The most important aspect of treating Pseudomonas otitis is to determine the primary cause and perpetuating factors of the otitis. Pseudomonas ear infection is almost always a secondary cause of otitis. After primary causes and perpetuating factors are managed then once the Pseudomonas is eliminated it will not recur. Often the emphasis is placed on treating Pseudomonas otitis with a topical antibiotic that it is sensitive to. When a very resistant strain is encountered then many veterinarians are asking for advice on what to do. The answer is that treating all Pseudomonas otitis cases should involve a multiple component therapeutic approach.

The first part is to get the ear canal, and middle ear if involved, as clean as possible eliminating nidus for organisms to be protected from topical therapies, reducing pro inflammatory toxins and eliminating the toxins and neutrophils that may interfere with some antibiotics by inactivating them. This is more of a problem when polymyxin and aminoglycosides are used as the antibiotic. When exudation is rapidly returning and often in ulcerative cases repetitive cleaning weekly and occasionally even alternate day flushes at home may be necessary. The level of cleaning is determined by what is required to keep the ear canal clean and free from exudate build up. The second part is the use of disinfectants prior to and in conjunction with a topical antibiotic, the third component. Disinfectants have the advantage or not inducing resistance and are often less expensive. Multiple disinfectants are available and effective though in general I tend to use acetic acid containing products. Acetic acid has been shown to be very effective in the treatment of otitis externa in humans. It is believed that its activity is not completely due to the pH because other acidic products are not as effective in killing Pseudomonas and Staphylococcus. However it is possible to get a disinfectant effect just by lowering the pH of the ear canal (Nuttal and Cole 2004). Acetic acid is most effective against Pseudomonas, with a 2% solution being lethal within one minute of contact (Griffin 1993; Thorp, Kruger et al. 1998). White vinegar is generally about 5% acetic acid and it has been recommended as an ear wash when diluted to 2.5% by mixing it in equal amounts with water or 25% water, 25% isopropyl alcohol and 50% white vinegar. Combinations with 2% boric and 2% acetic acid are available commercially. (Malacetic, Dermapet® and Otocet™ solution, Vedco) The disinfectant is used once daily as a rinse prior to application of a topical antibiotic glucocorticoid preparation. For resistant previously non responsive strains my favorite is the sequential use of two disinfectants followed by the topical antibiotic. The first is acetic acid which is then followed with a rinse with Tris-EDTA. Tris EDTA increases the permeability of bacterial cell membranes by binding Ca and Mg ions. This activity is mainly apparent in gram negative bacteria including Pseudomonas sp. Tris-EDTA was shown to have a sparing effect on the MIC of enrofloxacin against ciprofloxacin resistant Pseudomonas as well as resolve clinical cases resistant to cephalexin or enrofloxacin (Fanca, Pirovalli et al. 1997; Ghadamosis and Gottelf 2003). It was also shown effective in vivo in a small number of cases when combined with a low level (0.15%) of chlorhexidine digluconate (Gibaudo, Cornogiani et al. 2004). My preference for the tris EDTA combined with low strength (0.15%) chlorhexidine (TrizEDTA™ Plus, Dermapet). This is not rinsed out but allowed to be present when the antibiotic containing topical is then applied. This combination is done twice daily.

The third component is the use of a topical antibiotic. In some countries Polymyxin is available and also considered a first line antibiotic. It is very effective even for Pseudomonas at least in countries such as the United States where it is not routinely used. To get good effects though it is imperative to have a clean ear as purulent exudates bind it and greatly diminish polymyxin activity. Some of this may be beneficial as polymyxin E has been shown to bind endotoxin and could result in less inflammation and tissue damage (Senturk 2005). The most commonly used antibiotics are gentamicin (Mometamax®, Schering-Plough Animal Health) or fluoroquinolones such as enrofloxacin (Baytril Otic, Bayer) or in Europe marbofloxacin (Aurizon®, Vetroquinol). Ototoxicity is reported with all gentamicin topicals.
However, similar to chlorhexidine, this concern may be overstated. A study showed no vestibulotoxic or ototoxic effects from 21 days of otic gentamicin applied BID to ears with ruptured tympanic membranes (Strain, Merchant et al. 1995). A topical combination of enrofloxacin 0.5% and silver sulfadiazine 1.0% (Baytril Otic, Bayer Corp) is useful for the treatment of bacterial and yeast otitis. It may be effective though lacks a glucocorticoid in the formulation. Another option is in clinic formulated drops made by combining 4ml of injectable enrofloxacin 2.27% (Baytril, Bayer) with 4ml of injectable dexamethasone sodium phosphate (4mg/ml) and then 8 cc of saline or 8cc 1% miconazole lotion if Malassezia are also present. Third line topical antibiotic options to consider are amikacin, tobramycin and ticarcillin. Injectable amikacin is available at 50 or 250mg per ml and is diluted so that it is used at concentrations ranging from 25mg/ml to 5mg/ml. The higher concentrations are used when sensitivity testing has shown resistant organisms. It may be mixed with other ingredients similar to enrofloxacin though instead of saline Tris EDTA products may give a synergistic effect for resistant organisms.

The fourth component is the topical administration of a potent topical glucocorticoid which is often present in the antibiotic product. Mometasone, dexamethasone and betamethasone are the active agents used most commonly. They are used to decrease the exudation and if a case is not responsive to that alone then short term systemic glucocorticoids are indicated. Methylprednisolone at 1-1.5mg/kg/day for 4 days then tapered to eod is used until the inflammation and ulceration is resolved.

The fifth component is systemic antibiotic therapy. This component is only used when the ulcerative changes are not responding to the 4 component approach or initially is there is concurrent otitis media or marked proliferative changes present. Antibiotic selection should be based on a culture once cytology shows a pure, only one type of rod present on cytology. Prior to this empiric therapy is often used and most commonly the initial therapy when there is mixed rod or cocci and rod present on cytology is high dose fluoroquinolone. Marbofloxacin 5mg/kg/ q24h or enrofloxacin 12-15mg/kg q24h are most often used.

Since using this combination approach with the above agents I have not had a case that has required tobramycin or ticarcillin. Some veterinarians have recommended Imipenem and Cilastin (Primaxin®, Merck) and Piperacillin and tazobactam (Zosyn®, Wyeth) to be diluted and used as ear drops for resistant Pseudomonas. This practice should be seriously questioned as these are some the most effective rescue drugs for serious human infections and indiscriminate use in the veterinary field could jeopardize their value. I have not had a case that required these products.

References