

# Evidence review and ENT-UK consensus report for the use of aminoglycoside-containing ear drops in the presence of an open middle ear

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**Background and objectives of review:** The use of aminoglycoside drops in the presence of a perforation/grommet is still a common practice amongst the UK ENT community, in spite of theoretical risk of ototoxicity. Mindful of the need to produce clinical guidelines based on the best available evidence, it was the intention of the Clinical Audit and Practice Advisory Group of the British Association of Otolaryngologists – Head and Neck Surgeons (ENT-UK) to produce evidence-based guidelines. In the absence of good evidence, intentions were shifted towards producing consensus guidelines using validated methodology.

**Type of review:** Literature review, review of international guidelines and consensus guidelines.

**Search strategy:** A MEDLINE literature search (1966 to August 2006) was conducted, using the following strategies: ‘ototoxicity and drops’, ‘ototoxic and drops’, ‘vestibulotoxicity and drops’, ‘vestibulotoxic and drops’, ‘cochleotoxicity and drops’, ‘cochleotoxic and drops’.

Foreign language articles were not excluded.

**Results of the literature review:** The inclusion of foreign language articles and manually searching the reference sections of identified articles revealed further evidence

not considered in previous reviews on this subject. However, the available ‘evidence’ that does exist remains to be of poor quality, consisting of data from a number of case reports and small case series. Prospective studies into the ototoxic effects of aminoglycoside ear drops either support their use but lack power to statistically confirm this, or are performed in conditions that are not representative of normal clinical conditions.

**Evaluation method:** In the light of issues raised from the literature review, a questionnaire was produced. The questionnaire was initially completed by council members of the British Society of Otology, then revised and presented at a meeting of the British Society of Otology, where a consensus panel was formed.

**Conclusions:** ENT-UK recommends that when treating a patient with a discharging ear, in whom there is a perforation or patent grommet: if a topical aminoglycoside is used, this should only be in the presence of obvious infection. Topical aminoglycosides should be used for no longer than 2 weeks. The justification for using topical aminoglycosides should be explained to the patient. Baseline audiometry should be performed, if possible or practical, before treatment with topical aminoglycosides.

Renewed concerns about the safety of topical aminoglycoside-containing drops or sprays in the presence of a tympanic membrane perforation or grommet led the British Association of Otolaryngologists – Head & Neck Surgeons (ENT-UK) to initiate this review and produce a consensus document to guide specialist and non-specialist physicians in their use.

Much has been written about the *potential* ototoxicity of topical aminoglycoside eardrops when used *in vivo* in day-to-day clinical settings. The difficulty involved in separating the fact from anecdote is that there are deficiencies in the type and quality of evidence available on this subject. There is a large body of evidence demonstrating ototoxicity in experimental animals. However, there are many reasons why these animal models are unsuitable for direct comparison with the human subject.<sup>1,2</sup> These reasons include differences in middle and inner ear morphology, in particular, in the anatomy of the round-window niche and the thickness of the round-window

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membrane. In addition, fluids placed into the middle ear space of humans may not have extensive contact time with the round window membrane (unlike the situation seen in some experimental studies).

### **Efficacy of topical aminoglycosides in the treatment of CSOM: are they effective?**

It would be prudent to examine the evidence that topical aminoglycosides are of any benefit in CSOM before considering any ototoxic effects. A recent *Cochrane* review supported the treatment of aural discharge in CSOM with topical quinolone antibiotics.<sup>3</sup> The review was, however, inconclusive with regard to non-quinolone antibiotics. It should be noted that the review considered topical antibiotics without steroids. In the UK, the majority of the topical antibiotic preparations used to treat COSM contain a steroid as well as an antibiotic. No conclusions were reached regarding longer-term outcomes, such as producing a dry ear in the long term, preventing complications of CSOM, healing the tympanic membrane and improving hearing.

A review in *Clinical Evidence* identified three studies addressing the question of efficacy (<http://www.clinicalevidence.com/>). Two randomised controlled trials (RCTs) looked at the efficacy of gentamicin plus hydrocortisone compared with placebo.<sup>4,5</sup> Both studies found that gentamicin plus hydrocortisone reduced activity in chronic otitis media on otoscopy compared with placebo. The first study examined 123 adults with COM with no cholesteatoma and no open mastoid cavity; the second study examined 31 adults who had an open mastoid cavity. A third study compared topical gentamicin plus hydrocortisone with betamethasone and found that topical gentamicin plus hydrocortisone reduced the proportion of participants with persistent activity on otoscopy more readily than betamethasone alone.<sup>6</sup>

Alternatives to aminoglycosides include non-aminoglycoside antibiotics and antiseptics. Quinolones are a family of broad-spectrum antibiotics that include preparations such as ciprofloxacin and ofloxacin. The efficacy of quinolones has been demonstrated, but they are not licensed for use in the ear in the UK. There are no RCTs comparing topical antiseptics *versus* placebo or no treatment. One RCT demonstrated no significant difference between topical antiseptics plus ear cleansing under microscopic control and either topical or oral antibiotics.<sup>7</sup> Another RCT found no significant difference in resolution of ear discharge between topical povidone-iodine and topical quinolone.<sup>8</sup> Both RCTs contained too small a number of participants to establish or exclude a clinically significant benefit from topical antiseptics.

## **Methodology of evidence review**

### *Search strategy*

A MEDLINE literature search (1966 to August 2006) was conducted, using the following strategies: 'ototoxicity and drops', 'ototoxic and drops', 'vestibulotoxicity and drops', 'vestibulotoxic and drops', 'cochleotoxicity and drops', 'cochleotoxic and drops'. The titles and abstracts of the resultant articles were screened for adherence to the inclusion and exclusion criteria. The full text of articles fulfilling inclusion criteria and those containing ambiguous abstracts underwent further analysis. Foreign language articles were translated into English. The reference sections of all full text articles were reviewed to identify any further potentially relevant articles.

### *Inclusion criteria*

Articles describing case reports, case series or trials in which aminoglycoside drops were used in the presence of a documented tympanic membrane perforation or ventilation tube.

### *Exclusion criteria*

Articles describing ototoxicity in the animal subject. Articles that did not provide documented evidence (an audiogram) of normal auditory function (cochlear function) both pre- and post-treatment. Similarly, vestibular assessment was necessary to support alleged vestibular toxicity.

## **Review of case reports and small case series**

The most recently published study in which a MEDLINE search looked for documented cases of ototoxicity was by Matz *et al.* in 2004.<sup>9</sup> This was published in the same supplement that contained the AAO-HNS recommendations following its 'Consensus panel on role of potentially ototoxic antibiotics for topical middle ear use'. Matz *et al.* only considered articles in the English language. They identified seven articles containing a total of 48 retrospective cases of potential ototoxicity as a result of the topical application of aminoglycoside-containing drops.<sup>10-16</sup> Our literature search identified five further articles containing an additional 37 documented retrospective cases of potential ototoxicity.<sup>17-21</sup> Three of these extra articles were reported in foreign language journals so were originally excluded from the review by Matz *et al.* Two of the additional articles were discovered upon manually reviewing the reference sections of the originally described articles.

When we reviewed the cases identified by our literature search, we found the data to be significantly deficient, particularly as not all patients had formal tests of vestibular function or pre- and post-treatment audiograms. There seems to be little evidence linking the short-term use of aminoglycoside-containing drops in discharging ears with vertigo or hearing loss in clinical practice. The 'evidence' that does exist is of poor quality, consisting of data from a number of case reports and small case series. The phenomenon is undoubtedly very rare and we are unlikely to ever know the real incidence of this problem. Evidence of a genetic susceptibility to aminoglycoside ototoxicity with systemic therapy has been presented by a number of authors and may explain these rare cases.<sup>22</sup> Ascertaining whether a family history of aminoglycoside ototoxicity exists may be worthwhile before prescribing these drugs. Most clinical studies on ototoxicity looked at changes in hearing yet gentamicin (one of the most commonly used topical aminoglycosides) is known to be more vestibulotoxic than cochleotoxic. Few studies have systematically evaluated vestibular function, although this would be technically challenging in patients with discharging ears.

Table 1 summarises all those articles describing retrospective case reports or case series of potential ototoxicity as a consequence of topical aminoglycoside administration. The table does not include reports in which ototoxic effects were unsubstantiated and also those reports in which patients underwent significant concurrent middle ear surgery.

In addition to the retrospective studies outlined above, we identified five studies that prospectively examined the

use of topical aminoglycoside drops in the human subject (Table 2).

Three of these studies prospectively examined the result of instilling potentially ototoxic preparations into ear canals containing a grommet.<sup>23–25</sup> Rakover *et al.*<sup>23</sup> studied 446 children and were unable to demonstrate any ototoxicity after instilling three drops of a neomycin-containing preparation three times a day for 2 weeks into dry ears with grommets. Welling *et al.*<sup>24</sup> studied 50 children in a randomised trial and were unable to demonstrate any ototoxicity after instilling neomycin-containing drops once into the middle ear cavity at the time of myringotomy. Merifield *et al.*<sup>25</sup> studied 70 ears with persistent purulent otorrhoea through a ventilation tube. The authors measured bone conduction pre- and post-treatment, with five different types of aminoglycoside drops, for a duration ranging from 2 days to 2 weeks, and demonstrated no sensorineural hearing loss as a result of this treatment.

The main criticism of all three of these studies is that in studying such a rare complication, huge numbers of participants would be required to reduce the chance of a type II error (failing to identify an effect when one really exists because the study lacks statistical 'power'); the absence of any observed adverse event may be related to the low number of participants. Merifield *et al.* complicate the analysis further by using variable dose strategies and a variety of otological agents.

In contrast to these studies, which tend to support the premise that topical aminoglycoside drops are safe, a number of prospective studies have demonstrated the

**Table 1.** Retrospective cases reporting the ototoxic effects of commercially available aminoglycoside drops

Author	Type of study	Number of patients in study	Number of patients reported with ototoxicity because of topical aminoglycoside drops	Number of patients with corroboratory audiometric or vestibular testing*
Longridge <sup>10</sup>	Case reports	2	2	2
Chen <sup>11</sup>	Case reports	10	2	2
Marais <sup>12</sup>	Case series	9	9	9
Bath <sup>13</sup>	Case series	16	16	16
Dumas <sup>14</sup>	Case series	8	8	2
Linder <sup>15</sup>	Case reports	2	2	2
Lind <sup>16</sup>	Case report	1	1	1
Abello <sup>17</sup>	Case series	6	6	6
Martin <sup>18</sup>	Case series	14	14	13
Kellerhals <sup>19</sup>	Case series	15	14	14
Tommerup <sup>20</sup>	Case report	1	1	1
Nomura <sup>21</sup>	Case report	1	1	1
Total		85	76	69

\*Corroboratory data comprising a pre- and post-treatment audiogram or post-treatment electronystagmography testing. Additional cases in which symptoms occurred after significant middle ear surgery were excluded.

**Table 2.** Prospective trials and cases reporting the ototoxic effects of commercially available aminoglycoside drops

Author	Type of study	Number of patients in study	Number of patients reported with ototoxicity because of topical aminoglycoside drops	Number of patients with corroboratory audiometric or vestibular testing*
Rakover <sup>23</sup>	Non-randomised controlled trial (non-RCT)	446	0	0
Welling <sup>24</sup>	RCT	50	0	0
Merifield <sup>25</sup>	Non-randomised non-controlled study	70	0	0
Bath <sup>26</sup>	Case report	1	1	1
Kaplan <sup>27</sup>	Prospective case review	20	15	15
Podoshin <sup>28</sup>	Non-RCT	150	N/A	N/A
Total		737	16	16

\*Corroboratory data comprising a pre- and post-treatment audiogram or post-treatment electronystagmography testing.

opposite but in very different clinical settings. The ototoxic effects of commercially available Garasone® (Schering Canada Inc., Pointe-Claire, QC, Canada) eardrops (betamethasone sodium phosphate and gentamicin sulphate) in a patient with unilateral Menière's disease have been reported when the patient underwent deliberate therapeutic ablation of their vestibular function.<sup>26</sup> This study was followed by a similar study using commercially available gentamicin/betamethasone eardrops in 20 patients.<sup>27</sup> The method of administration of the drops differs significantly in these studies as might be expected from a regime which specifically seeks to produce ototoxic effects. Specifically, alternating tragal pressure was applied to the ear canal to 'pump' the drops into the middle ear while lying with the affected ear upright for 15 min. Participants were also instructed to continue applying drops until prolonged vertigo or imbalance occurred for longer than 24 h and then to continue instilling drops for another 2 days or for a maximum of 1 month. This regime is clearly quite different to any current, sensible practice aimed at treating a middle ear infection.

Podoshin *et al.*<sup>28</sup> enrolled 150 patients with CSOM (in the presence of a tympanic membrane perforation) into a prospective trial where they were split into three groups, each group receiving three drops of a neomycin-containing medication, three times a day for 6, 9, and 12 months, respectively. Unsurprisingly, all groups developed a sensorineural hearing loss, but this loss was interestingly small with average losses of 1.8 dB (SD 6.5) for the group being continuously treated for 6 months, 3.6 dB (SD 8.3) for the 9-month group and 10.9 dB (SD 10.8) for the 12-month group. Unfortunately, the exact number of patients who experienced a sensorineural hearing loss as a result of the topical aminoglycoside drops is not available – no absolute figures are published, only average losses. It would be interesting to know the range of hearing loss, as averaged data may hide a small number of large changes and this

may be relevant in considering the arguments for and against the use of topical aminoglycosides. Whatever the truth about the numbers of patients experiencing sensorineural hearing loss and the extent of those losses, the study in any event describes a therapeutic regime that is very different from standard clinical practice.

### International guidelines

The American Academy of Otolaryngology – Head and Neck Surgery – published a guideline on this topic in 2004.<sup>29</sup> The AAO-HNS initially published their recommendations as a supplement in *Otolaryngology – Head and Neck Surgery* and then again as a summary in *ENT – Ear Nose Throat Journal*.<sup>30</sup> These recommendations were in response to an increase in the number of claims lodged against physicians for allegedly causing iatrogenic ototoxic injury. The recommendations are:

*Recommendation 1.* When possible, topical antibiotic preparations that are free of potential ototoxicity are preferable to those that do have the potential for otologic injury in patients with an open middle ear or mastoid.

*Recommendation 2.* When a potentially ototoxic antibiotic is chosen, it should be used only in infected ears and it should be discontinued shortly after the infection has resolved.

*Recommendation 3.* When a potentially ototoxic antibiotic drop is prescribed for a patient with an open middle ear or mastoid, the patient or parent should be warned of the risk of ototoxicity.

*Recommendation 4.* If the tympanic membrane is known to be intact and the middle ear and mastoid are closed, the use of a potentially ototoxic preparation presents no risk of ototoxic injury'.

Rosenfeld *et al.* have recently published an American Academy of Otolaryngology – Head and Neck Surgery Clinical Practice Guideline for the treatment of acute

otitis externa<sup>31</sup> and briefly consider the use of ototoxic drops in the presence of a tympanic membrane perforation. They state:

Substances with ototoxic potential (e.g. aminoglycosides and alcohol) should not be used when the tympanic membrane is perforated and the middle ear space is open, because the risk of ototoxic injury outweighs the benefits compared with non-ototoxic antimicrobials with equal efficacy.

In Canada, recommendations for the use of topical aminoglycosides have also been published<sup>32</sup> and state that 'gentamicin-containing ear drops should not be used in patients with non-intact eardrum'.

### Need for ENT-UK recommendations

If quinolone ear drops were licensed for use in the UK, ENT-UK might have considered adopting the American Academy Guidelines. Although it is possible for individual doctors to use such drops 'off license', it is appropriate that ENT-UK should issue guidance on the continued use of aminoglycoside-containing drops.

### Methodology of producing ENT-UK consensus statement

The methods used to obtain an expert consensus were based on the recommendations of Raine *et al.*<sup>33</sup> The authors of the current paper identified the relevant issues and reviewed the evidence as outlined here. A questionnaire was prepared (Appendix 1) and mailed to 14 council members of the British Society of Otolaryngology, the otological arm of ENT-UK. They were asked to rate the statements on a 9-point Likert scale from strongly disagree to strongly agree. Twelve responses were received and discussed at an informal meeting. The statements were revised in the light of this and were presented at a meeting of British Society of Otolaryngology in December 2006, at which 39 consultants with an interest in otology formed the consensus panel.

After discussion, the members were asked whether or not they supported the five statements listed in Table 3. The group was unanimous, or nearly so, in its views on all but one question. The issue of the off-license use of topical quinolones was discussed. It was felt, *inter alia*, that the group did not possess the microbiological or pharmacotherapeutic expertise to determine the merits or otherwise of the off-license use of topical quinolones. It was felt that the association should seek appropriate expert advice on these issues to allow us to understand whether or not there are strong public health or other reasons (for example, related to the emergence of bacterial resistance) why these classes of drugs are not licensed in this country for use in this way.

**Table 3.** Questions submitted to expert consensus panel and the results obtained

Statement	Supporting, %
When treating a patient with a discharging ear, in whom there is a perforation or patent grommet:	
If a topical aminoglycoside is used, this should only be in the presence of obvious infection	100
Topical aminoglycosides should be used for no longer than 2 weeks	97
The justification for using topical aminoglycosides should be explained to the patient	100
Baseline audiometry should be performed, if possible or practical, before treatment with topical aminoglycosides	100
Unlicensed topical quinolones should be used instead of aminoglycosides	36

### ENT-UK consensus statement

This article provides background to the consensus statements that were presented to the ENT-UK Council for approval. Each council member, including 18 regional representatives, were given 2 months to give comment to the recommendations. There has been universal support of the recommendations, which have now been fully endorsed by the Council of ENT-UK. These guidelines are reproduced in Box 1. Full details regarding the consultation process and the consensus document in full can be found on the ENT-UK website.<sup>34</sup>

**Recommendation 1.** The following items have to be adopted (as formal ENT-UK guidances) when treating a patient with a discharging ear, in whom there is a perforation or patent grommet

1. If a topical aminoglycoside is used, this should only be in the presence of obvious infection.
2. Topical aminoglycosides should be used for no longer than 2 weeks.
3. The justification for using topical aminoglycosides should be explained to the patient.
4. Baseline audiometry should be performed, if possible or practical, before treatment with topical aminoglycosides.

**Recommendation 2.** ENT-UK should seek expert advice on the use of otological quinolones, specifically on the advisability of their un-licensed use for patients with a discharging ear, in whom there is a perforation or patent grommet. What are the potential adverse effects in terms of emergence of bacterial resistance?

**Box 1.** Formal ENT-UK guidance for the use of aminoglycoside-containing ear drops in the presence of a perforation.

### Keypoints

- There seems to be little evidence linking vertigo or hearing loss to the short-term use of aminoglycoside-containing drops in discharging ears, in the presence of a grommet or perforation.
- The 'evidence' that does exist is of poor quality, consisting of data from a number of case reports and small case series.
- Prospective studies into the ototoxic effects of aminoglycoside ear drops either support their use but lack power to statistically confirm this, or are performed in conditions that are not representative of normal clinical conditions.
- Guidelines produced outside the UK recommend the use of quinolone containing drops that are not licensed in this country.
- Although it is possible for individual doctors to use such drops 'off license', it is appropriate that ENT-UK should issue guidance on the continued use of aminoglycoside-containing drops.
- Mindful of the need to produce clinical guidelines based on the best available evidence, the Clinical Audit and Practice Advisory Group of the British Association of Otolaryngologists – Head and Neck Surgeons (ENT-UK) has produced recommendations based on the views of an expert consensus panel.

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### Conflict of Interest

None to declare.

### References

- 1 Kuhweide R. (1995) Experimental evidence of ototoxicity of ear drops. A review of the literature. *Acta. Otorhinolaryngol. Belg.* **49**, 293–298
- 2 Roland P.S. (1994) Clinical ototoxicity of topical antibiotic drops. *Otolaryngol. Head Neck Surg.* **110**, 598–602
- 3 Macfadyen C.A., Acuin J.M. & Gamble C. (2005) Topical antibiotics without steroids for chronically discharging ears with underlying eardrum perforations. *Cochrane Database Syst. Rev.* **4**, CD004618.
- 4 Browning G.G., Gatehouse S. & Calder I.T. (1988) Medical management of active chronic otitis media: a controlled study. *J. Laryngol. Otol.* **102**, 491–495
- 5 Picozzi G., Browning G. & Calder I. (1983) Controlled trial of gentamicin and hydrocortisone ear drops in the treatment of active chronic otitis media. *Clin. Otolaryngol.* **8**, 367–368
- 6 Crowther J.A. & Simpson D. (1991) Medical treatment of chronic otitis media: steroid or antibiotic with steroid ear-drops? *Clin. Otolaryngol.* **6**, 142–144
- 7 Browning G., Picozzi G., Calder I., *et al.* (1983) Controlled trial of medical treatment of active chronic otitis media. *BMJ* **287**, 1024
- 8 Jaya C., Job A., Mathai E., *et al.* (2003) Evaluation of topical povidone-iodine in chronic suppurative otitis media. *Arch. Otolaryngol. Head Neck Surg.* **129**, 1098–1100
- 9 Matz G., Rybak L., Roland P.S. *et al.* (2004) Ototoxicity of ototopical antibiotic drops in humans. *Otolaryngol. Head Neck Surg.* **130** (3 Suppl), S79–S82
- 10 Longridge N.S. (1994) Topical gentamicin vestibular toxicity. *J. Otolaryngol.* **23**, 444–446
- 11 Chen J.M., Williamson P.A., Hutchin T. *et al.* (1996) Topical gentamicin-induced hearing loss: a mitochondrial ribosomal RNA study of genetic susceptibility. *Am. J. Otol.* **17**, 850–852
- 12 Marais J. & Rutka J.A. (1998) Ototoxicity and topical eardrops. *Clin. Otolaryngol. Allied Sci.* **23**, 360–367
- 13 Bath A.P., Walsh R.M., Bance M.L. *et al.* (1999) Ototoxicity of topical gentamicin preparations. *Laryngoscope* **109** (7 Pt 1), 1088–1093
- 14 Dumas G., Bessard G., Gavend M. *et al.* (1980) Risk of deafness following ototopical administration of aminoglycoside antibiotic (author's transl). *Therapie* **35**, 357–363
- 15 Linder T.E., Zwicky S. & Brandle P. (1995) Ototoxicity of ear drops: a clinical perspective. *Am. J. Otol.* **16**, 653–657
- 16 Lind O. & Kristiansen B. (1986) Deafness after treatment with ear drops containing neomycin, gramicidin and dexamethasone. A case report. *ORL J. Otorhinolaryngol. Relat. Spec.* **48**, 52–54
- 17 Abello P., Vinas J.B. & Vega J. (1998) [Topical ototoxicity: review over a 6-year period]. *Acta Otorrinolaryngol. Esp.* **49**, 353–356
- 18 Martin H. & Martin C. (1980) Ototoxicity of ear drops. *J. Fr. Otorhinolaryngol. Audiophonol. Chir. Maxillofac.* **29**, 19–37
- 19 Kellerhals B. (1978) [Risk of inner ear damage from ototoxic eardrops]. *HNO* **26**, 49–52
- 20 Tommerup B. & Moller K. (1984) A case of profound hearing impairment following the prolonged use of framycetin ear drops. *J. Laryngol. Otol.* **98**, 1135–1137
- 21 Nomura Y. (1984) Otological significance of the round window. *Adv. Otorhinolaryngol.* **33**, 1–162
- 22 Tang H.Y., Hutcheson E., Neill S. *et al.* (2002) Genetic susceptibility to aminoglycoside ototoxicity: how many are at risk? *Genet. Med.* **4**, 336–345
- 23 Rakover Y., Keywan K. & Rosen G. (1997) Safety of topical ear drops containing ototoxic antibiotics. *J. Otolaryngol.* **26**, 194–196
- 24 Welling D.B., Forrest L.A., Goll 3rd F. (1995) Safety of ototopical antibiotics. *Laryngoscope* **105**, 472
- 25 Merifield D.O., Parker N.J. & Nicholson N.C. (1993) Therapeutic management of chronic suppurative otitis media with otic drops. *Otolaryngol. Head Neck Surg.* **109**, 77–82

- 26 Bath A.P., Walsh R.M. & Bance M.L. (1999) Presumed reduction of vestibular function in unilateral Meniere's disease with aminoglycoside eardrops. *J. Laryngol. Otol.* **113**, 916–918
- 27 Kaplan D.M., Hehar S.S., Bance M.L. et al. (2002) Intentional ablation of vestibular function using commercially available topical gentamicin-betamethasone eardrops in patients with Meniere's disease: further evidence for topical eardrop ototoxicity. *Laryngoscope* **112**, 689–695
- 28 Podoshin L., Fradis M. & Ben David J. (1989) Ototoxicity of ear drops in patients suffering from chronic otitis media. *J. Laryngol. Otol.* **103**, 46–50
- 29 Roland P.S., Stewart M.G., Hannley M. et al. (2004) Consensus panel on role of potentially ototoxic antibiotics for topical middle ear use: introduction, methodology, and recommendations. *Otolaryngol. Head Neck Surg.* **130** (Suppl. 3), 0S51–0S56
- 30 Roland P.S. (2004) Consensus panel on role of potentially ototoxic antibiotics for topical middle ear use. Summary of the findings of a joint consensus panel on the use of potentially ototoxic ototopicals. *Ear Nose Throat J.* **83** (Suppl. 4), 13–14
- 31 Rosenfeld R.M., Brown L., Cannon C.R. et al. (2006) American Academy of Otolaryngology – Head and Neck Surgery Foundation. Clinical practice guideline: acute otitis externa. *Otolaryngol. Head Neck Surg.* **134** (Suppl. 4), S4–S23
- 32 Rosser W., Pennie R., Pilla N. and The Anti-infective Review Panel. (2005) Anti-Infective Guidelines for Community-Acquired Infections. MUMS (Medication Use Management Services) Guideline Clearinghouse, Toronto
- 33 Raine R., Sanderson C. & Black N. (2005) Developing clinical guidelines: a challenge to current methods. *BMJ* **331**, 631–633
- 34 Phillips J.S., Yung M.W., Burton M.J. & Swan I.R.C. (2007) Use of aminoglycoside-containing ear drops in the presence of a perforation: evidence review and ENT-UK consensus statement. *Clinical Audit and Practice Advisory Group Guidelines, British Association of Otolaryngologists – Head & Neck Surgeons (ENT-UK)* <http://www.entuk.org/>

**Appendix**

**Appendix 1.** Treatment of active mucosal chronic otitis media with tympanic membrane perforation: questionnaire to develop guidelines based on ENT-UK consensus. Please highlight your opinion.

	Strongly disagree							Strongly agree	
	1	2	3	4	5	6	7	8	9
If a topical aminoglycoside is used, this should only be in the presence of obvious infection.	1	2	3	4	5	6	7	8	9
Topical aminoglycosides should not be used for longer than 2 weeks.	1	2	3	4	5	6	7	8	9
The justification for using topical aminoglycosides should be explained to the patient.	1	2	3	4	5	6	7	8	9
Baseline audiometry should be performed before treatment with topical aminoglycosides.	1	2	3	4	5	6	7	8	9
Unlicensed topical quinolones should be used instead of aminoglycosides.	1	2	3	4	5	6	7	8	9

Other recommendations: .....