include:

1. Multiple strains with different susceptibilities
2. Single strain with heteroresistances

In both of the cases the selection of which colonies are selected to be tested for susceptibility may vary from technician to technician. . A 3<sup>rd</sup> study was performed in which duplicate samples were sent to the same lab. Seventy percent of the *Pseudomonas aeruginosa* had different susceptibility profiles.

These results should give you great pause as to the reliability of cultures. The author will only take a culture in cases of OE when there are proliferative changes present AND there are numerous rods present on cytology AND the dog has failed to respond to empirical antimicrobial therapy. This is a very uncommon scenario. This approach is supported by a study in which the author evaluated if there was any correlation between topical antibiotic selection, in vitro bacterial antibiotic sensitivity and clinical response in 16 cases of canine otitis externa complicated by *Pseudomonas aeruginosa*. For these cases empirically selected topical antibiotic therapy was dispensed after collecting bacterial cultures from the affected ears. All dogs had *Pseudomonas aeruginosa* isolated on culture. In 10 cases, the antibiotic selected was deemed to be resistant based on the culture, yet 8/10 responded to the selected antibiotic. One of the 10 resistant cases needed to have a second antibiotic selected to successfully treat the infection. This supports the observation that there is no value to performing cultures in cases of canine otitis externa.

The MIC (broth microdilution technique) method is the "gold standard" for culture technique therefore if a c/s is submitted, the MIC method should be used to determine the susceptibility of the organism(s) rather than the disc diffusion method (Kirby-Bauer). This is because the disk-diffusion susceptibility test (DDST) is only semi quantitative. This means that the drug concentration achieved in the agar surrounding the disc can be roughly correlated with the concentration achieved in the patient's serum. It will only report the organism's susceptibility (susceptible, intermediate or resistant) based on an approximation of the effect of an antibiotic on bacterial growth on a solid medium. Tube dilution (MIC) is quantitative, not only reporting SIR but also the amount of drug necessary to inhibit microbial growth. The MIC is reported as the amount of antibiotic (in µmg/ml) necessary to inhibit 90% of the tested bacteria (the lowest concentration in the tube that is clear). This allows a clinician to not only decide susceptible or resistant but also the proper dosage and frequency of administration of the antibiotic. Note that if the MIC for the bacterial isolate is reported to be susceptible, there is a greater likelihood of successful treatment (cure) than if the isolate was classified as resistant. Treatment failure is still possible due to other drug or patient factors such as the location of the infection and the immunologic status of the host. If the MIC value is in the intermediate category, therapy with this drug at the usual dose will likely be unsuccessful in establishing a cure. However, successful therapy is possible when doses higher than the label dose is used or if the drug is concentrated in the affected organ (eg urine) or is used topically (ear). If the MIC is in the resistant category, treatment failure is more likely because of resistance mechanisms or inadequate drug concentrations. Lastly not only does the MIC method indicate susceptibility, but it also implies the relative risk of emerging resistance and thus the need for a high dose.

The other limitation to the Kirby-Bauer results in regards to *Pseudomonas* susceptibility is the discrepancy between it and MIC. In two studies, Kirby-Bauer underestimated *P. aeruginosa* sensitivity to enrofloxacin (when compared with MIC) whereas in 2 other studies Kirby-Bauer overestimated enrofloxacin susceptibility. Since *Pseudomonas* infections is one of the most common reasons cultures are performed in cases of otitis externa, and enrofloxacin is a commonly used antibiotic for this infection, this inability to properly identify susceptible vs resistance to enrofloxacin is an important limitation in using Kirby-Bauer testing..

With the information gathered above, the treatment is directed toward the primary cause(s) (eg parasitocidal treatment, food trial, intradermal testing and allergen specific immunotherapy, etc) and perpetuating factors. Ear cleaning is performed in the clinic with a bulb syringe, AuriFlush<sup>TM</sup> system or by retrograde tube flushing (under anesthesia). If on the initial examination the ear canals are swollen and painful, ear cleaning may not be performed on the first visit, preferring to use topical glucocorticoids (GC) and systemic GC for 10-14 days to decrease the swelling. Once the swelling has decreased it will be much easier to examine the ear canals and visualize the TM.

Cleaning agents contain substances that soften and emulsify wax and lipids. This initial cleaning is necessary in order to remove debris that may interfere with the effectiveness of topical agents and to reduce inflammatory debris (bacterial toxins). The author doesn't usually have the owner do cleaning after the initial exam since it seems that many owners have trouble with just medicating the ear, let alone cleaning too. Many of the cleaners have a low pH leading to discomfort if used in an inflamed ear. A study comparing 2 ear cleaners (original formulation and then a new formulation) noted that in 38% of the cases with the old formulation and 37.5% of the cases with the new formulation dogs had a moderate to marked avoidance to having the cleaner instilled. This behavior was believed to be due to either a reaction to the ear cleaner or just overall animal irritability. Also the base in the otic ointments/suspensions (mineral oil, liquid paraffin) acts as a ceruminolytic agent. In addition, a recent study calls into question whether any of the ear cleaners have any ceruminolytic activity. In this study the ceruminolytic activity of 13 ear cleansers was evaluated using a standardized synthetic cerumen (SSC) that mimics the composition and texture of canine cerumen. Of the tested products only Cerumene®, Epiotic® and Vet Solutions Ear Cleaner® are available in the US. The test products were incubated with mild agitation for 20 min with 500 mg of SSC previously compacted at the bottom of a test tube. Ceruminolytic activity was then assessed by quantifying the SSC removed by decantation. Overall, Otoclean® (OT) was most efficacious, reaching an activity of 86–90% followed by Netaural® (NET) with a 39%, Specicare® (SP) with a 23% and Cerumene® (CE) with an 8% ceruminolytic activity. None of the other products displayed any ceruminolytic activity. It was concluded that, in the experimental conditions used in this study, only 1/13 products had significant ceruminolytic activity. Please note that the company that manufactures OT funded this study. A follow up study by Robson, et al using Australian and US products revealed that 15/24 cleaners had <5% efficacy while only 6/24 ear cleaners had >80% efficacy- none of which are available in the US.

There is frequently a discussion of the ototoxicity of agents put into ears. Remember that it is inner ear damage, specifically vestibular and/or cochlear damage that occurs with ototoxic agents, not middle ear damage. In order for a drug to cause damage to the inner ear it must either get to the inner ear hematogenously or by traveling thru the middle ear and entering the inner ear thru the vestibular (oval) or cochlear (round) window(s).

In humans because ofloxacin otic solution (Floxin Otic®) is the only topical agent to be labeled by the U.S. Food and Drug Administration (FDA) for use when the tympanic membrane is perforated, oral antibiotics have traditionally been used in this situation. However, according to otolaryngologists because the risk of cochlear damage with the use of other topical medications seems quite small, perforation alone is not an indication for oral antibiotics.

The opinion of this author is that the concern for ototoxicity due to topical medications is overstated. This position is supported by a consensus panel on reviewing the use of ototopical antibiotics. In their report they stated "There have been very few irrefutable cases of ototoxicity reported (after proper use of a topical otic preparation). Under many circumstances, it is difficult to separate the underlying disease process, which is also known to cause ototoxicity, from ototopical drug use." They go on to state "For more than 40 years, the most common treatment has been aminoglycoside combination drops. A longstanding debate over the safety of these drops centers on ototoxicity. Even though the theoretical risk exists, there have been few reported cases in the literature, considering the millions of doses given".

The author has only seen one ototoxic reaction that was suspected to be due to a topical agent and in that case the TM was intact! Therefore, agents are chosen more for their effectiveness than the concern about ototoxicity, especially since there are very few agents that have been proven to be safe in cases of a ruptured TM. It is more important to get rid of the infection than to avoid (effective) drugs because of ototoxicity concerns. Also, just because the TM is intact doesn't mean that the barrier function is complete, therefore, even in the presence of an intact TM it is possible to get drugs into the middle/inner ear.

After ear cleaning topical agents are dispensed. The author prefers ointments over drops because of the impression that ointments get the drugs to the region of the tympanic membrane better than drops do (this may be a volume issue more than the formulation- it has been reported that it takes 1.0 cc of medication to get down to the TM in a medium sized (40 pound) sized dog - personal communication). The other advantage of ointments is that the base vehicle in the otic ointments (mineral oil/liquid paraffin) acts as a ceruminolytic agent.

Most topical products contain a combination of glucocorticoids, antibacterial and antifungal agents. Antibacterial agents used topically include:

1. Broad spectrum agents (gram positive and negative organisms) –
  - a. Aminoglycosides
    - i. Decreased effectiveness in an acidified ear
    - ii. Inactivated by purulent debris (so they must be put in a clean ear)
    - ii. Examples of first line
      - a. Neomycin
      - b. Gentamicin – note injectable water based gentamicin is non toxic even if the dog has a ruptured tympanic membrane- this has not been studied when using commercial ear products that contain more than just gentamicin.
    - iii. Silver sulfadiazine - inactivated by purulent debris so they must be put in a clean ear. It needs

- to be compounded to a 1% solution
      - a. Spectrum also includes yeast
      - b. Inactivated by purulent debris so they must be put in a clean ear
- 2. Narrow spectrum agents (gram negative rods) – most are reserved for resistant gram negative infections
  - a. Polymyxin B - inactivated by purulent material
  - b. Fluoroquinolone — decreased effectiveness in an acidified ear
    - i. Never a first line choice
    - ii. Enrofloxacin
    - iii. Orbifloxacin
  - c. Extended-spectrum penicillins (anti- *Pseudomonas* penicillins)
    - i. Susceptible to beta lactamase
    - ii. Penetrate *Pseudomonas* cell wall better than other antibiotics
    - iii. Increase gram negative activity but less activity gram positive and anaerobes compared to other penicillins
    - iv. Carboxypenicillin
      - a. Ticarcillin
    - v. Ureidopenicillins
      - a. Piperacillin
      - b. More effective against *Pseudomonas* than are the Carboxypenicillin
  - d. Aminoglycoside
    - i. Amikacin and tobramycin
      - a. Gram negative bacteria (including some *Pseudomonas*) have less resistance to amikacin or tobramycin than gentamicin or neomycin
      - b. Decreased effectiveness in an acidified ear
      - c. Inactivated by purulent debris so they must be put in a clean ear

Antifungal agents used include thiabendazole (anecdotally reported to have poor efficacy against *Malassezia*- is it volume related?), nystatin, clotrimazole 1%, miconazole 1 or 2%, posaconazole 0.1% and ketoconazole 1 or 2%

When gram negative organisms are present treatment of OE should include EDTA. To understand the action of ethylenediaminetetraacetic acid (EDTA) solution we need to review some microbiology. A capsule surrounds bacteria. Under the capsule is the cell wall that contains peptidoglycans. Under the cell wall is the cytoplasmic membrane (plasma membrane, cell membrane). The cytoplasmic membrane surrounds the cytoplasm and nuclear body. Gram negative have 2 additional layers. The outer most is the outer cell membrane that lies between the capsule and the cell wall. The outer cell membrane is composed of lipopolysaccharides. The other additional layer is between the cell wall and cytoplasmic membrane, called the periplasmic space. This space contains a variety of enzymes and other proteins that help digest and move nutrients into the cell. Gram positives do not have the outer cell membrane (and therefore no lipopolysaccharides) or a periplasmic space but do have a thick layer of peptidoglycans in the cell wall (vs. gram negatives which only have a thin layer). Note the peptidoglycans are the site of action for beta-lactam antibiotics.

Topical EDTA solution has a direct bactericidal action against bacteria by chelating metal ions important for the integrity of the bacterial cell wall. EDTA also stimulates the release of outer cell membrane lipopolysaccharides (LPS), proteins, and other cell contents. The end result of these actions is the leakage of cell solutes leading to cell death and better drug penetration and antimicrobial activity. Note - since EDTA stimulates the release of LPS from the outer membrane it is less effective at inhibiting gram-positive than gram-negative bacteria because gram-positive bacteria lack an outer membrane.

*Pseudomonas* bacteria have an efflux pump that is mediated by the MEX gene. This protein pumps the drugs out the bacteria, rendering the antibiotic ineffective. EDTA blocks this pump thereby allowing the antibiotic to accumulate in the bacteria.

To maximize its bactericidal activity it is essential for EDTA to be in an environment with an alkaline pH. Appropriate pH (8.0) is maintained by combining it with buffers such as tromethamine (TRIS) hydrochloride. This alkaline pH also decreases the bacterial MIC for an aminoglycoside or a fluoroquinolone. It is therefore useful to use TrisEDTA prior to instilling either of these antibiotics. Two commercial veterinary preparations are available - TrizEDTA®, (Dechra) or Tris Flush® (Sogeval). The ear canal should be filled with the solution prior to instilling the topical antibiotic (15-30 minutes before is ideal). This is done q 12 hrs. EDTA is used primarily for treatment of otitis externa and/or media caused by gram-negative organisms especially *Pseudomonas*.

A product made by Dechra, TrizChlor® contains 0.15% chlorhexidene in addition to the trisEDTA. The combination of these 2 ingredients is beneficial due to the synergistic effect between EDTA and chlorhexidene. The addition of the chlorhexidene extends the antimicrobial spectrum to include cocci in addition to the rods. There are 2 studies that support the effectiveness of this combination. The limitations of these studies are they in vitro studies and they used a 30 minute contact time. Whether these results can be repeated in vivo has not been studied. Since the author uses this product in combination with other topical agents, it is impossible to draw an accurate conclusion.

In regards to safety of the chlorhexidene in otic products, a study reported the effects of instilling 0.2% chlorhexidene into the ear canals of dogs with experimentally ruptured tympanic membranes. In this study, 0.2% chlorhexidene was instilled in greyhound's ear canals bid for 21 days. At the end of the study there were neither clinical vestibular signs nor BAER changes noted. THIS DOESN'T APPLY TO CATS!!!. A study instilling 0.05% chlorhexidene once every other day for 3 treatments into the middle ear of cats concluded that even this concentration of chlorhexidene may cause hearing loss in a cat. The authors did a subsequent study in which they evaluated vestibular effects of infusing chlorhexidene into the middle ear of cats. That study concluded that exposure of the middle ear to even dilute concentrations of chlorhexidene (0.05%) were likely to cause vestibular disturbances.

Any otic cleaner that contains EDTA-Tris would be appropriate to use when otitis externa/media is complicated by both rod shaped bacteria and Malassezia. Some contain ketoconazole. An unanswered concern about using ketoconazole chronically as a maintenance treatment is whether (when?) resistance will to ketoconazole will develop. Also acidifying the ear canal is one of the best treatments/prevention for Malassezia otitis and these products alkalinize the ear.

GC's are an essential component of topical treatment. Successful treatment of OE frequently requires topical GC and in fact the author has seen cases resolve where the only change in therapy was the addition of topical GC. GC are antipruritic, anti-inflammatory, decreases glandular secretions (cerumen), decreases pain and swelling and decreases hyperplasia- all properties that can help restore the normal barrier function to the epithelium of the ear canal. When using topical GC it is best to begin with the most potent form and if GC are needed long term go to less potent (and less side effects) forms (in decreasing potency- mometasone>betamethasone= hydrocortisone aceponate > fluocinolone> triamcinolone>dexamethasone> prednisolone> hydrocortisone). Note- even though hydrocortisone aceponate is classified as an intermediate potent glucocorticoid, equal to that of betamethasone 17-valerate, it has an improved benefit/risk ratio due to its decrease incidence of skin atrophy. REMEMBER topical steroids are systemically absorbed and can lower thyroid hormone concentrations; elevate liver enzymes, suppress the hypothalamus-pituitary-adrenal axis and even cause pu/pd.

The author has rarely used systemic antibiotics when treating OE. This approach is supported by the previously mentioned consensus panel who stated "In most cases of uncomplicated AOE, topical antibiotics are the first-line treatment choice. There is no evidence that systemic antibiotics alone or combined with topical preparations improve treatment outcome compared with topical antibiotics alone".

In addition systemic antibiotics increase the risks of adverse effects and enhancing the environment for the production of resistant organisms. In humans it has been reported to increase the time to clinical cure and do not improve outcomes compared with a topical agent alone in uncomplicated otitis externa, In humans systemic antibiotics are recommended to be used only when the infection has spread beyond the ear canal, or when there is uncontrolled diabetes, immunocompromise, a history of local radiotherapy, or an inability to deliver topical antibiotics.

Systemic antibiotics or antifungal agents are used only if otitis media with bacteria, other than Pseudomonas (see below about Pseudomonas), or Malassezia are present on cytology, compliance and follow up has been good and topical treatment has been unsuccessful (very rare occurrence). Once again this approach is supported by the consensus panel (for humans) in which they state "The initial therapy of otherwise normal, healthy patients with CSOM (chronic suppurative otitis media)... should consist of ototopical drops and thorough cleaning of the canal."

Empirical choices for cocci include cephalosporins, amoxicillin-clavulanic acid, clindamycin and potentiated sulfas. Empirical choices for rods include cephalosporins, amoxicillin-clavulanic acid (use TID vs. BID for gram negative organisms) and potentiated sulfas. Fluoroquinolones should be reserved for culture-proven resistant gram-negative rods. The antifungal agents that the author prefers include ketoconazole (5 to 10 mg/kg sid, given with food to enhance absorption), fluconazole (10 mg/kg sid), and itraconazole (5 mg/kg sid).

If the OM infection is due to Pseudomonas it is unlikely that systemic antibiotics will be useful. This is because systemic administration of antibiotics, including the fluoroquinolones, can't exceed the MIC for P. aeruginosa in the ear canal. Since P. aeruginosa is the most common pathogen associated with OM in dogs, systemic administration of antibiotics will only select for more resistant organisms. Since it has been documented in humans that high drug concentration may be achieved in the middle ear when topical antibiotics are used, in cases of OM, topical treatment is the author's mainstay therapy.

Systemic glucocorticoids are used if the ear canals are edematous, ulcerated and/or stenotic. Even proliferative changes may decrease with steroid administration since secondary edema may be present. Prednisone at 0.25-.50 mg/# bid for 7-14 days is dispensed and a reassessment is made in 7-14 days. At that time if the canals are completely open and the ulcers are healed, the prednisone can be discontinued. If the ears are better but not normal then make a clinical decision is made whether to maintain or decrease the dose for another 7-14 days. Again reassessment should be done in 7-14 days. If the ear canals are not opened by this second recheck, a total ear canal ablation with a bullae osteotomy would most likely need to be performed.

#### Specific scenarios

1. Acute otitis (and/or infrequent) externa treatment overview. It is important to differentiate whether this is a first time occurrence, a recurrence or an unresolved infection. The only way to know this is to do follow-up examinations on

ALL cases of OE. Remember that the absence of symptoms is not synonymous with resolution of the disease. This means that owners are unable to determine whether the infection is resolved and the dog must be rechecked. If this is the first episode, discuss the possible predisposing, primary and perpetuating causes and foreshadow that additional testing may be necessary in the future. In this situation, begin with eliminating easily diagnosed primary causes (foreign bodies, parasites, masses, etc). During the examination be sure to evaluate the status of the tympanic membrane. Perform a cytology to identify secondary infections. Treatment should be directed toward both the infectious component and the inflammatory component. Treatment should be for 7-14 days, unless using Easotic® (Virbac). At the end of the treatment, while still on therapy, a recheck examination should be performed!! Traditionally once the OE has clinically resolved the author has treated cases for an additional 7 days. More recently the author has begun to use a product with a unique delivery system- Easotic® (Virbac). When using this product, the dog is only treated for 5 days, in contrast to the 7-14 day schedule as previously mentioned, and then rechecked. The author has found this product to be very effective- most likely due to better compliance. Unless contraindicated, a topical GC containing product should be used as part of the therapy. The author prefers ointments over drops when treating otitis externa. Since all the otic ointments contain steroids and an antimicrobial agent, the author uses a combination product.

- a. In cases of an acute infection there are a variety of products that are effective and would be appropriate to dispense (note most products will contain a combination of 3 of these drugs- antifungal, antibiotic and steroid). Typical ingredients include miconazole polymyxin B, prednisolone, nystatin, neomycin sulfate, thioestrepton, triamcinolone acetonide, gentamicin, hydrocortisone aceponate, betamethasone valerate and clotrimazole.
  - b. The only time this is altered is if there are heavy rods or just rods present, which is very rare in this scenario. In that case the author would use TrisEDTA, silver sulfadiazine and either gentamicin or polymyxin B (see below – Pseudomonas)
  - c. If the dog is painful, systemic GC and analgesics (tramadol, gabapentin and/or Tylenol with codeine) are added to the treatment.
2. If initially TM the is not visible due to swelling of the ear canals oral prednisone ½-1mg/#/day for 10-14 days will be added to the topical treatment. Because of the potency of fluocinolone or mometasone, Synotic® (fluocinolone with DMSO) and/or Mometamax® (mometasone) will be included in the therapy. Many times an analgesic is added as previously described (NO NSAID!).
- a. A recheck examination will be performed in 10-14 days. If the TM is visible and the swelling resolved, then only the prednisone can be stopped. All the other treatment should be continued.
  - b. If the TM is not visible but the swelling has resolved, then an ear lavage via FEVO under general anesthesia should be performed.
  - c. If at the 10-14 day recheck the TM is not visible and the swelling has NOT resolved, continue the prednisone for another 10-14 days and then recheck.
    - i. If the ear canals are still narrowed at the next recheck, perform (or refer) a total ear ablation with a bullae osteotomy.
3. In cases of chronic (recurrent and/or unresolved) otitis externa, it is essential to determine if it is recurrent or unresolved. If it is unresolved is it because of owner compliance? If it is poor compliance then this problem must be resolved! If it is recurrent (or unresolved with good owner compliance) in addition to the above, a very aggressive search is performed to identify and treat the primary, perpetuating and secondary factors. Treatment should be for a minimum of 30 days. As above, GC will be an important component of therapy.
- a. If there is only yeast, then the depending on what products have already been used, consider using clotrimazole 1%, miconazole 2%, 0.1% posaconazole or 2% ketoconazole lotion compounded with dexamethasone 0.1%.
  - b. If cocci are the only organism present then use gentamicin, mupirocin or 5% cefazolin (1 gm vial mixed with 20 cc Triz-Edta plus).
  - c. If rods +/- cocci are present then use-Triz-Edta (+/- chlorhexidene if cocci are present) along with gentamicin or polymyxin B and silver sulfadiazine
  - d. Because of the association of the use of fluoroquinolones and the development of MRSA, and E.coli, the author rarely uses fluoroquinolones for the treatment of otitis externa. This concern is supported by many different sources. In the BSAVA “Guide to the Use of Veterinary Medicines” it discusses the prudent use of antimicrobial agents. In regards to all fluoroquinolones (FQ) it states “that in all species fluoroquinolones and third- and fourth-generation cephalosporins should be used judiciously and never considered as first-choice options”. The concern with using FQ is that, according to information from the CDC website, “a major

limitation of fluoroquinolones is that resistant mutants can be selected with relative ease, leading to relapse and treatment failure". In addition it has been observed that there is a significant association between total fluoroquinolone use within human hospitals and percentage of *S. aureus* isolates that were MRSA and between total fluoroquinolone use in the community and percentage of *E. coli* isolates that were fluoroquinolone-resistant *E. coli*. Association between fluoroquinolone exposure and the induction of *mecA*-positive *S. aureus* (MRSA) and the increase in the resistance index for methicillin resistance has been noted.

Lastly it has been widely reported that there is an association between FQ use and clinically significant MRSA

- i. The only time the author will use enrofloxacin or orbifloxacin is when the infection has failed to respond to the author's aggressive therapy. The author prefers the later product due to the inclusion of steroids in the lotion. If using the former, dexamethasone should be added to achieve a final concentration of 0.1% dexamethasone.

*Pseudomonas* infections are especially challenging because of *Pseudomonas*' intrinsic multidrug resistance (MDR). Many of the clinically relevant resistance mechanisms in *Pseudomonas aeruginosa* are attributed to synergy between its outer membrane that has a very low permeability to drugs and the presence of an active drug efflux pump (MEX). Because of the intrinsic MDR, *Pseudomonas* infections successful treatment must be aggressive before other resistance develops.