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Dr Tim Nuttall is an RCVS Specialist in Veterinary Dermatology. After 12 years at the University of Liverpool he returned to the Royal (Dick) School of Veterinary Studies as Head of Dermatology where he runs a busy referral dermatology clinic, with particular interests in atopic dermatitis and antimicrobial resistance.

Tim has written over 100 clinical and scientific publications, and has presented lectures throughout the world. In addition, Tim has served on RCVS, BSAVA, ESVD, WCVD and DEFRA scientific committees. In 2014 he received the BSAVA Woodrow Award for outstanding contributions to veterinary medicine.

> In his spare time Tim enjoys Munro-bagging (all 282 were completed in July), cycling and single malt whisky.



\*Suggested Personal & Professional Development (PPD)



DERMATOLOGY

# Managing chronic and recurrent otitis externa in dogs

Most cases of acute otitis externa can be managed with ear cleaning and use of an appropriate topical antimicrobial/glucocorticoid product. However, recurrent or chronic cases require a more thorough approach to achieve resolution and prevent relapses (Figure 1).



Figure 1. Approach to recurrent and chronic otitis externa in dogs.

Ear infections are secondary and involve commensal (staphylococci and *Malassezia*) or environmental (*Pseudomonas*) opportunists.

The primary cause is the actual trigger for the ear inflammation and this must be identified and managed. Predisposing factors rarely cause otitis by themselves, but make an otitis or progression to severe disease more likely in a dog. Perpetuating problems arise from repeated cycles of inflammation and infection, and will eventually cause 'end-stage' otitis that requires surgical intervention.

This whole cycle – involving primary, predisposing, perpetuating and secondary causes of otitis - can be summarised as the PPPS approach (**Tables 1**, **2** & **3**).

#### Clinical examination

Otitis is erythroceruminous or suppurative (**Figure 2**). Erythroceruminous otitis is usually associated with *Malassezia* and staphylococcal overgrowths - Gram-negative bacteria are much less common. Gramnegative bacteria, particularly *Pseudomonas*, are more likely in suppurative otitis, where staphylococci are less common and *Malassezia* rare.

Healthy ear canals should be non-painful, non-pruritic, flexible and mobile. Careful palpation of the ears will reveal the extent and

"The primary cause is the actual trigger for the ear inflammation and this must be identified and managed" severity of pain, pruritus and inflammatory changes. Very firm and fixed ear canals may be irreversibly mineralised and stenosed.

#### Otoscopy

Otoscopy should be carried out wherever possible, using sedation and cleaning when necessary. This will allow you to assess the state of the ear canals, the type and amount of discharge, the condition of the tympanic membrane, presence of foreign bodies and *Otodectes* mites.

Use the following procedure:

- raise the pinna to expose the opening to the vertical ear canal, which is behind the tragus (Figure 3)
- insert the otoscope cone into the vertical ear canal
- advance the cone while moving the pinna ventrally and laterally – this aligns the vertical and horizontal ear canals and allows access to the horizontal ear canal

Condition	Clinical picture
Atopic dermatitis and/or adverse food reactions	Chronic/recurrent bilateral otitis; pruritus; diffuse erythema of the ventral pinnae
Otodectes	Bilateral otitis; pruritus; dark, granular exudate
Foreign bodies	Acute unilateral otitis; painful
Pemphigus foliaceus	Bilateral otitis; pustules & crusts on the ventral pinna
Sterile lymphangitis/lymphadenitis (juvenile cellulitis)	Bilateral exudate; young dogs; severe swelling of the pinnae and opening to the ear canals
Other immune-mediated diseases	Ulceration of the ventral pinnae and/or ear canals
Neoplasia and polyps	Unilateral otitis; obstruction
Endocrinopathies	Bilateral otitis; look for clinical signs elsewhere
Keratinisation disorders	Bilateral otitis; severe seborrheic otitis; scaling; look for clinical signs elsewhere

#### Table 1. Common primary triggers of otitis in dogs

Conformation	Pendulous, narrow or hairy ears; high density of ceruminous glands	
Environment	Warm, humid conditions	
latrogenic	Over-cleaning, wetting and maceration, traumatic cleaning, plucking hairs, irritation from ear cleaners etc.	
Swimming	Wetting and maceration of the ear canals; dirty, stagnant water is often contaminated by Pseudomonas	

#### Table 2. Predisposing factors in canine otitis

Epidermal and dermal hyperplasia and fibrosis	<ul> <li>ear canal stenosis</li> </ul>
Ceruminous gland hyperplasia	<ul> <li>increased discharge</li> <li>polyp and cyst formation</li> <li>stenosis and obstruction</li> </ul>
Loss of epidermal migration	<ul><li>build-up of ceruminous, seborrhoeic and keratinised debris</li><li>ceruminolith formation</li></ul>
Tympanic membrane invagination	<ul><li>impaired hearing</li><li>cholesteatoma formation</li></ul>
Tympanic membrane rupture	<ul> <li>otitis media</li> <li>tympanic bulla osteomyelitis</li> <li>otitis interna (vestibular syndrome)</li> </ul>
Ear canal mineralisation	<ul> <li>irreversible stenosis</li> </ul>

Table 3. Perpetuating factors in canine otitis - chronic inflammatory changes

 the tympanic membrane is fixed to the skull and faces horizontally – to properly assess it your otoscope must be horizontal to the dog's head (Figure 4).

Healthy ear canals should be open with a thin, smooth and pale pink lining. Sebaceous hyperplasia leads to a roughened 'cobblestone' appearance (**Figure 5**). This is an early sign of chronic inflammation and requires prompt intervention. The tympanic membrane should be taut, translucent, slightly concave and angled ventromedially. The dorsal fleshy pars flaccida can be flat or slightly bulge into the ear canal (**Figure 6**).

#### **Biofilms**

Biofilms have a major impact on treatment and antimicrobial resistance. They are common and can be identified easily on otoscopy forming a darkbrown or black adherent, thick and slimy discharge (**Figure 7**). On cytology, they appear as variably thick, veil-like material that may obscure bacteria and cells (Figure 8).

Biofilms inhibit cleaning and antimicrobial penetration and efficacy, and help bacteria adhere to surfaces. They effectively increase minimum inhibitory concentrations (MICs) resulting in subtherapeutic antimicrobial levels, which leads to treatment failure and resistance.

#### Cytology

Cytology is the most useful and effective way to identify

the organisms in the infection and to monitor progress. It is quick and easy to prepare smears using Diff-Quik-type stains. However, the alcohol fixative can remove waxy material and it is better to heat-fix or use one-stain methods with samples that have a high oil content. Interpretation is quick and straightforward in most cases. Malassezia, staphylococci and rod bacteria are easily differentiated allowing rational treatment choices (Figure 9).



*Figure 2.* (a) Erythroceruminous otitis with erythema and a ceruminous (waxy) discharge. This dog had atopic dermatitis with a secondary Malassezia otitis; (b) suppurative otitis with erythema, ulceration, a purulent discharge and crusting in an atopic dog with a secondary Pseudomonas otitis.



Figure 3. Ventral surface of the pinna in a dog with suppurative otitis. The arrow shows the tragus – the opening to the vertical ear canal is behind the tragus.



**Figure 4.** The tympanic membrane is fixed to the skull and faces horizontally. You must move the pinna ventrally to align the vertical and horizontal ear canals to advance your otoscope into the horizontal ear canal and assess the tympanic membrane (B = tympanic bulla; AnC = horizontal ear canal; AuC = vertical ear canal).



*Figure 5.* Early chronic inflammation with sebaceous hyperplasia giving a 'cobbled' appearance to the ear canals.

You can also evaluate the numbers of cells and organisms, interpret mixed and/or evolving infections, and identify unusual organisms that may be difficult to culture, such as anaerobes, filamentous bacteria and *Aspergillus*.

The likely antimicrobial sensitivity patterns of *Malassezia* and staphylococci can be estimated from local resistance patterns and previous treatment; although the susceptibility patterns of Gram-negative bacteria are harder to predict. *Pseudomonas* readily acquire resistance and most isolates from recurrent infections will be multi-drug resistant.

### Bacterial culture and sensitivity testing

Bacterial culture and sensitivity testing identifies the bacteria definitively, which can be useful for less common organisms that are hard to differentiate on cytology – streptococci, enterococci, *E. coli, Klebsiella, Proteus* and coryneforms. Knowledge of their likely sensitivity patterns can then help guide treatment choices. However, antimicrobial susceptibility test results are less useful in otitis, especially with topical treatment.

The break points used to determine susceptibility or resistance assume systemic treatment and are in  $\mu g/$ ml concentrations. These are poorly predictive of the response to topical therapy where the antimicrobials can achieve mg/ml concentrations. The response to treatment is, therefore, best assessed using clinical criteria and cytology. Antibiotic sensitivity data can be used to predict the efficacy of systemic drugs; but the concentration in the ear tissues is often low and high doses are needed.

#### Ear flushing and cleaning

Removing all the debris from the ear canals and middle ear cavity allows proper inspection and enhances antimicrobial treatment – especially with aminoglycosides and polymixin B. However, acidic ear cleaners may



*Figure 6.* Healthy tympanic membrane (*A* = pars tensa; *B* = pars flaccida; *C* = malleus; *D* = cerumen).



*Figure 7. Biofilm from a dog with a* Pseudomonas *otitis.* 



*Figure 8.* Cytology of the biofilm from Figure 7 – the neutrophils and bacteria are embedded in a thick veil-like matrix.

inactivate antibiotics and residual cleaner may inhibit the penetration of topical drugs. The antibiotic and/ or glucocorticoids can be applied 20 minutes or more after cleaning, if necessary.

The nature of the discharge can indicate which ear cleaner will be most appropriate, because not all are suitable for all types of exudate (**Figure 10**). Antimicrobial compounds – alcohols, parachlorometaxylenol [PCMX], chlorhexidine and acids – in ear cleaners can retard microbial proliferation; and polysaccharide and monosaccharide complexes can reduce microbial adherence to keratinocytes. Biofilms can be physically broken up and removed by thorough flushing and aspiration; and topical trizEDTA and n-acetylcysteine (2% in trizEDTA or saline) can disrupt biofims.

TrizEDTA damages bacterial cell walls and increases antimicrobial efficacy. It shows additive efficacy with chlorhexidine, gentamicin and fluoroquinolones at concentrations of 35.6/9.4 mg/ml or more, but not at lower concentrations. It is best given 20-30 minutes before the antibiotic, but can be co-administered. It is well tolerated and non-ototoxic. Gentle manual cleaning may be performed conscious or under light sedation. Bulb syringes are very effective, but should only be used in-clinic as inadvertently sealing the ear canal during flushing can rupture tympanic membranes. More thorough ear flushing requires general

anaesthesia. This is best done using a video otoscope; but can be performed using a cut-down urinary catheter or feeding tube and a hand-held operating otoscope.

#### Antimicrobial therapy Topical versus systemic therapy

Systemic antimicrobial therapy is less effective in erythroceruminous otitis because micro-organisms are only present in the external ear canal and cerumen. Systemic treatment may be more useful in suppurative otitis externa and/or otitis media, where there is an active inflammatory discharge and ulceration.

Topical therapy achieves mg/ml local concentrations compared to  $\mu g/ml$  ranges after systemic therapy, and is, therefore, much more effective. In addition, total body exposure is lower, reducing the risk of selecting for resistance among bacteria in non-target sites. Systemic antibiotic or antifungal treatment is only indicated when the ear canal cannot be treated topically - for instance, when there is stenosis or compliance problems, or topical adverse reactions.

#### **Topical therapy**

**Topical products** containing florfenicol, polymixin B, fusidic acid, gentamicin, enrofloxacin and marbofloxacin are suitable for most bacterial infections. Clotrimazole, miconazole, posaconazole and nystatin are effective against Malassezia. Polymixin B and miconazole have synergistic activity against Pseudomonas; and framycetin and fucidic acid show synergistic activity against staphylococci and streptococci. Fluoroquinolones, gentamicin and polymixin B are effective against most first-line Pseudomonas infections; and fusidic acid







*Figure 9.* Diff-Quik-stained cytology from dogs with otitis: (a) Malassezia overgrowth; (b) staphylococcal overgrowth; (c) purulent Pseudomonas infection.

Ciprofloxacin*	0.2% sol. 0.15-0.3 ml/ear q24h			
Enrofloxacin	15-20mg/kg PO q24h; 2.5% injectable sol. diluted 1:4 with saline or EpiOtic topically q24h; 22.7mg/ml sol. 1ml/ear q24h			
Marbofloxacin	5-10/kg PO q24h; Aurizon and Marbodex; 1% injectable sol. diluted 1:4 with saline topically q24h; 20mg/ml sol. 1ml/ear q24h			
Ofloxacin	Ofloxacin 0.3% 0.15-0.3 ml/ear q24h			
Carbenicillin*	10-20mg/kg IV q8h			
Clavulanate-ticarcillin*#	15-40 mg/kg IV q8h; reconstituted injectable sol. 0.15- 0.3 ml/ear q12-24h; 160mg/ml sol. 1ml/ear q12-24h			
Ceftazidime*#	25-50mg/kg IV q8h; 100mg/ml 1ml/ear q12-24h			
Silver sulfadiazine¶	Dilute 0.1-0.5% in saline or trizEDTA; apply 1ml q24h			
Polymixin B	Surolan			
Amikacin*	10-15mg/kg SC q24h; 50mg/ml 1ml/ear q24h			
Gentamicin	5-10mg/kg SC q24h; Otomax or Easotic			
Tobramycin*	Use eye drops or 8mg/ml injectable sol. 0.15-0.3ml/ear q24h			

\* not licensed for animals;

- # reconstituted solution stable for up to seven days at 4°C or one month frozen;

**Table 4.** Antibiotics that can be effective in multi-drug resistantPseudomonas otitis

and florfenicol are effective against MRSA and MRSP.

It is important to use an adequate volume to penetrate into the ear canals – 1ml is sufficient for most ears. Where necessary, products can be drawn up into a syringe for administration ensuring that an appropriate dose is delivered each time.

'Leave-in' products offer significant advantages in terms of compliance and quality of life compared to daily treatment. However, daily cleaning and treatment is better in heavily exudative otitis where leave-in products could be pushed out or diluted.

#### Pseudomonas otitis

*Pseudomonas* is resistant to many antibiotics and readily develops further resistance if treatment is ineffective. A wide variety of treatment options have been used in multi-drug-resistant *Pseudomonas* infections (**Table 4**).

## Anti-inflammatory treatment

Reducing pruritus, swelling, exudation and tissue proliferation is a key goal, and proactive maintenance treatment is necessary in ongoing conditions such as atopic dermatitis (**Figure 11**).

## Topical or systemic glucocorticoids

Topical therapy is preferred as this delivers the drug to the affected site, avoiding systemic exposure. Systemic treatment is necessary if there is stenosis, severe fibrosis or mineralisation, or if topical therapy can't be administered safely. It is usually possible to switch to topical therapy once the ear canals have opened.

#### **Topical glucocorticoids**

The glucocorticoids in topical ear medications are appropriate for mild to moderate inflammation in acute otitis externa. Use of antimicrobial-containing products, however, is not indicated in the absence of infection. There is a variety of glucocorticoid products available for eyes, ears and skin, although these may not be licensed for use in animals or in ears. Soluble glucocorticoid preparations can also be added to trizEDTA solutions or ear cleaners to create rinses with an appropriate glucocorticoid concentration (e.g. 0.1% dexamethasone). Once the otitis has resolved, topical glucocorticoids should be used at the lowest frequency that controls the inflammation.

#### Systemic glucocorticoids

Prednisolone (1-2mg/kg q12-24h) or methylprednisolone for one to three weeks

Colour	Dark brown	Pale brown to grey	Pale brown to yellow	Yellow to green	Dark green to black
Consistency	Waxy and adherent	Waxy to seborrhoeic	Seborrhoeic to purulent	Purulent	Thick and slimy
Association	Ceruminous otitis	Malassezia	Staphylococci	Pseudomonas	Biofilm
Ceruminoltic and ceruminosolvent cleaners		TrizEDTA or 2% n-acetyl cysteine (NAC)			
Surfactant and detergent flushing cleaners					

#### Figure 10. Choosing an appropriate ear cleaner.

is sufficient to control inflammation and stenosis in most cases. Patients with severe fibrosis and stenosis, however, may respond better to dexamethasone (7.5 to 10 times as potent as prednisolone). Three to four injections of 0.05ml depot dexamethasone or triamcinolone into the wall of stenosed ears can be very effective, although short-term iatrogenic hyperadrenocorticism is common.



Figure 11. Reactive and proactive management of otitis externa. Simple reactive treatment of each bout of infection (red line) misses the ongoing inflammation that underlies the infections. Repeated cycles of inflammation and infection will lead to chronic inflammation and an 'end-stage' ear. Proactive management (blue line) with regular topical glucocorticoids controls the inflammation and prevents flares.

#### Further reading

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## **PPD** Questions

- 1. You see a two-year-old Labrador retriever that presents with ear scratching and head shaking for the fourth time in the last nine months. Cytology has previously shown a *Malassezia* overgrowth, and the otitis quickly responds to topical antimicrobial/glucocorticoid products. Cytology today shows large numbers of coccoid bacteria. No other abnormalities are detected on clinical examination. What is the most likely problem that explains the clinical history?
  - A. undetected Otodectes cynotis
  - B. a foreign body in the ear canal
  - C. hypothyroidism
  - D. swimming
  - E. atopic dermatitis.
- 2. What does a roughened 'cobbled' lining of the ear canal indicate?
  - A. Malassezia overgrowth
  - B. staphylococcal overgrowth
  - C. sebaceous and ceruminous hyperplasia
  - D. ear canal fibrosis
  - E. ear canal mineralisation.
- 3. You see a dog with a three-month history of otitis externa. The ear canal is narrow and you can't insert an otoscope beyond the upper part of the vertical ear canal. This is lichenified and hyperpigmented with a greasy discharge protruding. Cytology shows mixed coccoid and rod bacteria. The dog scratches his ears and shakes his head during the consult. What is your treatment priority?
  - A. topical ear medication with fusidic acid
  - B. topical ear medication with marbofloxacin
  - C. topical ceruminolytic ear cleaner and glucocorticoids
  - D. systemic glucocorticoid
  - E. systemic ocalcitinib.
- 4. You see a five-year-old male neutered cocker spaniel. He has had a history of recurrent ear infections for the last three years, although these always respond to topical ear medications. Three days ago, he started to shake his head and scratch at his left ear after a day spent hill-walking. Examination of the skin reveals mild erythema of the interdigital skin and ventral pinnae. You see the following on otoscopic examination:



Left ear



Right ear

- What is the most likely cause of the otitis?
- A. Malassezia pachydermatis
- B. Trombicula autumnalis
- C. foreign body
- D. atopic dermatitis
- E. adverse food reaction.
- 5. Why are bacterial culture and antimicrobial susceptibility test results misleading in otitis externa?
  - A. the susceptibility/resistance break points underestimate topical antimicrobial concentrations
  - B. topical antimicrobials can't be tested in vitro
  - C. there is often a mixed infection
  - D. it's difficult to grow most micro-organisms involved in otitis externa
  - E. treatment uses mixed antibiotic/antifungal/steroid products.

Answers 1.E 2.C 3.D 4.C 5.A.