Diagnosis and Medical Management of Canine Otitis

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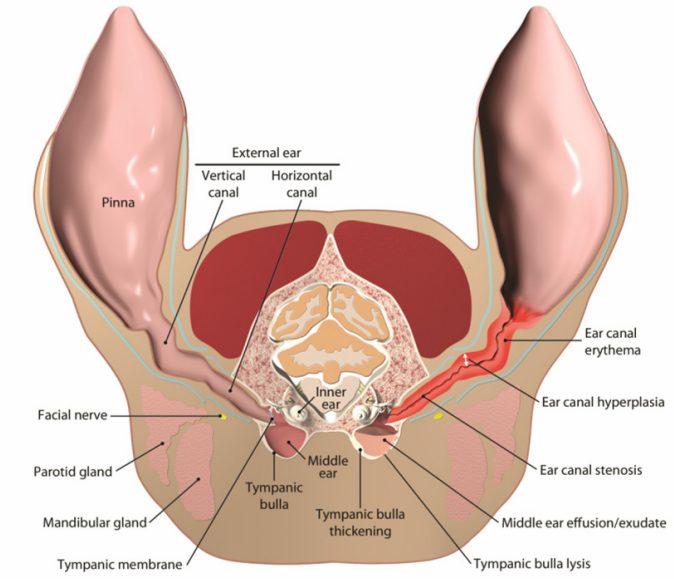
Canine otitis externa is defined as inflammation of the external ear canal which may also include the pinna. Otitis media is present when the middle ear is also involved, usually by extension of infection through the tympanic membrane.



From Logas D and Kwochka KW. *Illustrated Reference Guide of Basic Veterinary Dermatology*. American College of Veterinary Dermatology and Bayer Corporation

Canine otitis is one of the most common, challenging and frustrating conditions in veterinary medicine. The major reason for this is that it is not a single disease but a complex of interrelated etiologic components. Successful management requires: I) Identification and control of the various pathogenic factors which may be contributing to the otitis. This becomes especially important with recurrent and chronic otitis. II) Identification and treatment of the inflammation, pruritus, discomfort and infectious agent(s) present at the time of examination for a long enough period of time to control the infection and minimize the development of chronic changes. III) Establishment of a maintenance plan to control redevelopment of inflammation and secondary infections.

IDENTIFICATION AND CONTROL OF THE PATHOGENIC FACTORS WHICH MAY CONTRIBUTE TO OTITIS – PPSP – PREDISPOSING, PRIMARY, SECONDARY AND PERPETUATING FACTORS

This classification system or modifications of it have been used for many years. A detailed description is available.[1]

Predisposing Factors are pre-existent conditions that increase the risk of development of otitis when other factors are present. They include conformation (pendulous pinnae, narrow ear canals, high concentration of glandular tissue in the canal, etc.), previous treatments (aggressive use of cotton swabs for routine cleaning, irritant cleaning solutions, etc.) and excessive moisture. A fairly common example is a golden or Labrador retriever that swims

regularly with no problem unless the dog has some atopic inflammation in the canal. The moisture and inflammation together predispose to secondary infection and clinical otitis externa.

Primary Factors directly result in inflammation, hypersensitivity reactions, trauma or other damage to the ear canal either individually or in combination, usually resulting in secondary infections and chronic changes over time if left untreated. Primary factors are sometimes not diagnosed because changes are subtle, a proper diagnostic plan is not implemented or owners elect not to pursue the recommended plan. Factors include foreign bodies, ear mites and other parasites, trauma, atopic dermatitis, cutaneous adverse food reactions, endocrinopathies, epithelialization abnormalities and autoimmune diseases. Depending on history and clinical lesions, diagnostics include otoscopic examination, cytology, dietary changes, biopsy of the ear canal and/or pinna, therapeutic trials and serum or intradermal testing for reactions to environmental allergens.

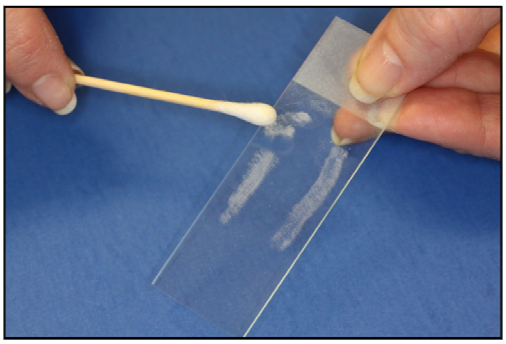
Secondary Factors, as the name implies, do not cause otitis by themselves but cause further pathology when present with primary causes and predisposing factors. Secondary factors are bacterial and yeast infections which are diagnosed by cytology and, when indicated, bacterial culture and susceptibility. These infections need to be treated aggressively until resolved and recurrence prevented by managing primary factors and/or instituting a long-term maintenance plan.

Staphylococcus pseudintermedius (*Sp*) and *Malassezia pachydermatis* (*Mp*) are the two most common otic pathogens associated with canine otitis. In a study of 100 clinical specimens from 50 dogs with bilateral otitis externa, *Sp* was isolated in 70 and *Mp* in 73 with *Proteus mirabilis* (*Pm*) in 7, *Pseudomonas aeruginosa* (*Pa*) in 3 and *Escherichia coli* (*Ec*) in 1.[2] Two microorganisms were isolated in 62% of the samples with *Sp* and *Mp* the most frequent association observed in 54.8%. In another study of bacterial isolates in 92 cultures from dogs with otitis externa, *Sp* was isolated from 73.9%, *Pa* from 10.9%, *Pm* from 3.3% and *Ec* from 1.1%.[3] In an 11-year study of lipophilic yeast of the external ear canals of 188 dogs with otitis externa, *Mp* was isolated from 62.2% of the dogs with 76.1% of the isolates showing heavy growth of the yeast.[4]

Perpetuating Factors are anatomic and physiologic changes which occur when inflammation and infection have been present with chronic otitis, generally over a long period of time. These factors include hyperplastic changes and fibroplasia of the ear canal tissue, disruption of normal epithelial migration, apocrine gland hyperplasia and rupture, furunculosis with a foreign body reaction to keratin in the dermis, false middle ear cavity, otitis media, ossification of cartilage and progressive hearing loss. Once these changes occur ears become more prone to recurrence of inflammation and infection. With time, these changes become irreversible leading to failure of medical therapy.

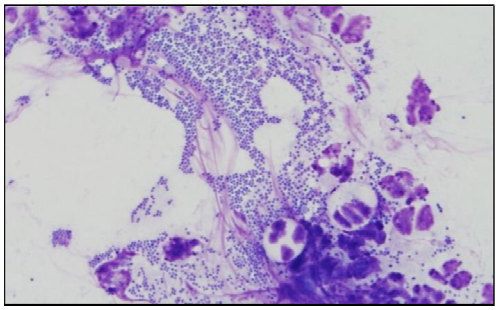
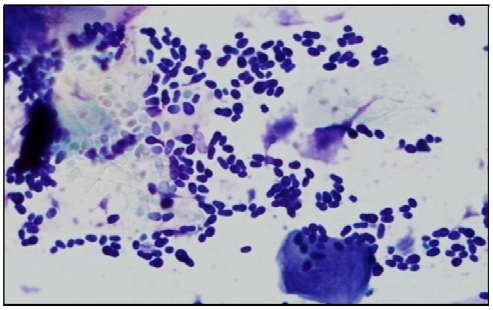
DIAGNOSIS

Ear Canal Cytology should be performed with a cotton-tipped applicator in all cases of otitis! Repeat cytology at recheck visits is the only way to monitor response to prescribed treatments and to be sure that pathogens have not changed in the ear canal. Samples should be taken from the entrance to the horizontal canal if possible, being careful not to rupture an intact tympanic membrane, or as deep in the vertical canal as possible. Gentle lateral traction of the pinna will facilitate passage of the applicator into the canal. Cytologic preps are then made by firmly rolling the swabs onto a clean microscope slide, heat fixing (personal preference), staining with modified Wright Giemsa (Diff-Quik) and examination at oil immersion 1000x.

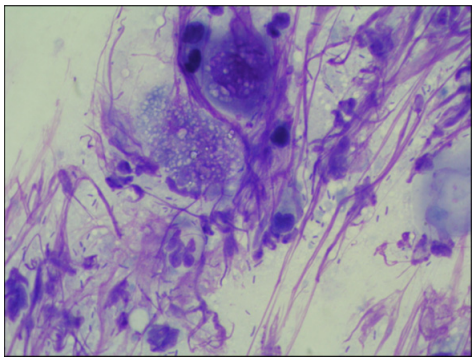
The value of the initial cytology is that the results will guide selection of an appropriate topical product to specifically treat the existing infection. The decision to treat and with what is based on the clinical condition of the ear canal, organisms identified, numbers of organisms and presence of inflammatory cells.

Staph. pseudintermedius *Malassezia pachydermatis*

Chronic gram-negative otic infections have a high prevalence of otitis media.[5] Patients with otitis media also need a cytology sample taken from the middle ear using swabs made for small body cavities such as 5.5 inch sterile calcium alginate swabs (Calgiswab®, Puritan Medical) or material from the tip of the catheter or needle used to perform a myringotomy. Cytology associated with gram-negative otitis is characterized by a predominant population of rods with neutrophils, phagocytized bacteria, red blood cells and proteinaceous debris.

Pseudomonas aeruginosa



Bacterial Culture and Susceptibility Testing (CS) is not needed for cases of acute otitis externa to be treated with ear cleaning, anti-inflammatory drugs and topical antimicrobials alone. It is indicated for severe chronic cases of otitis externa, when rods and inflammatory cells are found on cytology, when otitis media is present, when systemic antibiotics are deemed necessary and in cases not responding to empirical therapy. The sample should be taken from the middle ear (when otitis media is present) and/or within the horizontal canal using a sterile culturette passed through a sterile otoscope cone before cleaning or treatment. In a prospective study of 23 dogs

with chronic bilateral otitis externa of at least 6-months' duration, concurrent otitis media was present in at least one tympanic bulla in 22 of the dogs (38 of 46 ears).[5] Of the 38 ears evaluated, a difference in total number of isolates or susceptibility patterns between organisms from the horizontal ear canal and middle ear was found in 34 (89.5%) ears.

Even when CS is indicated, variable results may be obtained due to interference by concurrent antibiotic use, sample location, multiple strains of the same organism present in the ear canal, and variability among laboratories. CS results are not reproducible 100% of the time in samples taken from a badly infected ear canal or tympanic bulla.

BASIC TREATMENT PRINCIPLES

1) Identify and treat predisposing and primary factors. Especially consider the most common ones seen in practice: otic foreign bodies, ear mites, atopic dermatitis, cutaneous adverse food reactions, scaling/glandular abnormalities and swimming.

2) When needed, use topical and/or systemic corticosteroids to increase patency of a chronically affected stenotic ear canal to facilitate full examination, sample collection and flushing:

- Topical mometasone, betamethasone, triamcinolone, dexamethasone or fluocinolone/DMSO for 1-2 weeks. Most of these steroids are available in commercial otic formulations.
- Triamcinolone: 0.1 mg/kg total dose injected in a ring-like fashion with a 22-gauge spinal needle through an otoscope cone into proliferative tissue at various depths in the ear canal[6]
- Systemic dexamethasone: 0.1 mg/kg, IM or SQ
- Prednisone or prednisolone: 0.5-2.0 mg/kg/day for 1-2 weeks

3) Completely clean and flush the ear canal and tympanic bulla (if indicated) initially and keep the ear clean thereafter. In addition to physically removing debris and pathogens from the ear, cleaning the canal facilitates movement and penetration of topically-applied medications down the canal and removes organic material that may interfere with some topical antibiotics (aminoglycosides and polymyxin). The reader is directed to other references which describe in detail initial cleaning and flushing of the external ear and tympanic bulla.[1,7,8] Depending on the nature of the otic exudate, condition of the ear canal, and integrity of the tympanic membrane, various techniques and agents may be utilized for in-hospital or at-home cleaning.

- Mild to moderate cases may be adequately cleaned by filling the canal with the cleaner, massaging the canal for several minutes if possible, letting the patient shake debris out of the ears and drying with a cotton ball. With proper instruction, clients may be able to perform these cleanings at home if necessary.

- The goal is to start with a clean ear canal and then repeat as needed during the time that the infection is being treated if debris re-accumulates in the canal. When using the newer residual otic antibiotic/antifungal/corticosteroid treatment formulations (Claro™, Bayer; Osurnia®, Elanco), cleaning should not be repeated during the treatment duration. If cleaning is deemed necessary based on the condition of the ear at recheck then the medication may need to be re-applied.

- For moderate to severe cases, in-clinic deep flushing under general anesthesia is recommended. This may be accomplished with a bulb syringe, however, more directed flushing deep in the canal and middle ear may be done with a syringe (usually 12 mL) attached to a catheter or red rubber feeding tube passed through a hand-held otoscope. Fiberoptic video otoscopy (Karl Storz Otoscopy, https://www.karlstorz.com/ar/en/small-animals.htm) is very helpful when cleaning of the deep horizontal canal and tympanic bulla is necessary. This equipment allows superior visualization, magnification, a channel for diagnostic instruments and flushing tubes and the ability to capture digital images for clients

to enhance communication and compliance.

- Cleaning Agents
    - *Ceruminolytic Agents* purportedly act by emulsification of waxes and lipids to more readily flush ceruminous debris from the canal. Ingredients include calcium or sodium dioctyl sulfosuccinate, triethanolamine polypeptide oleate condensate, carbamide peroxide, sodium lauryl sulfate and squalene. Examples of commercial formulations include: Cerumene®, Vetoquinol; Cerulytic®, Virbac; Douxo® Micellar, Ceva; and OtiRinse®, Bayer. These have commonly been used in-clinic where they are applied 5-10 minutes before cleaning and then flushed out of the canal with water or saline after exerting their effect to avoid potential irritancy and ototoxicity. They may also be used for at-home maintenance flushing in dogs with intact tympanic membranes that accumulate ceruminous exudate in their canals regularly such as seborrheic cocker spaniels. There are no published studies in dogs or cats documenting the clinical efficacy of ceruminolytic agents.
    - *Mild Cleaning /Antiseptic/Drying Agents* are most often used for in-clinic flushing, at-home cleaning and long-term maintenance of chronic and recurrent otitis. Common ingredients include alcohol, chlorhexidine*, parachlorometaxylenol (PCMX), tris-ethylenediaminetetraacetic acid (tris-EDTA), ketoconazole, miconazole, propylene glycol, sulfur, aluminum acetate, enzyme combinations and various types of acids at low concentrations. Examples of commercial formulations include: Epi-Otic® and Epi-Otic Advanced®, Virbac; MalAcetic® Otic, Dechra; Mal-A-Ket Plus TrizEDTA® Flush, Dechra; Malaseb® Flush, Bayer; OtiRinse®, Bayer; OtiSoothe®, Ceva; T8 Keto® Flush, Bayer; TrizULTRA + Keto®, Dechra.
      (*Chlorhexidine acetate (0.2%) was applied twice a day for 3 weeks to the external ear canals of dogs with surgically perforated tympanic membranes. There were no observed abnormalities in vestibular or auditory function over the course of the study.[9] However, chlorhexidine may be ototoxic in some individuals and should be used with caution in dogs with confirmed or suspected ruptured tympanic membranes. Chlorhexidine is also a difficult molecule to formulate correctly and it is advised not to compound other ingredients into commercial formulations of chlorhexidine or risk it losing activity.[10])
    - For in-clinic flushing if there is concern that the tympanic membrane might be ruptured, the author has most commonly used warm isotonic saline and solutions containing trisEDTA. TrisEDTA also offers the advantage of destabilizing and increasing permeability of gram-negative bacterial cell walls thus potentially enhancing the activity of topically applied antibiotics.[11] It should be noted that there is no veterinary commercial product approved by the FDA for use in middle ears of dogs or cats.

4) If at all possible, eliminate swimming in dogs with a history of recurrent otitis. For dogs that cannot be completely kept out of the water and have problems with recurrent infections, regular use of the cleansing, antiseptic drying agents listed above may be helpful. Additionally, the combination of Burow's solution and 1% hydrocortisone (Cort/Astrin Solution, Vedco) is effective applied after swimming and as needed between swimming.

5) Use a sufficient volume of topical medication to adequately coat the ear canal. Most commercial veterinary products as labeled do not provide adequate volumes to achieve this.

- Depending on the size of the dog, 0.25-1.0 mL is needed, q12-24h (per product label).
- Use a dosing syringe.
- Claro, Easotic® (Virbac) and Osurnia deliver 1 mL of medication directly from their applicators and thus achieve adequate volumes for dogs of all sizes.[12]
- To facilitate more complete penetration into the canal, apply to the deep portion of the vertical canal and gently massage the ear for 30 seconds after instillation.

6) Continue antimicrobial treatments for 2 weeks after the infection is cytologically resolved.

7) Utilize a long-term maintenance program to prevent recurrence. This is generally accomplished by regular use of the cleansing, antiseptic drying agents listed above and topical steroids as needed to control inflammation (usually from allergies) which initiates the secondary infections. Ideally, the primary allergy should be diagnosed and treated to best eliminate recurrence of otitis.

8) Consider a surgical option for an ear that cannot be medically salvaged.[1]

TOPICAL THERAPY

Topical therapy alone is usually sufficient to successfully treat and control otitis externa. Systemic antibiotics, antifungals and corticosteroids may be needed with chronic proliferative otitis externa, otitis media, severe recurrent infectious otitis and when owner or patient compliance issues preclude the use of topical formulations that need to be administered once or twice a day for days or weeks. Clinical experience suggests that compliance is a major factor in treatment failures and recurrence of otitis. Recently approved products such as Claro and Osurnia address this issue with the former approved for single administration and the latter for 2 applications at a 7-day interval for *S. pseudintermedius* and *M. pachydermatis*.

The topical products approved by the FDA for otitis externa (see table below) contain combinations of ingredients including antibiotics, antifungals and corticosteroids. The appropriate product should be chosen based on clinical condition of the ear canal, cytologic findings of infectious agents (cocci, yeast, rods) and approved spectrum of activity. Culture and susceptibility results may also help guide selection of topical treatments. However, CS typically underestimates *in vivo* efficacy of topicals since topical antibiotics are used at concentrations many times those attainable in plasma and tissues and may be formulated with vehicles that enhance the efficacy of the antibiotic.

The staphylococcal and/or yeast infections most commonly seen in practice, as described above, generally do not require topical formulations with broad-spectrum aminoglycosides, fluoroquinolones or polymyxin. These are better reserved when needed for the less common gram-negative infections associated with *P. aeruginosa*, *E. coli* and *P. mirabilis*. Over usage when not indicated may lead to development of resistance to these important antibiotics for serious infections in animals and humans.[5]

Some commercial formulations (see table below) are in petrolatum, hydrocarbon oil or paraffin silicon suspension and ointment vehicles. While they may adhere well to the lining of the ear canal, they may occlude and further moisturize an already macerated epithelium, especially with once or twice daily application over several days. If the ointment or suspension does enter the middle ear with a ruptured tympanic membrane, it is uncertain how long it takes for normal metabolic processes to remove it. In most ears, commercial formulations with non-occlusive water-soluble and aqueous solution vehicles are more desirable.[12]

Compounded otic preparations for the treatment of ear infections in dogs have been utilized for many years. It should be noted that these are not FDA-approved so their use is considered extra-label and efficacy is based on anecdotal reports with lack of published scientific evidence. Over time, approval of new products has decreased the need for compounding. Compounding of active ingredients in lanolin and other occlusive vehicles was done to enhance residual activity and improve convenience and compliance. Residual activity has now been achieved in the FDA-approved topicals, Claro and Osurnia. There may still be occasions when commercial formulations are not clinically effective or tolerated by a patient. For these situations the reader is referred to a drug formulary for various compounding options.[13]

Combination Ear Treatment Products
(modified and updated from reference 1)

Brand, MFG	Active Ingredients	Vehicle	Indications*	Dosage and Duration
Baytril® Otic, Bayer	0.5% enrofloxacin, 1% silver sulfadiazine	Water-based emulsion	*CPS, Mp, Pa, E, Pm, S, Ah, A, Ca, Kp*	5-15 drops, Q12h, for 14 days
Claro™, Bayer	1.5% florfenicol, 1.33% terbinafine, 0.2% mometasone furoate	Clear, liquid solution	*Sp, Mp*	1 mL, single administration
Easotic®, Virbac	0.15% gentamicin, 1.51% miconazole, 0.11% hydrocortisone aceponate	Semi-liquid petrolatum jelly	*Sp, Mp*	1 mL, Q24h, for 5 days
GentaOtic™, Henry Schein	0.3% gentamicin, 0.1% betamethasone	Solution	Bacteria susceptible to gentamicin**	3-8 drops, q12h, for 7-14 days
Mometamax®, Merck	0.3% gentamicin, 1% clotrimazole, 0.1% mometasone furoate	Plasticized hydrocarbon oil suspension	*CPS, Mp, Pa, Ef, Pm, S*	4-8 drops, q24h, for 7 days
Osurnia®, Elanco	1% florfenicol, 1% terbinafine, 0.1% betamethasone acetate	Translucent gel	*Sp, Mp*	1 mL, repeat in 7 days
Otomax®, Merck; Tri-Otic®, Med-Pharmex	0.3% gentamicin, 1% clotrimazole, 0.1% betamethasone	Plasticized hydrocarbon oil suspension	*Mp* and bacteria susceptible to gentamicin**	4-8 drops, q12h, for 7 days
Panalog®, Zoetis; Anamax®, Dechra	0.25% neomycin, 2,500 IU/mL thiostrepton, 100,000 IU/mL nystatin, 0.1% triamcinolone	Cream or plasticized carbon polyethelene ointment	Bacterial and *Candida* infections**	No specific dosing recommendation for otitis
Posatex®, Merck	1.0% orbifloxacin, 0.1% posaconazole, 0.1% mometasone furoate	Plasticized hydrocarbon oil suspension	*CPS, Mp, Pa, Ef*	4-8 drops, q24h, for 7 days
Surolan®, Elanco	0.053% polymyxin B, 2.3% miconazole nitrate, 0.5% prednisolone acetate	Liquid paraffin silicon suspension	*Sp, Mp*	5 drops, q12h, for 7 days
Tresaderm®, Merial	0.32% neomycin, 9% alcohols, 4% thiabendazole, 0.1% dexamethasone	Propylene glycol solution	Acute and chronic otitis externa**	5-15 drops, q12h, for 7 days

**CPS* (coagulase-positive *Staphylococcus* spp.), *Mp* (*Malassezia pachydermatis*), *Pa* (*Pseudomonas aeruginosa*), *E* (*Enterobacter* spp.), *Pm* (*Proteus mirabilis*), *S* (*Streptococci* spp.), Ah (*Aeromonas hydrophila*), A (*Aspergillus* spp.), Ca (*Candida albicans*), Kp (*Klebsiella pneumoniae*), *Ef* (*Enterococcus faecalis*) **Older products with no specific organisms indicated

SYSTEMIC THERAPY

Systemic antimicrobials.[1,14] Routine systemic antimicrobial therapy for infectious otitis externa and otitis media is controversial. Some dermatologists have stated that there is not a difference in success rate managing otitis with or without systemic antibiotics. However, there are no credible data comparing efficacy using topical therapy alone, systemic therapy alone and topical and systemic treatments. Indications for use of systemic antibiotics include otitis media, a pure gram-negative infection, proliferative chronic otitis externa, purulent ulcerative otitis externa and when owners cannot treat their pet's ears with topical therapy. If at all possible, systemic antibiotics should be selected based on CS results. If an empirical choice is made, it should be based on cytologic findings and guided by a current antimicrobial reference.[15] Depending on the pathogen and the severity and chronicity of the infection, systemic antimicrobial treatment should be continued for 1-2 weeks after negative cytology followed by a topical maintenance program to prevent recurrence of infection.

For gram-positive infections associated with *Staphylococcus*, cephalosporins, clindamycin and amoxicillin trihydrate/clavulanate potassium are generally good initial choices. The only oral antibiotics that may be efficacious for gram-negatives such as *Pseudomonas* are the fluoroquinolones, enrofloxacin and marbofloxacin. They should be used at the high end of the approved dosage range to avoid the development of resistance. The human fluoroquinolone, ciprofloxacin, should only be used when CS indicates resistance to the veterinary-approved drugs but continued susceptibility to ciprofloxacin based on MIC's. Even in this situation, oral ciprofloxacin tablets may not achieve effective plasma and tissue concentrations because of extremely variable absorption after oral administration in dogs.[16]

When *Pseudomonas* has become multi-drug resistant and topical therapy alone does not resolve the infection, parenteral antibiotic treatment is required.[14] Options in dogs based on CS generally include ticarcillin disodium/clavulanate potassium (15-25 mg/kg, q8h, IV), meropenem (12 mg/kg, q8h, SQ; 24 mg/kg, q8h, IV), ceftazidime sodium (30 mg/kg, q6h, IV, IM; 30 mg/kg, q4h, SQ), amikacin (15-30 mg/kg, q24h, IM, SQ, IV), and gentamicin (10-14 mg/kg, q24h, IM, SQ, IV).[14] Patients on the aminoglycosides must be monitored for nephrotoxicity with urinalysis for protein and tubular casts and serum for BUN and creatinine every 1-2 weeks. Meropenem and ceftazidime should be used as a last resort due to implications for human health.

When *Malassezia* infections have failed to respond to topical therapy alone or if yeast otitis media is present, ketoconazole, fluconazole or itraconazole at 5-10 mg/kg, q24h or terbinafine at 30-40 mg/kg, q24h may be effective.

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