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# Clinical Practice Guideline: Acute Otitis Externa

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## Abstract

**Objective.** This clinical practice guideline is an update and replacement for an earlier guideline published in 2006 by the American Academy of Otolaryngology—Head and Neck Surgery Foundation. This update provides evidence-based recommendations to manage acute otitis externa (AOE), defined as diffuse inflammation of the external ear canal, which may also involve the pinna or tympanic membrane. The variations in management of AOE and the importance of accurate diagnosis suggest a need for updating the clinical practice guideline. The primary outcome considered in this guideline is clinical resolution of AOE.

**Purpose.** The primary purpose of the original guideline was to promote appropriate use of oral and topical antimicrobials for AOE and to highlight the need for adequate pain relief. An updated guideline is needed because of new clinical trials, new systematic reviews, and the lack of consumer participation in the initial guideline development group. The target patient is aged 2 years or older with diffuse AOE. Differential diagnosis will be discussed, but recommendations for management will be limited to diffuse AOE, which is almost exclusively a bacterial infection. This guideline is intended for primary care and specialist clinicians, including otolaryngologists—head and neck surgeons, pediatricians, family physicians, emergency physicians, internists, nurse practitioners, and physician assistants. This guideline is applicable in any setting in which patients with diffuse AOE would be identified, monitored, or managed.

**Action Statements.** The development group made *strong recommendations* that (1) clinicians should assess patients with AOE for pain and recommend analgesic treatment based on the severity of pain and (2) clinicians should not prescribe systemic antimicrobials as initial therapy for diffuse, uncomplicated AOE unless there is extension outside the ear canal or the presence of specific host factors that would indicate a need for systemic therapy. The development group made *recommendations* that (1) clinicians should distinguish diffuse

AOE from other causes of otalgia, otorrhea, and inflammation of the external ear canal; (2) clinicians should assess the patient with diffuse AOE for factors that modify management (nonintact tympanic membrane, tympanostomy tube, diabetes, immunocompromised state, prior radiotherapy); (3) clinicians should prescribe topical preparations for initial therapy of diffuse, uncomplicated AOE; (4) clinicians should enhance the delivery of topical drops by informing the patient how to administer topical drops and by performing aural toilet, placing a wick, or both, when the ear canal is obstructed; (5) clinicians should prescribe a non-ototoxic preparation when the patient has a known or suspected perforation of the tympanic membrane, including a tympanostomy tube; and (6) clinicians should reassess the patient who fails to respond to the initial therapeutic option within 48 to 72 hours to confirm the diagnosis of diffuse AOE and to exclude other causes of illness.

## Keywords

acute otitis externa, clinical practice guideline, topical antimicrobial therapy, randomized controlled trials, meta-analysis

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## Differences from Prior Guideline

This clinical practice guideline is as an update, and replacement, for an earlier guideline published in 2006 by the American Academy of Otolaryngology—Head and Neck Surgery Foundation.<sup>1</sup> Changes in content and methodology from the prior guideline include the following:

- Addition of a dermatologist and consumer advocate to the guideline development group
- Expanded action statement profiles to explicitly state confidence in the evidence, intentional vagueness, and differences of opinion
- Enhanced external review process to include public comment and journal peer review
- New evidence from 12 randomized controlled trials and 2 systematic reviews

- Review and update of all supporting text
- Emphasis on patient education and counseling with new tables that list common questions with clear, simple answers and provide instructions for properly administering ear drops

## Introduction

Acute otitis externa (AOE) as discussed in this guideline is defined as diffuse inflammation of the external ear canal, which may also involve the pinna or tympanic membrane. A diagnosis of diffuse AOE requires rapid onset (generally within 48 hours) in the past 3 weeks of symptoms and signs of ear canal inflammation, as detailed in **Table 1**. A hallmark sign of diffuse AOE is tenderness of the tragus, pinna, or both that is often intense and disproportionate to what might be expected based on visual inspection.

AOE is a cellulitis of the ear canal skin and subdermis, with acute inflammation and variable edema. Nearly all (98%) AOE in North America is bacterial.<sup>2</sup> The most common pathogens are *Pseudomonas aeruginosa* (20%-60% prevalence) and *Staphylococcus aureus* (10%-70% prevalence), often occurring as a polymicrobial infection. Other pathogens are principally gram-negative organisms (other than *P aeruginosa*), any one of which causes no more than 2% to 3% of cases in large clinical series.<sup>3-10</sup> Fungal involvement is distinctly uncommon in primary AOE but may be more common in chronic otitis externa or after treatment of AOE with topical, or less often systemic, antibiotics.<sup>11</sup>

Topical antimicrobials are beneficial for AOE, but oral antibiotics have limited utility.<sup>12</sup> Nonetheless, about 20% to 40% of patients with AOE receive oral antibiotics, with or without concurrent topical therapy.<sup>3,13,14</sup> The oral antibiotics selected are usually inactive against *P aeruginosa* and *S aureus*, may have undesirable side effects, and, because they are widely distributed throughout the body, serve to select out resistant organisms.<sup>15,16</sup>

Bacterial resistance is likely of far less concern with topical antimicrobials because the high local concentration of drug in the ear canal will generally eradicate all susceptible organisms plus those resistant to systemically administered antibiotics (which only achieve concentrations at the site of infection several magnitudes lower than when topically administered).<sup>5</sup> The efficacy of topical therapy against resistant organisms is of increasing importance given the rising incidence of drug-resistant *Staphylococcus* and community-acquired strains of *Pseudomonas*.<sup>17</sup>

**Table 1.** Elements of the diagnosis of diffuse acute otitis externa.

1. Rapid onset (generally within 48 hours) in the past 3 weeks, AND...
2. Symptoms of ear canal inflammation, which include: otalgia (often severe), itching, or fullness, WITH OR WITHOUT hearing loss or jaw pain,<sup>a</sup> AND...
3. Signs of ear canal inflammation, which include: tenderness of the tragus, pinna, or both OR diffuse ear canal edema, erythema, or both WITH OR WITHOUT otorrhea, regional lymphadenitis, tympanic membrane erythema, or cellulitis of the pinna and adjacent skin

<sup>a</sup>Pain in the ear canal and temporomandibular joint region intensified by jaw motion.

The etiology of AOE is multifactorial. Regular cleaning of the ear canal removes cerumen, which is an important barrier to moisture and infection.<sup>18</sup> Cerumen creates a slightly acidic pH that inhibits infection (especially by *P aeruginosa*) but can be altered by water exposure, aggressive cleaning, soapy deposits, or alkaline eardrops.<sup>19,20</sup> Debris from dermatologic conditions may also encourage infections,<sup>7,21</sup> as can local trauma from attempts at self-cleaning, irrigation,<sup>22</sup> and wearing hearing aids.<sup>23,24</sup> Other factors such as sweating, allergy, and stress have also been implicated in the pathogenesis of AOE.<sup>25</sup>

AOE is more common in regions with warmer climates, increased humidity, or increased water exposure from swimming.<sup>26,27</sup> Most, but not all, studies have found an association with water quality (in terms of bacterial load) and the risk of AOE. The causative organisms are present in most swimming pools and hot tubs; however, even those that comply with water quality standards may still contain AOE pathogens.<sup>28-31</sup> In addition, these organisms are present in the healthy external auditory canal, and thus the external auditory canal may be a source of AOE.<sup>32</sup> Some individuals appear more susceptible to AOE on a genetic basis (those with type A blood group).<sup>33</sup> The subspecies of *Pseudomonas* causing AOE may be different from those causing other *Pseudomonas* infections.<sup>34,35</sup>

Strategies to prevent AOE are aimed at limiting water accumulation and moisture retention in the external auditory canal and maintaining a healthy skin barrier. No randomized trials have compared the efficacy of different strategies to prevent AOE. Available reports include case series and expert opinion, which emphasize preventing moisture and water retention in the external auditory canal. Recommendations to

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prevent AOE include removing obstructing cerumen; using acidifying ear drops shortly before swimming, after swimming, at bedtime, or all three; drying the ear canal with a hair dryer; using ear plugs while swimming; and avoiding trauma to the external auditory canal.<sup>36-39</sup>

The continued variations in managing AOE and the importance of accurate diagnosis suggest a need for updating this evidence-based clinical practice guideline. Failure to distinguish AOE from other causes of “the draining ear” (eg, chronic external otitis, malignant otitis externa, middle ear disease, cholesteatoma) may prolong morbidity or cause serious complications. Because topical therapy is efficacious, systemic antibiotics are often prescribed inappropriately.<sup>15,40</sup> When topical therapy is prescribed, confusion exists about whether to use an antiseptic (eg, acetic acid), antibiotic, corticosteroid, or a combination product. Antibiotic choice is controversial, particularly regarding the role of newer quinolone drops. Lastly, the optimal methods for cleaning the ear canal (aural toilet) and drug delivery are defined.

The primary outcome considered in this guideline is clinical resolution of AOE, which implies resolution of all presenting signs and symptoms (eg, pain, fever, otorrhea). Additional outcomes considered include minimizing the use of ineffective treatments; eradicating pathogens; minimizing recurrence, cost, complications, and adverse events; maximizing the health-related quality of life of individuals afflicted with AOE; increasing patient satisfaction<sup>41</sup>; and permitting the continued use of necessary hearing aids. The relatively high incidence of AOE and the diversity of interventions in practice (**Table 2**) make AOE an important condition for the use of an up-to-date, evidence-based practice guideline.

## Purpose

The primary purpose of the original guideline was to promote appropriate use of oral and topical antimicrobials for AOE and to highlight the need for adequate pain relief. An updated guideline is needed because of new clinical trials, new systematic reviews, and the lack of consumer participation in the initial guideline development group. The target patient is aged 2 years or older with diffuse AOE, defined as generalized inflammation of the external ear canal, with or without involvement of the pinna or tympanic membrane. This guideline does not apply to children younger than 2 years or to patients of any age with chronic or malignant (progressive necrotizing) otitis externa. AOE is uncommon before 2 years of age, and very limited evidence exists regarding treatment or outcomes in this age group.<sup>42</sup> Although the differential diagnosis of the “draining ear” will be discussed, recommendations for management will be limited to diffuse AOE, which is almost exclusively a bacterial infection. The following conditions will be briefly discussed but not considered in detail: furunculosis (localized AOE), otomycosis, herpes zoster oticus (Ramsay Hunt syndrome), and contact dermatitis.

The guideline is intended for primary care and specialist clinicians, including otolaryngologists—head and neck surgeons, pediatricians, family physicians, emergency physicians, internists, nurse practitioners, and physician assistants.

**Table 2.** Interventions considered in acute otitis externa guideline development.

Diagnosis	History and physical examination Otoscopy Pneumatic otoscopy Otomicroscopy Tympanometry Acoustic reflectometry Culture Imaging studies Audiometry (excluded from guideline)
Treatment	Aural toilet (suction, dry mopping, irrigation, removal of obstructing cerumen or foreign object) Non-antibiotic (antiseptic or acidifying) drops Antibiotic drops Steroid drops Oral antibiotics Analgesics Complementary and alternative medicine Ear canal wick Biopsy (excluded from guideline) Surgery (excluded from guideline)
Prevention	Water precautions Prophylactic drops Environmental control (eg, hot tubs) Avoiding neomycin drops (if allergic) Addressing allergy to ear molds or water protector Addressing underlying dermatitis Specific preventive measures for diabetics or immunocompromised state

The guideline is applicable to any setting in which children, adolescents, or adults with diffuse AOE would be identified, monitored, or managed.

## Health Care Burden

Also known as “swimmer’s ear” or “tropical ear,” AOE is one of the most common infections encountered by clinicians, with regional variations based on age and geography. In 2007, 44% of AOE visits occurred in June through August, and the disease was least frequent in winter. Ambulatory visits for AOE were most common in the South (9.1 per 1000 population) and least common in the West (4.3 per 1000 population).<sup>43</sup>

Data from ambulatory care centers and emergency departments indicate that in 2007 there were about 2.4 million visits for AOE (8.1 visits per 1000 population), affecting 1 in 123 persons in the United States. Just less than half of all visits were for children 5 to 14 years of age. Lifetime incidence is up to 10%.<sup>44</sup> Medical costs include physician visits and prescriptions for analgesics and systemic medications, such as antibiotics, steroids, or both. Direct costs are estimated at about half a billion dollars annually, and ambulatory care providers spent about 600,000 hours treating AOE.<sup>43</sup> The indirect costs of AOE have not been calculated but are likely to be substantial because of severe and persistent otalgia that limits activities, especially work.

## Methods

In developing this update of the evidence-based clinical practice guideline on managing AOE, the American Academy of Otolaryngology—Head and Neck Surgery Foundation (AAO-HNSF) assembled a working group representing the disciplines of otolaryngology—head and neck surgery, pediatrics, infectious disease, family medicine, dermatology, and a consumer advocate. The panel followed the methodology for updating guidelines detailed in the AAO-HNSF's guideline development manual.<sup>45</sup>

The original MEDLINE search was updated from July 2005 to October 2012 on PubMed using “otitis externa” (MeSH term) and “swimmer’s ear.” The English-language search, which was supplemented by manual cross-checks of bibliographies from systematic reviews, identified 6 clinical practice guidelines, 4 systematic reviews, and 52 randomized controlled trials (RCTs). After assessing quality and relevance, we retained none of the guidelines, 2 of the systematic reviews, and 12 RCTs. A systematic review had been conducted to support initial guideline development,<sup>46</sup> but an update was deemed unnecessary because of only limited new evidence that was incorporated into the newer systematic reviews identified. An executive summary of the existing guideline was then sent to a panel of reviewers. They were asked to assess the statements in the original guideline and recommend if they should be kept as is, amended, or removed based on relevancy, omissions, or controversies that the guideline spurred and any new literature or treatments that might affect the guideline recommendations.

The working group then had 1 conference call and 1 face-to-face meeting during which these comments and the literature search were reviewed for each action statement. The panel then decided to leave the statement unaltered, change slightly, or rewrite the statement based on the impact of the literature search and the reviewer’s comments. The supporting text was then edited to explain any changes from the original action statement and recommendation level.

The evidence profile for each statement was then converted into an action statement profile, which was moved up in the text to immediately follow the action statement. Statements about the level of confidence in the evidence, any intentional vagueness included in the action statement, and any exclusions to whom the action statement does not apply were added to the action statement profile. These additions reflect the current methodology for guideline development by the AAO-HNSF and conform to the Institute of Medicine’s standards for developing trustworthy guidelines.<sup>45,47</sup>

The updated guideline then underwent Guideline Implementability Appraisal, to appraise adherence to methodologic standards, to improve the clarity of recommendations, and to predict potential obstacles to implementation. The final draft of the updated clinical practice guideline underwent extensive external peer review. Comments were compiled and reviewed by the group chairperson. The recommendations contained in the guideline are based on the best available published data through October 2012. Where data were lacking, a

combination of clinical experience and expert consensus was used. A scheduled review process will occur at 5 years from publication or sooner if new compelling evidence warrants earlier consideration.

## Classification of Evidence-Based Statements

Guidelines are intended to produce optimal health outcomes for patients, to minimize harm, and to reduce inappropriate variations in clinical care. The evidence-based approach to guideline development requires that the evidence supporting a policy be identified, appraised, and summarized and that an explicit link between evidence and statements be defined. Evidence-based statements reflect both the quality of evidence and the balance of benefit and harm that is anticipated when the statement is followed. The definitions for evidence-based statements are listed in **Tables 3 and 4.**<sup>48,49</sup>

Guidelines are not intended to supersede professional judgment; rather, they may be viewed as a relative constraint on individual clinician discretion in a particular clinical circumstance. Less frequent variation in practice is expected for a “strong recommendation” than might be expected with a “recommendation.” “Options” offer the most opportunity for practice variability.<sup>50</sup> Clinicians should always act and decide in a way that they believe will best serve their patients’ interests and needs, regardless of guideline recommendations. They must also operate within their scope of practice and according to their training. Guidelines represent the best judgment of a team of experienced clinicians and methodologists addressing the scientific evidence for a particular topic.<sup>48</sup>

Making recommendations about health practices involves value judgments on the desirability of various outcomes associated with management options. Values applied by the guideline panel sought to minimize harm and diminish unnecessary and inappropriate therapy. A major goal of the panel was to be transparent and explicit about how values were applied and to document the process.

## Financial Disclosure and Conflicts of Interest

The cost of updating this guideline, including travel expenses of all panel members, was covered in full by the AAO-HNSF. Potential conflicts of interest for all panel members were compiled and distributed before the first in-person meeting. After review and discussion of these disclosures,<sup>51</sup> the panel concluded that individuals with potential conflicts could remain on the panel if they (1) reminded the panel of potential conflicts before any related discussion, (2) recused themselves from a related discussion if asked by the panel, and (3) agreed not to discuss any aspect of the guideline with industry before publication. Lastly, panelists were reminded that conflicts of interest extend beyond financial relationships and may include personal experiences, how a participant earns a living, and the participant’s previously established “stake” in an issue.<sup>52</sup>

**Table 3.** Guideline definitions for evidence-based statements.

Statement	Definition	Implication
Strong recommendation	A strong recommendation means the benefits of the recommended approach clearly exceed the harms (or that the harms clearly exceed the benefits in the case of a strong negative recommendation) and that the quality of the supporting evidence is excellent (Grade A or B). <sup>a</sup> In some clearly identified circumstances, strong recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	A recommendation means the benefits exceed the harms (or that the harms exceed the benefits in the case of a negative recommendation) but the quality of evidence is not as strong (Grade B or C). <sup>a</sup> In some clearly identified circumstances, recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits outweigh the harms.	Clinicians should also generally follow a recommendation but should remain alert to new information and sensitive to patient preferences.
Option	An option means that either the quality of evidence that exists is suspect (Grade D) <sup>a</sup> or that well-done studies (Grade A, B, or C) <sup>a</sup> show little clear advantage to one approach versus another.	Clinicians should be flexible in their decision making regarding appropriate practice, although they may set bounds on alternatives; patient preference should have a substantial influencing role.
No recommendation	No recommendation means there is both a lack of pertinent evidence (Grade D) <sup>a</sup> and an unclear balance between benefits and harms.	Clinicians should feel little constraint in their decision making and be alert to new published evidence that clarifies the balance of benefit versus harm; patient preference should have a substantial influencing role.

<sup>a</sup>See **Table 4** for definition of evidence grades.

**Table 4.** Evidence quality for grades of evidence.<sup>a</sup>

Grade	Evidence Quality for Diagnosis	Evidence Quality for Treatment and Harm
A	Systematic review of cross-sectional studies with consistently applied reference standard and blinding	Well-designed randomized controlled trials performed on a population similar to the guideline's target population
B	Individual cross-sectional studies with consistently applied reference standard and blinding	Randomized controlled trials; overwhelmingly consistent evidence from observational studies
C	Nonconsecutive studies, case-control studies, or studies with poor, nonindependent, or inconsistently applied reference standards	Observational studies (case control and cohort design)
D	Mechanism-based reasoning or case reports	
X	Exceptional situations in which validating studies cannot be performed and there is a clear preponderance of benefit over harm	

<sup>a</sup>American Academy of Pediatrics (AAP)<sup>48</sup> classification scheme updated for consistency with current level of evidence definitions.<sup>49</sup>

## Guideline Key Action Statements

Each evidence-based statement is organized in a similar fashion: an **evidence-based key action statement in bold**, followed by the *strength of the recommendation in italics*. Each key action statement is followed by an action statement profile that outlines the aggregate evidence quality, our confidence in the evidence, and the guideline development group's benefit-harm assessment. In addition, there is an explicit statement of any value judgments, clarification of any intentional vagueness, the role of patient preferences, the policy level, and a discussion of any differences of opinion. Several paragraphs subsequently discuss the evidence base supporting

the statement. **Table 5** summarizes the evidence-based statements within the guideline.

The role of patient preferences in making decisions deserves further clarification. For some statements, where the evidence base demonstrates clear benefit, although the role of patient preference for a range of treatments may not be relevant (such as with intraoperative decision making), clinicians should provide patients with clear and comprehensible information on the benefits in order to facilitate patient understanding and shared decision making, which in turn leads to better patient adherence and outcomes. In cases in which evidence is weak or benefits unclear, the practice of shared decision

**Table 5.** Summary of evidence-based statements.

Statement	Action	Strength
1. Differential diagnosis	Clinicians should distinguish diffuse acute otitis externa (AOE) from other causes of otalgia, otorrhea, and inflammation of the external ear canal.	Recommendation
2. Modifying factors	Clinicians should assess the patient with diffuse AOE for factors that modify management (nonintact tympanic membrane, tympanostomy tube, diabetes, immunocompromised state, prior radiotherapy).	Recommendation
3. Pain management	The clinician should assess patients with AOE for pain and recommend analgesic treatment based on the severity of pain.	Strong recommendation
4. Systemic antimicrobials	Clinicians should not prescribe systemic antimicrobials as initial therapy for diffuse, uncomplicated AOE unless there is extension outside the ear canal or the presence of specific host factors that would indicate a need for systemic therapy.	Strong recommendation
5. Topical therapy	Clinicians should use topical preparations for initial therapy of diffuse, uncomplicated AOE.	Recommendation
6. Drug delivery	Clinicians should inform patients how to administer topical drops and should enhance delivery of topical drops when the ear canal is obstructed by performing aural toilet, placing a wick, or both.	Recommendation
7. Nonintact tympanic membrane	When the patient has a known or suspected perforation of the tympanic membrane, including a tympanostomy tube, the clinician should recommend a non-ototoxic topical preparation.	Recommendation
8. Outcome assessment	If the patient fails to respond to the initial therapeutic option within 48 to 72 hours, the clinician should reassess the patient to confirm the diagnosis of diffuse AOE and to exclude other causes of illness.	Recommendation

making, again where the management decision is made by a collaborative effort between the clinician and an informed patient, is extremely useful. Factors related to patient preference include (but are not limited to) absolute benefits (numbers needed to treat), adverse effects (number needed to harm), cost of drugs or procedures, and frequency and duration of treatment.

**STATEMENT 1. DIFFERENTIAL DIAGNOSIS: Clinicians should distinguish diffuse AOE from other causes of otalgia, otorrhea, and inflammation of the external ear canal.**

*Recommendation based on observational studies with a preponderance of benefit over risk.*

**Action Statement Profile**

- Aggregate evidence quality: Grade C, observational studies, and Grade D, reasoning from first principles
- Level of confidence in evidence: High
- Benefit: Improved diagnostic accuracy
- Risks, harms, costs: None in following the recommended action
- Benefits-harm assessment: Preponderance of benefit over harm
- Value judgments: Importance of accurate diagnosis
- Intentional vagueness: None
- Role of patient preferences: None, regarding the need for a proper diagnosis
- Exceptions: None

- Policy level: Recommendation
- Differences of opinion: None

**Supporting Text**

The purpose of this statement is to underscore the importance of distinguishing AOE from other causes of otalgia, otorrhea, and inflammation of the external ear canal. The clinician should make every effort to identify the cause of ear pain and make an accurate diagnosis of AOE, which will enable the clinician to treat the condition appropriately. A diagnosis of diffuse AOE requires rapid onset with signs and symptoms of ear canal inflammation (**Table 1**). Clinical history should identify various predisposing factors including exposure to potentially contaminated water.

Symptoms of AOE include otalgia (70%), itching (60%), or fullness (22%), with or without hearing loss (32%) or ear canal pain on chewing. A hallmark sign of diffuse AOE is tenderness of the tragus (when pushed), the pinna (when pulled), or both. The tenderness is often intense and disproportionate to what might be expected based on appearance of the ear canal on inspection. Otoscopy will reveal diffuse ear canal edema, erythema, or both, with or without otorrhea or material in the ear canal. Regional lymphadenitis or cellulitis of the pinna and adjacent skin may be present in some patients.<sup>7,53</sup>

AOE can mimic the appearance of acute otitis media (AOM) because of erythema involving the tympanic membrane. Distinguishing AOE from AOM is important, because the latter may require systemic antimicrobials.<sup>54</sup> If pneumatic otoscopy can be performed, it will demonstrate good tympanic

membrane mobility with AOE but will show absent or limited mobility with AOM and associated middle-ear effusion. Similarly, tympanometry will show a normal peaked curve (type A) with AOE but a flat tracing (type B) with AOM. The validity of acoustic reflectometry with AOE is unknown.

Anything that disrupts the epithelium of the ear canal can permit invasion by bacteria that cause diffuse AOE. Common predisposing factors for AOE<sup>25</sup> are humidity or prolonged exposure to water, dermatologic conditions (eczema, seborrhea, psoriasis), anatomic abnormalities (narrow canal, exostoses), trauma or external devices (wax removal, inserting earplugs, using hearing aids), and otorrhea caused by middle-ear disease. AOE may also occur secondary to ear canal obstruction by impacted cerumen, a foreign object, a dermoid cyst, a sebaceous cyst, or a furuncle.

### Dermatoses of the Ear Canal

Eczema (atopic dermatitis), seborrhea (seborrheic dermatitis), and other inflammatory dermatoses involving the ear canal and surrounding tissue are relatively common and can mimic AOE. Patients with eczema present with chronic pruritus typically starting in childhood with involvement of multiple areas of the body. Skin lesions demonstrate different clinical features such as erythema, xerotic scaling, lichenification, and hyperpigmentation depending on the stage of eczema. Management includes gentle skin care, application of emollients, prevention of secondary skin infection, and the use of topical corticosteroids and other antipruritics. Seborrheic dermatitis is a common condition affecting the ears, scalp, central face, and other sebaceous areas of the skin. Presenting with greasy yellowish scaling, itching, and secondary inflammation from *Malassezia* yeast, seborrheic dermatitis is more pronounced in patients with Down syndrome, HIV infection, and Parkinson disease.<sup>55</sup> Treatment includes the use of topical antifungal medications to reduce the amount of yeast present and topical anti-inflammatory medications to reduce inflammation and itch. Other skin disorders that can mimic AOE include psoriasis and discoid lupus erythematosus, which have characteristic skin lesions and often involvement of other areas of the skin.

Contact dermatitis of the ear canal is common and divided into irritant contact dermatitis and allergic contact dermatitis. Irritant contact dermatitis is inflammation of the skin caused from direct chemical damage usually from acids or alkalis.<sup>56</sup> Resultant release of inflammatory mediators from damaged epidermal cells leads to erythema, edema, scaling, itch, and occasional pain. All individuals are susceptible to an irritant contact dermatitis in a dose-dependent manner.

In contrast, allergic contact dermatitis occurs only in susceptible individuals with a predisposition to an allergic reaction to antigens such as metals (nickel, silver), chemicals (cosmetics, soaps, detergents, shampoos, hair sprays), plastics, rubber, leather, or drugs. Nickel is the most common contact allergen, affecting about 10% of women with pierced ears.<sup>57-59</sup> Contact allergy also occurs in some patients wearing hearing aids as a reaction to the plastics and other chemicals used in hearing aid molds.<sup>60,61</sup>

Some otic preparations (antibiotics and vehicle substances) have been reported to cause sensitization. Neomycin is the most common substance, causing reactions in about 5% to 15% of patients with chronic external otitis.<sup>62</sup> Patch testing has demonstrated that 13% of normal volunteers are hypersensitive to neomycin.<sup>63</sup> A maculopapular and often eczematous eruption on the conchal bowl and in the ear canal is consistent with an allergic reaction to a topical agent; an erythematous streak may extend down the pinna where drops contact the auricular skin.<sup>64</sup> Management involves removing the sensitizing agent and applying a topical steroid or other anti-inflammatory topical such as a calcineurin inhibitors (eg, tacrolimus 0.1% ointment or pimecrolimus 1% cream).<sup>65-69</sup>

### Other Causes of Otagia or Otorrhea That May Mimic AOE

Furunculosis is the presence of an infected hair follicle on the outer third of the ear canal, sometimes referred to as localized otitis externa. Clinical findings can include otalgia, otorrhea, localized tenderness, focal swelling, and pustular lesions. Treatment may include local heat, incision and drainage, or systemic antibiotics that cover *S aureus*, the most common causative agent.<sup>70</sup>

Viral infections of the external ear, caused by varicella, measles, or herpes virus, are rare but are important on the differential of AOE. Herpes zoster oticus (Ramsay Hunt syndrome) causes vesicles on the external ear canal and posterior surface of the auricle, severe otalgia, facial paralysis or paresis, loss of taste on the anterior two-thirds of the tongue, and decreased lacrimation on the involved side.<sup>71</sup> Management involves prompt systemic antiviral therapy and systemic steroids.<sup>72</sup>

Complaints of otalgia in the absence of swelling of the ear canal and without apparent middle ear disease should arouse suspicion of pathology outside the ear. Perhaps the most common cause of referred otalgia is that of temporomandibular joint (TMJ) syndrome. These patients commonly complain of pain not only in the ear but also radiating to the periauricular area, temple, or neck. There may be a history of gum chewing, bruxism, or recent dental procedure with subsequent malocclusion. On examination, they are tender over the affected TMJ and may have associated crepitus.<sup>73</sup> On occasion, the only symptom of patients with upper aerodigestive tract cancer is that of otalgia. Older patients with a long history of tobacco and ethanol use, and more recently younger patients with human papillomavirus infection, suggest this possibility. A complete head and neck examination with visualization of the mucosal surfaces of the head and neck, assessment of any neck masses, and palpation of the tongue base is recommended. Other potential etiologies are dental pathologies (caries, impacted molars), tonsillitis, peritonsillar abscesses, retropharyngeal abscesses, carotidynia, styloid process elongation, angina, intrathoracic aneurysms, glossopharyngeal neuralgia, and geniculate neuralgia.

Although otorrhea may accompany AOE, other causes of otorrhea should be considered in the differential diagnosis. Cholesteatoma may be mistaken for AOE or chronic external otitis but is typically painless and associated with abnormalities

of the tympanic membrane that include perforation, retraction pockets, and granulation tissue. Any patient with suspected cholesteatoma should be referred to an otolaryngologist for definitive management. AOM with tympanostomy tubes is a common cause of otorrhea, which is painless at first and caused by either a primary bacterial AOM episode or by water penetration into the middle ear from swimming or bathing. Topical antibiotic eardrops are the treatment of choice for acute tympanostomy tube otorrhea.<sup>74</sup>

**STATEMENT 2. MODIFYING FACTORS: Clinicians should assess the patient with diffuse AOE for factors that modify management (nonintact tympanic membrane, tympanostomy tube, diabetes, immunocompromised state, prior radiotherapy).** *Recommendation based on observational studies with a preponderance of benefit over risk.*

#### Action Statement Profile

- Aggregate evidence quality: Grade C, observational studies
- Level of confidence in evidence: High
- Benefit: Optimizing treatment of AOE through appropriate diagnosis and recognition of factors or comorbid conditions that might alter management
- Risks, harms, costs: None from following the recommendation; additional expense of diagnostic tests or imaging studies to identify modifying factors
- Benefits-harm assessment: Preponderance of benefits over harm
- Value judgments: Avoiding complications that could potentially be prevented by modifying the management approach based on the specific factors identified
- Intentional vagueness: None
- Role of patient preferences: None
- Exceptions: None
- Policy level: Recommendation
- Differences of opinion: None

#### Supporting Text

The purpose of this statement is to emphasize the importance of identifying patients with AOE who may have other disease processes that could seriously affect the outcome of AOE.

The key components of the clinical history that can modify management of diffuse AOE include (1) diabetes<sup>75-77</sup>; (2) HIV infection, AIDS,<sup>78</sup> or other immunocompromised states, such as patients with malignancies receiving chemotherapy<sup>79</sup>; (3) history of radiotherapy; and (4) presence of tympanostomy tubes or perforated tympanic membrane (nonintact tympanic membrane).

Patients with diabetes, an immunocompromised state, or both require special consideration because they are susceptible to otomycosis and necrotizing otitis externa, which may present similar to AOE but require different management. In addition, as discussed later in this guideline, they are more likely to require systemic antibiotics (in addition to topical therapy) when managing AOE and should not have their ear

canals irrigated to remove debris, since it may predispose to necrotizing otitis externa.<sup>80</sup>

Necrotizing (malignant) otitis externa is an aggressive infection that predominantly affects elderly, diabetic, or immunocompromised patients.<sup>81</sup> *P aeruginosa* is isolated from exudate in the ear canal in more than 90% of cases. Initial signs and symptoms are those of the initiating AOE, but untreated disease develops into a skull base osteomyelitis that can invade soft tissue, the middle ear, inner ear, or brain. Facial nerve paralysis may be an early sign, with the glossopharyngeal and spinal accessory nerves less frequently involved. Granulation tissue is classically seen on the floor of the canal and at the bony-cartilaginous junction.

A clinical diagnosis of necrotizing otitis externa can be confirmed with a raised erythrocyte sedimentation rate plus an abnormal computed tomography or magnetic resonance imaging scan<sup>81,82</sup>; other imaging modalities include gallium scan, indium-labeled leukocyte scan, technetium bone scan, and single-photon emission tomographs. Treatment includes surgical debridement and systemic antibiotics adequate to cover pseudomonal and staphylococcal infection, including methicillin-resistant *S aureus*. Biopsy may be necessary to detect neoplasia if the diagnosis of malignant otitis externa is uncertain or response to therapy is incomplete.

Otomycosis, or fungal infection of the external ear canal, is common in tropical countries, humid locations, after long-term topical antibiotic therapy, and in those with diabetes, HIV infection, or an immunocompromised state. *Aspergillus* species (60%-90%) and *Candida* species (10%-40%) are often cultured.<sup>83</sup> Symptoms include pruritus and thickened otorrhea, which may be black, gray, bluish green, yellow, or white. Candidal otitis externa generally results in white debris sprouting hyphae,<sup>84</sup> best seen with an otologic microscope. *Aspergillus niger* usually appears as a moist white plug dotted with black debris ("wet newspaper").<sup>84,85</sup> Fungal otitis externa should also be suspected if a patient fails to respond to initial topical therapy. Management may include debridement plus topical antifungal therapy, rarely systemic antifungal therapy,<sup>86</sup> or both. Topical antibiotic therapy, which is the mainstay of managing AOE, is contraindicated in managing otomycosis because it is ineffective and may promote further fungal overgrowth.

Radiotherapy can damage the external ear by causing acute and late skin reactions involving the pinna, external canal, and periauricular region.<sup>87</sup> Acute events include erythema, desquamation, or ulceration of the auricle and ear canal, thus leading to pain and otorrhea. Late skin changes include atrophy, necrosis or ulceration, external otitis, and external canal stenosis. Damage to the epithelium of sebaceous and apocrine glands can diminish cerumen production. Management of AOE in patients after radiotherapy may require systemic antimicrobials.<sup>87</sup>

Concurrent middle ear disease can modify treatment of AOE. Patients with a tympanostomy tube or tympanic membrane perforation may develop diffuse AOE because of purulent middle-ear secretions that enter the external ear canal. This condition has been called infectious eczematoid

dermatitis because the skin changes resemble eczema as well as infection.<sup>53</sup> Management of the underlying middle-ear disease may also require systemic antimicrobials, imaging studies, or surgery. Patients with AOE may also develop AOM without perforation of the tympanic membrane independent of AOE. Fluid may be present in the middle ear or mastoid in patients with AOE.<sup>88</sup> Patients with concurrent AOM and AOE may require systemic antibiotic therapy. As discussed later in the guideline, clinicians should recommend a non-ototoxic topical preparation when the tympanic membrane is not intact.

**STATEMENT 3. PAIN MANAGEMENT: The clinician should assess patients with AOE for pain and recommend analgesic treatment based on the severity of pain.** *Strong recommendation based on well-designed randomized trials with a preponderance of benefit over harm.*

#### Action Statement Profile

- Aggregate evidence quality: Grade B, 1 randomized controlled trial limited to AOE; consistent, well-designed randomized trials of analgesics for pain relief in general
- Level of confidence in evidence: High
- Benefit: Increase patient satisfaction, allow faster return to normal activities
- Risks, harms, costs: Adverse effects of analgesics; direct cost of medication
- Benefits-harms assessment: Preponderance of benefit over harm
- Value judgments: Consensus among guideline development group that the severity of pain associated with AOE is underrecognized; preeminent role of pain relief as an outcome when managing AOE
- Intentional vagueness: None
- Role of patient preferences: Moderate, choice of analgesic and degree of pain tolerance
- Exceptions: None
- Policy level: Strong recommendation
- Differences of opinion: None

#### Supporting Text

The purpose of this statement is to emphasize the importance of acute pain assessment and management in patients with AOE, because the accompanying pain may be severe and the intensity of the pain underappreciated (and inadequately treated) by clinicians.

Pain relief is an essential component of managing AOE. Pain caused by AOE can be intense and severe, because the highly sensitive periosteum of the underlying bone is in close proximity to the ear canal skin, especially in the deeper portion of the canal. Frequent use of appropriate analgesics at adequate doses is necessary to permit patients to achieve comfort, rest, and resume normal activities.<sup>89-91</sup> Ongoing assessment of the severity of discomfort is essential for proper management. Use of a faces,<sup>92</sup> Oucher,<sup>93</sup> or visual analog<sup>94</sup> scale may help determine the level of pain, particularly for children and non-English-speaking patients.

Adequate pain control requires knowing the dose, timing, routes of delivery, and possible adverse effects of an analgesic.<sup>89-91,95</sup> Mild to moderate pain usually responds to acetaminophen or nonsteroidal anti-inflammatory drugs given alone or in fixed combination with an opioid (eg, oxycodone or hydrocodone; ibuprofen with oxycodone). Administering a nonsteroidal anti-inflammatory drug during the acute phase of diffuse AOE significantly reduces pain compared with placebo.<sup>96</sup>

Convenience, ease of use, and cost make orally administered analgesics the preferred route of administration whenever possible. Rarely, parenteral analgesia may be necessary to achieve adequate pain relief in a timely fashion. In all cases, analgesic therapy should be guided by the recognition that pain is easier to prevent than treat. Thus, early treatment at an appropriate starting dose is always indicated. When frequent dosing is required to maintain adequate pain relief, administering analgesics at fixed intervals rather than on a pro re nata (prn) basis may be more effective. Nonpharmacologic therapies such as heat or cold, relaxation, and distraction are of unproven value.

Acute analgesia and, occasionally, procedure-related sedation,<sup>97</sup> may be required to accomplish adequate aural toilet in patients with severe inflammation and tenderness of the canal. In one study,<sup>98</sup> analgesic cream was applied to the ear canal in adults and cooperative children to relieve pain and anesthetize the external auditory meatus if the tympanic membrane was intact. Opioids such as fentanyl citrate, morphine sulfate, and hydromorphone hydrochloride are indicated for procedure-related pain and moderate to severe around-the-clock pain.

Benzocaine otic solution, with or without antipyrine, is available for topical anesthesia of the ear canal but is not approved by the US Food and Drug Administration (FDA) for safety, effectiveness, or quality.<sup>99</sup> There is no specific indication for using topical anesthetic drops in treating AOE, and using them may mask progression of underlying disease while pain is being suppressed.

If a topical anesthetic drop is prescribed for temporary pain relief, the patient should be reexamined within 48 hours to ensure that AOE has responded appropriately to primary therapy. Topical anesthetic drops should not be used if a tympanostomy tube is present or there is uncertainty regarding the integrity of the tympanic membrane, because these drops are not approved for use in the middle ear.

Adding a topical steroid to topical antimicrobial drops has been shown to hasten pain relief in some randomized trials,<sup>100</sup> but other studies have shown no significant benefits.<sup>101,102</sup>

Because of concerns of inappropriate opioid use by patients, physicians and other providers may have apprehension in prescribing these potent analgesics even when indicated for pain relief. However, given that symptoms of uncomplicated AOE should improve within 48 to 72 hours of initiating appropriate topical therapy, prescribing a limited number of doses of opioid-containing analgesic for this initial treatment period should mitigate risks of opioid misuse or diversion. Patients should be instructed explicitly that if pain

relief is not adequate or if there is no improvement within the expected time period, clinical reassessment is indicated.

**STATEMENT 4. SYSTEMIC ANTIMICROBIALS: Clinicians should not prescribe systemic antimicrobials as initial therapy for diffuse, uncomplicated AOE unless there is extension outside the ear canal or the presence of specific host factors that would indicate a need for systemic therapy.**

*Strong recommendation based on randomized controlled trials with minor limitations and a preponderance of benefit over harm.*

#### Action Statement Profile

- Aggregate evidence quality: Grade B, randomized controlled trials with minor limitations; no direct comparisons of topical versus systemic therapy
- Level of confidence in evidence: High
- Benefit: Avoid side effects from ineffective therapy, reduce antibiotic resistance by avoiding systemic antibiotics
- Risks, harms, costs: None
- Benefits-harms assessment: Preponderance of benefit over harm
- Value judgments: Desire to decrease the use of ineffective treatments, societal benefit from avoiding the development of antibiotic resistance
- Intentional vagueness: None
- Role of patient preferences: None
- Exceptions: None
- Policy level: Strong recommendation
- Differences of opinion: None

#### Supporting Text

The purpose of this statement is to emphasize that clinicians should not prescribe systemic antimicrobials as initial therapy for diffuse, uncomplicated AOE unless there is extension outside the ear canal or the presence of specific host factors that would indicate a need for systemic therapy.

#### Efficacy of Topical Therapy

Three randomized trials have compared topical antimicrobial versus placebo for treating diffuse AOE.<sup>103-105</sup> A meta-analysis of the 2 trials with similar methodology<sup>106,107</sup> yields a combined absolute rate difference (RD) of 0.46 based on 89 patients (95% confidence interval [CI], 0.28 to 0.63), suggesting that only 2 patients need to be treated (NNT) with topical antimicrobials to achieve 1 additional cure. Bacteriologic efficacy (RD = 0.61) was higher than clinical efficacy. Another trial<sup>108</sup> reported significantly less edema and itching 3 days after initiating therapy and less edema, itching, redness, scaling, and weeping 7 days after initiating therapy. Conversely, another study<sup>109</sup> showed no benefit for an antimicrobial-steroid drop versus placebo, but patients with chronic otitis externa, otomycosis, and furunculosis were also included.

Topical preparations are recommended as initial therapy for diffuse, uncomplicated AOE because of safety, efficacy over placebo in randomized trials, and excellent clinical and

bacteriologic outcomes in comparative studies. The recent Cochrane review affirms this recommendation and states, "Topical treatments alone, as distinct from systemic ones, are effective for uncomplicated AOE."<sup>110</sup> There are no data on the efficacy of systemic therapy using appropriate antibacterials and stratified by severity of the infection. Moreover, orally administered antibiotics have significant adverse effects that include rashes, vomiting, diarrhea, allergic reactions, altered nasopharyngeal flora, and development of bacterial resistance.<sup>20,107,111,112</sup> Societal consequences include direct transmission of resistant bacterial pathogens in homes and child care centers.<sup>19</sup>

Despite the well-demonstrated safety and efficacy of topical preparations for treating AOE, about 20% to 40% of subjects with AOE nonetheless receive oral antibiotics, often in addition to topical antimicrobials.<sup>3,16,18</sup> Despite a strong recommendation against the use of systemic (oral or parenteral) antibiotics in the initial guideline, clinicians actually prescribed more systemic antibiotics postpublication (31% vs 22%).<sup>113</sup> Many of the oral antibiotics selected are inactive against *P aeruginosa* and *S aureus*, the most common pathogens identified in cases of AOE. Further, treatment with penicillins, macrolides, or cephalosporins increases disease persistence (rate ratios 1.56 to 1.91), and treatment with cephalosporins also increases recurrence (rate ratio 1.28; 95% CI, 1.03 to 1.58).<sup>3</sup>

#### Lack of Efficacy of Systemic Antibiotic Therapy

Two studies directly address the use of oral antibiotics in treating diffuse AOE.<sup>107</sup> When patients were randomized to topical ointment plus oral antibiotic (trimethoprim-sulfamethoxazole) versus topical ointment plus placebo, there was no significant difference in cure rates at 2 to 4 days (RD = -0.01; 95% CI, -0.21 to 0.18) or at 5 to 6 days (RD = 0.08; 95% CI, -0.15 to 0.30). The ointment (Kenacomb) contained an antifungal, an antibiotic active against gram-negative organisms, an antibiotic active against gram-positive organisms, and a steroid. Another randomized multicenter trial showed no differences in pain duration or bacteriologic efficacy between topical ciprofloxacin/hydrocortisone (Cipro HC) and combination therapy with oral amoxicillin and topical neomycin/polymyxin b/hydrocortisone.<sup>114</sup>

An argument against the use of oral antibiotics for diffuse AOE limited to the ear canal is the efficacy of topical treatments that do not include antibiotics. Effective topical treatments include acetic acid,<sup>100,106,108,115</sup> boric acid,<sup>101</sup> aluminum acetate,<sup>116,117</sup> silver nitrate,<sup>118,119</sup> and an endogenous antiseptic N-chlorotaurine.<sup>120</sup> Topical steroids are also effective as a single agent<sup>121-123</sup> or in combination with acetic acid<sup>100,108,115</sup> or an antifungal preparation.<sup>124</sup> Considering the success of these non-antibiotic therapies, it is likely that for cases of uncomplicated AOE, oral antibiotics, particularly those with no activity against *P aeruginosa* or *S aureus*, are unnecessary.

#### Benefits of Topical Therapy

An advantage of topical therapy is the very high concentration of antimicrobial that can be delivered to infected tissue, often 100 to 1000 times higher than can be achieved with systemic

therapy. For example, a 0.3% solution of antibiotic (a typical concentration in commercial otic drops) has a concentration of 3000 µg/mL. Since there are between 10 to 20 drops/mL, depending on the nature of the liquid (solution vs suspension, viscosity, etc), each dose of 3 to 5 drops contains about 0.5 to 1.5 mg of antibiotic.

Topical therapy avoids prolonged exposure of bacteria to subtherapeutic concentrations of antibiotic and may therefore be less likely than systemic therapy to result in selective pressure for resistant organisms.<sup>5,125</sup> Avoiding antibiotic exposure of host bacteria resident outside the ear canal, as occurs with systemic therapy, provides a further advantage to reducing the selection of resistant microorganisms. Restrictive use of oral antibiotics for AOE is important because of increasing resistance among common AOE pathogens, especially *S aureus* and *P aeruginosa*.<sup>126,127</sup>

The recommendation for initial topical therapy applies to the otherwise healthy patient with diffuse AOE that is not complicated by osteitis, abscess formation, middle ear disease, or recurrent episodes of infection. Topical therapy should be supplemented by systemic antibiotics if the affected individual has a condition, especially diabetes, that is associated with markedly increased morbidity, or HIV infection/AIDS with immune deficiency, that could impair host defenses; if the infection has spread beyond the confines of the ear canal into the pinna, skin of the neck or face, or into deeper tissues such as occurs with malignant external otitis; or if there is good reason to believe that topical therapy cannot be delivered effectively (see Statement 6).<sup>3,128</sup> Systemic antibiotics, if indicated, should include coverage for common AOE pathogens, including *P aeruginosa* and *S aureus*.

**STATEMENT 5. TOPICAL THERAPY: Clinicians should prescribe topical preparations for initial therapy of diffuse, uncomplicated AOE.** *Recommendation based on randomized trials with some heterogeneity and a preponderance of benefit over harm.*

#### Action Statement Profile

- Aggregate evidence quality: Grade B, meta-analyses of randomized controlled trials with significant limitations and heterogeneity
- Level of confidence in evidence: High for the efficacy of topical therapy as initial management, but low regarding comparative benefits of different classes of drugs or combinations of ototopical drugs
- Benefit: Effective therapy, low incidence of adverse events
- Risks, harms, costs: Direct cost of medication (varies greatly depending on drug class and selection), risk of secondary fungal infection (otomycosis) with prolonged use of topical antibiotics
- Benefits-harms assessment: Preponderance of benefit over harm
- Value judgments: RCT results from largely specialty settings may not be generalizable to patients seen in

primary care settings, where the ability to perform effective aural toilet may be limited

- Intentional vagueness: No specific recommendations regarding the choice of ototopical agent
- Role of patient preferences: Substantial role for patient preference in choice of topical therapeutic agent
- Exceptions: Patients with a nonintact tympanic membrane (see Statement 7 on “Nonintact Tympanic Membrane”)
- Policy level: Recommendation
- Differences of opinion: None

#### Supporting Text

The purpose of this statement is to emphasize the importance of topical therapy, without systemic antibiotics, for initial management of uncomplicated AOE. A variety of topical preparations are approved by the US FDA for treating AOE (Table 6). Most of those currently available in the United States provide antimicrobial activity through (1) an antibiotic, which may be an aminoglycoside, polymyxin B, a quinolone, or a combination of these agents; (2) a steroid, such as hydrocortisone or dexamethasone; or (3) a low-pH antiseptic.

#### Efficacy of Topical Therapy

Efficacy is best summarized using meta-analysis of randomized controlled trials, of which 3 have been published: one to support the initial version of this clinical practice guideline,<sup>46</sup> another under the auspices of the Cochrane Collaboration,<sup>110</sup> and the most recent supported by industry to assess the comparative efficacy of quinolone versus nonquinolone preparations.<sup>129</sup> Although these 3 meta-analyses differ in study design, trial selection, and methods of statistical pooling, they all conclude that topical therapy is highly effective first-line therapy for diffuse AOE. Similarly, they do not find any meaningful differences in clinical outcomes based on class of drug (antibiotic vs antiseptic), use of a quinolone versus a nonquinolone preparation, or for monotherapy versus combination drugs with or without a concurrent steroid.

Randomized trials used in the 3 AOE meta-analyses are summarized in Table 7. Of the 31 listed trials, 3 were included in all of the meta-analyses, 14 trials were included in 2, and 15 in only 1. This reflects the authors' differing philosophies regarding article selection criteria and the ability to pool data from studies, with the Cochrane review being the most restrictive in this regard. Whereas all analyses conclude that topical therapy is efficacious, the internal validity is limited by the low methodological quality in most of the included studies.<sup>130</sup> Further, the analyses that combine multiple trials show large heterogeneity for the pooled estimate of treatment effect. Lastly, the generalizability of results is limited by the paucity of trials conducted in a primary care setting (Table 7) and the frequent use of aural toilet, wicks, or both, which may not be available in primary care.

Rosenfeld and colleagues<sup>46</sup> found no significant differences in clinical outcomes of AOE for antiseptic versus antimicrobial, quinolone antibiotic versus nonquinolone antibiotic(s), or steroid-antimicrobial versus antimicrobial

**Table 6.** Common topical otic preparations approved by the Food and Drug Administration for treating diffuse acute otitis externa.

Active Drug(s)	Name	Bottle	Cost, US\$ <sup>a</sup>	
		Size, mL	Trade	Generic
Acetic acid 2.0% solution	Acetic acid otic (generic)	15.0	—	33
Acetic acid 2.0%, hydrocortisone 1.0%	Acetasol HC (generic)	10.0	—	23
Ciprofloxacin 0.2%, hydrocortisone 1.0%	Cipro HC (trade)	10.0	170	—
Ciprofloxacin 0.3%, dexamethasone 0.1%	Ciprodex (trade)	7.5	144	—
Neomycin, polymyxin B, hydrocortisone	Cortisporin Otic (trade)	10.0	85	30
Ofloxacin 0.3%	Floxin Otic (trade)	5.0	76	18

<sup>a</sup>Approximate price in New York metropolitan region (<http://www.goodrx.com>).

**Table 7.** Randomized controlled trials included in published systematic reviews of acute otitis externa treatment.

Author Year, Country	N	Topical Treatment Groups	Setting	Aural Toilet	Systematic Review(s)
Arnes 1993, Norway	30	Cipro vs oxytet/polymyx/HC	S	No	M, R
Cannon 1967, USA	40	Neo/methylpred vs placebo	S	Yes	R
Cannon 1970, USA	43	Acetic/glyceryl vs placebo	S	Yes	R
Clayton 1990, UK	66	Alum-acetate vs gentamicin	S	No	R
Drehobl 2008, USA	630	Cipro vs polymyx/neo/HC	NS	NS	M
Emgard 2005, Sweden	51	Betamethasone vs oxytet/polymyx/HC	S	No	K, R
Freedman 1978, USA	91	Neo/colistin/HC vs placebo	S	Wick	K, R
Goldenberg 2002, Israel	120	Cipro vs tobramycin	S	No	M, R
Gydé 1982,	55	Gentamicin vs colistin/neo/HC	S	Yes	K
Johnston 2006, UK	109	Acetic vs acetic/neo/dex (spray)	S	Yes	K
Jones 1997, USA	601	Oflox vs neo/polymyx/HC	P	No	K, M, R
Kime 1978, USA	102	Acetic/HC vs neo/colistin/HC	NS	Wick	M, R
Lambert 1981, Cyprus	126	Alum-acetate vs neo/polymyx/HC	P	Yes	R
Masood 2008, UK	64	Glycerine vs. triamcin/neo/nystatin/gramicidin	S	Wick	K
Mösges 2007, Germany	152	Polymyx/bacitracin vs polymyx/bacitracin/HC	S	Wick	K
Mösges 2008, Germany	338	Polymx/neo vs polymyx/neo/dex	S	NS	K
Neher 2004, Austria	50	NCT vs neo/polymyx/HC	S	Wick	K, R
Olivera 2004, Argentina	33	Cipro vs cipro/glycerin	NS	NS	K
Ordonez 1978, USA	181	Acetic/HC vs neo/polymyx/HC	NS	Yes	R
Pistorius 1999, USA	842	Cipro vs cipro/HC vs neo/polymyx/HC	P, S	Yes	M, R
Psifidis 2005, Greece	91	Cipro vs cipro/dex vs neo/polymyx/HC	P, S	No	R
Roland 2004, USA	468	Cipro/dex vs neo/polymyx/HC	S	Yes	K, R
Roland 2007, USA	524	Cipro/dex vs neo/polymyx/HC	NS	NS	K
Roland 2008, USA	206	Cipro/HC vs neo/polymyx/HC + amoxicillin PO	NS	Yes	K
Ruth 1990, Sweden	53	HC butyrate vs oxytet/polymyx/HC	P, S	No	M, R
Sabater 1996, Spain	54	Cipro vs gentamicin	S	No	K, R
Schwartz 2006, USA	278	Oflox vs polymyx/neo/HC	P	NS	M, K
Slack 1987, UK	28	Boric/ethyl vs neo/polymyx/HC	S	Yes	K, R
Tsikoudas 2002, UK	39	Betamethasone vs betamethasone/neo	S	Yes	K, R
van Balen 2003, Netherlands	213	Acetic vs acetic/triamcin vs neo/polymyx/dex	P	Yes	K, M, R
Wadsten 1985, Sweden	64	Framycetin/gramicidin/dex vs oxytet/polymyx/HC	S	Yes	K, M

Abbreviations: acetic, acetic acid 2%; alum-acetate, aluminum acetate 8%; boric, boric acid 4%; cipro, ciprofloxacin; dex, dexamethasone; ethyl, ethyl alcohol 25%; glyceryl, glyceryl acetate 88%; HC, hydrocortisone; K, Kaushik 2010<sup>10</sup>; M, Mosges 2011<sup>129</sup>; methylpred, methylprednisolone; NCT, N-chlorotaurine (antiseptic); neo, neomycin; NS, not specified; oflox, ofloxacin; oxytet, oxytetracycline; P, primary care; PO, per oral; polymyx, polymyxin B; R, Rosenfeld 2006<sup>46</sup>; S, specialty practice; triamcin, triamcinolone.

alone. Regardless of topical agent used, about 65% to 90% of patients had clinical resolution within 7 to 10 days. Kaushik and coworkers<sup>110</sup> reached the same conclusion in their more recent Cochrane review, which included 7 newer trials with more than 1600 patients. In contrast, Mösges and colleagues<sup>129</sup> found superior clinical cure rates for topical quinolones versus other antibiotic-steroid combination drugs (odds ratio, 1.29; 95% CI, 1.06-1.57). However, the validity of this finding must take into consideration industry funding, substantial heterogeneity in the pooled analysis, and the possibility of a trivial effect size as suggested by the lower bound of the 95% CI (near unity). Furthermore, the superiority of quinolones found in the network meta-analysis was no longer significant in the direct comparisons.

Topical treatment with a quinolone-containing otic drop resulted in improved rates of bacteriologic cure in 2 meta-analyses. Rosenfeld and colleagues<sup>46</sup> found that 87% of patients with AOE have bacteriologic cure after nonquinolone therapy, with an 8% absolute increase when a quinolone antibiotic is used. The clinical significance of this modest effect (NNT of 12 patients) is reduced when considering that persistent bacteria in the ear canal after treatment does not necessarily imply persistent AOE symptoms. Mösges and colleagues<sup>129</sup> also found a higher bacteriologic cure rate when quinolones were used (odds ratio, 1.44; 95% CI, 1.03-2.02). The validity of this finding, however, must again take into consideration industry funding, substantial heterogeneity in the pooled analysis, and possibility of a trivial effect size as suggested by the lower bound of the 95% CI (near unity). Generalizability of bacteriologic results is further limited because not all patients had positive cultures before treatment and posttreatment cultures were not always obtained for those who were initially positive.

### Adverse Events, Adherence to Therapy, and Cost

The lack of differences in efficacy among most topical antimicrobial and steroid preparations suggests that patient preference and clinician experience are important aspects in selecting therapy. Cost, adherence to therapy, and adverse effects must also be considered.

Only a few studies report detailed information on adverse events, showing an overall low incidence and comparable rates among treatment groups.<sup>46,110</sup> The most common problems are pruritus (about 5% to 7%) and site reaction (4% to 5%); other events with an incidence less than 2% include rash, discomfort, otalgia, dizziness, vertigo, superinfection, and reduced hearing. None of the randomized trials reported otomycosis after topical antibiotics, although otomycosis has been described anecdotally following topical ofloxacin therapy for AOE.<sup>131</sup> There have been no additional published reports of otomycosis associated with topical quinolone use (through January 2013).

Contact dermatitis is a potential sequela of topical antimicrobial or steroid therapy but is rare after a single course of therapy for diffuse AOE. Two meta-analyses have compared a quinolone drop versus neomycin-polymyxin B-hydrocortisone

drop for diffuse AOE, with no significant difference in adverse events individually or when combined.<sup>46,110</sup> Conversely, about 30% to 60% of patients with chronic or eczematous external otitis develop a contact dermatitis, most often to aminoglycosides such as neomycin and framycetin.<sup>62,131-135</sup> No studies are limited specifically to patients with recurrent AOE, chronic external otitis, or eczematous external otitis, but it would appear prudent to avoid using aminoglycoside drops in these populations.

Remaining factors to consider when prescribing topical therapy include adherence to therapy and cost. Adherence to therapy and patient satisfaction are highest when drops are easy to administer,<sup>41</sup> which would entail a less frequent dosing schedule, shorter duration of therapy, or both. There are no comparative studies, but drops administered 4 times daily (eg, neomycin, polymyxin, hydrocortisone) may be less acceptable to some patients. Cost varies widely among available otic preparations (**Table 6**), ranging from a few dollars for antiseptics or generic products (eg, neomycin, polymyxin B, hydrocortisone) to more than \$100 for quinolones, with or without a steroid.

Dosing schedules for AOE have not been studied systematically, but available data suggest that, at least with quinolone drops (and perhaps also with the other concentration-dependent drugs such as the aminoglycosides), a twice-daily dosing regimen is adequate. One open-label study showed good clinical outcomes when ofloxacin was given once daily.<sup>136</sup> The optimal duration of therapy has not been determined and varies from a few days up to several weeks in published trials. More recent trials recommend 7 to 10 days of topical therapy.

### Patient Counseling

Patient education is important to maximize adherence to therapy when eardrops are prescribed as initial therapy for AOE. **Table 8** summarizes frequently asked questions from patients and provides suggested responses for counseling. Clinicians may distribute this table as stands or modify it to suit their needs. Additional patient instructions regarding the specific technique for administering eardrops are provided in the subsequent section of this guideline.

Clinicians should advise patients with AOE to resist manipulating the ear to minimize trauma and should discuss issues pertaining to water restrictions during treatment. Inserting earplugs or cotton (with petroleum jelly) prior to showering or swimming can reduce the introduction of moisture into the ear. The external auditory canal can be dried after swimming or bathing with a hair dryer on the lowest heat setting.

Patients with AOE should preferably abstain from water sports for 7 to 10 days during treatment. Entering a swimming pool, as long as prolonged submersion is avoided, can be allowed in mild cases. Competitive swimmers sometimes return to competition after 2 to 3 days after completing treatment or, if using well-fitting earplugs, after pain resolution.<sup>37,137,138</sup> Patients with hearing aids or ear phones, which enter the ear canal, should limit insertion until pain and discharge (if present) have subsided.

**Table 8.** Patient information for topical therapy of acute otitis externa (AOE).

Frequently Asked Question	Answer
Are eardrops alone sufficient to treat my infection or do I also need to take an antibiotic by mouth?	Eardrops alone are the most effective treatment for AOE and may contain antibiotics, antiseptics, steroids, or a combination. Antibiotics taken by mouth do not kill most germs that cause AOE and should be used only when infection spreads beyond the ear canal, eardrops cannot get into the ear, or the immune system is weak.
Which eardrop is best for treating my ear infection?	All eardrops approved for treating AOE ( <b>Table 5</b> ) are highly effective, with no consistent advantage shown for any one specific drug.
If all eardrops are equally effective, why do doctors prescribe different ones?	Your doctor will discuss with you the reasoning behind his or her eardrop recommendation, but some of the factors considered include cost, dosing frequency, status of the eardrum, and the doctor's experience. Your opinion and preferences should also factor into this decision.
Is there anything I should be sure to tell my doctor that might help in deciding which eardrop is best?	Let your doctor know if you had any prior ear surgery, if there is an opening (hole or perforation) of the eardrum, or if an ear tube is in place. If 1 or more of these conditions apply, then your doctor will need to use an eardrop that is approved for use in the middle ear, just in case some of it gets past the eardrum. Also let your doctor know if you have recently used other ear products or medications or if you have had a reaction in the past to a particular eardrop or antibiotic. Last, tell your doctor if you have, or are suspected to have, diabetes, since this could alter management.
Once I start using the eardrops, how long should it take until I feel better?	Most people feel better within 48 to 72 hours and have minimal or no symptoms by 7 days. Notify your doctor if your pain or other symptoms fail to respond within this time frame.
If it usually takes at least 48 hours to feel better from the eardrops, what should I do for earlier relief?	Pain medicine is especially important to use for relief in the first few days, until the eardrops begin working. Discuss with your doctor which pain medicines are best for you. Pain-relieving (anesthetic) eardrops are not recommended because they are not intended for use during an active ear canal infection and can mask symptoms of a delayed response to therapy.
For how long will I need to use the eardrops?	Eardrops should be used for at least 7 days, even if you feel better sooner, to prevent relapse of infection. If symptoms persist beyond 7 days, you should notify your doctor and continue the drops until the symptoms resolve for a maximum of 7 additional days.
Are there any activity restrictions or special precautions that will help my ear recover faster?	Avoid scratching or touching the ear, and do not insert anything into the ear canal, including cotton-tipped swabs. Cover the opening of ear canal with an earplug or cotton (with petroleum jelly) prior to showering or hair washing to minimize water entry. Check with your doctor regarding swimming or other water activities that may take place during, or soon after, your infection.
Do eardrops have side effects that I should be aware of?	Eardrops are, in general, very safe and well tolerated. Some people report local rash, itching, irritation, or discomfort, but it is rarely bad enough to require stopping the medication. If you taste the eardrops, it means there is likely a hole or perforation of the eardrum, so inform your doctor (if you have not already done so). Also call your doctor if the drops become painful or you develop unexpected symptoms.

### Complementary and Alternative Therapies

There are no data regarding the efficacy of complementary and alternative therapies for AOE. Isopropyl ("rubbing") alcohol, as well as 5% acetic acid (white vinegar) mixed with equal parts of isopropyl alcohol or water, are time honored "home remedies" but have never been formally evaluated in clinical trials. The similarity of these preparations to some antiseptic or acidifying agents that have been studied suggests that they may be effective. Although tea tree oil has been found to be effective in vitro against 71% of organisms cultured from 52 patients with AOE,<sup>139</sup> *Pseudomonas* was resistant in 75% of cases, and no controlled efficacy trials evaluating this form of therapy have been described.

Ear candles should never be used in treating AOE. Ear candles have never been shown to be efficacious for AOE but have been shown to produce harm.<sup>140</sup> Obstruction of the ear canal with paraffin and associated hearing loss and perforation of the tympanic membrane have been reported.<sup>141</sup> Since the initial publication of this guideline in 2006, there have been no studies published to

suggest a role for ear candles in managing AOE, but there has been 1 new report of hearing loss caused by candling.<sup>142</sup>

**STATEMENT 6. DRUG DELIVERY:** The clinician should enhance the delivery of topical drops by informing the patient how to administer topical drops and by performing aural toilet, placing a wick, or both, when the ear canal is obstructed. *Recommendation based on observational studies with a preponderance of benefit over harm.*

### Action Statement Profile

- Aggregate evidence quality: Grade C, observational studies and D, first principles
- Level of confidence in evidence: High
- Benefit: Improved adherence to therapy and drug delivery
- Risks, harms, costs: Pain and local trauma caused by inappropriate aural toilet or wick insertion; direct cost of wick (inexpensive)

**Table 9.** Instructions for patients.

- If possible, get someone to put the drops in the ear canal for you.
- Lie down with the affected ear up. Put enough drops in the ear canal to fill it up.
- Once the drops are in place, stay in this position for 3 to 5 minutes. Use a timer to help measure the time. It is important to allow adequate time for the drops to penetrate into the ear canal.
- A gentle to-and-fro movement of the ear will sometimes help in getting the drops to their intended destination. An alternate method is to press with an in/out movement on the small piece of cartilage (tragus) in front of the ear.
- You may then get up and resume your normal activities. Wipe off any excess drops.
- Keeping the ear dry is generally a good idea while using ear drops.
- Try not to clean the ear yourself as the ear is very tender and you could possibly damage the ear canal or even the eardrum.
- If the drops do not easily run into the ear canal, you may need to have the ear canal cleaned by your clinician or have a wick placed in the ear canal to help in getting the drops into the ear canal.
- If you do have a wick placed, it may fall out on its own. This is a good sign as it means the inflammation is clearing and the infection subsiding.
- Do not remove the wick yourself unless instructed to do so.

- Benefits-harms assessment: Preponderance of benefit over harm
- Value judgments: Despite an absence of RCTs demonstrating a benefit of aural toilet, the guideline development group agreed that cleaning was appropriate, when necessary, to improve penetration of the drops into the ear canal
- Intentional vagueness: None
- Role of patient preferences: Choice of self-administering drops versus using assistant
- Exceptions: None
- Policy level: Recommendation
- Differences of opinion: None

### Supporting Text

The purpose of this statement is to maximize the efficacy of topical therapy by ensuring that it penetrates the ear canal and reaches the site of infection. To achieve this goal, it is important that the clinician inform patients how to administer ear drops and advise them that they may need to have the ear canal cleaned if it is obstructed by debris (**Table 9**).

For topical treatment to be effective, the drug must be delivered to the infected tissues. While most patients with uncomplicated AOE will require only topical medication, for some patients additional management is needed to ensure appropriate drug delivery. Ensuring adequate delivery of the topical medication may require removing a foreign body, performing aural toilet to remove obstructing debris, placing a wick to permit drug delivery through the length of the ear canal, or all three.

Drug delivery may be impaired by poor adherence to therapy, poor application (ie, “missing” the ear canal), debris filling the canal, or edema closing the canal. Poor adherence to therapy and ineffective administration of topical medication must be dealt with by providing clear instructions. Self-administration of eardrops is difficult because it must be done by feel. Only 40% of patients who self-medicate do so appropriately during the first 3 days,<sup>143</sup> often tending to undermedicate. Adherence to therapy increases significantly when someone other than the patient applies the drops,<sup>144</sup> making this the preferred method of administration when feasible.

### Administering Otological Drops

Otological drops should be applied with the patient lying down and the affected ear upward. Drop should be run along the side of the canal until it is filled. The amount required will vary with the age and size of the patient. Gentle to-and-fro movement of the pinna is often necessary to eliminate trapped air and to ensure filling, particularly when a viscous solution is used. An alternative method is that of tragal pumping to aid in getting the drops into the ear canal. The patient should remain in this position for about 3 to 5 minutes. Use of a timer to mark the minutes is often helpful to facilitate the cooperation of young children. After placing drops, the canal is best left open to dry and to avoid trapping moisture and infected debris.

The ear canal should be cleared of inflammatory debris, obstructing cerumen, or any foreign object. There are no randomized studies of the use of aural toilet in AOE, but some investigators have proposed that aural toilet by itself (without antimicrobials) is therapeutic.<sup>122</sup> Aural toilet may be performed by the clinician with a gentle lavage using body-temperature water, saline solution, or hydrogen peroxide. Alternative methods of aural toilet include physically removing the obstructing debris with suction or dry mop (blotting with cotton tipped applicator). Adequate visualization for suctioning may be facilitated by using an otoscope with an open head or a binocular otologic microscope, which may require referral to a facility with the appropriate equipment to do so.

There are no randomized trials that address the safety of aural lavage in diabetic patients or immunocompromised patients with AOE. Lavage of the ear canal for cerumen impaction in elderly or diabetic patients, however, has been implicated as a contributing factor in malignant otitis externa.<sup>145-147</sup> The pathophysiology of malignant (necrotizing) otitis externa is poorly understood, but irrigation of the ear canal with tap water is a potential iatrogenic factor.<sup>81</sup> Patients with risk factors such as diabetes or immunocompromised state, as well as those with established malignant otitis externa, may require atraumatic cleaning with aural suctioning under microscopic guidance.

### Wicks to Promote Drug Delivery

Clinicians may place a wick in the ear canal if there is edema preventing drop entry<sup>118</sup> or if most of the tympanic membrane cannot be visualized.<sup>100</sup> The wick should preferably be made of compressed cellulose because it expands when exposed to moisture, facilitating drug delivery and reducing ear canal edema. Alternatively, ribbon gauze can be used.<sup>148</sup> Once a dry wick is placed in the ear canal, some experts recommend moistening and thus expanding the wick with an aqueous solution (water, saline, aluminum acetate) before the first application of an otic suspension or a nonaqueous viscous medication (for better penetration). Aqueous solutions, however, can be directly applied to expand a dry wick. A wick should not be made of a simple cotton ball since the cotton can fall apart and be retained in the ear canal.

Many treatment studies uniformly use a wick to improve drug delivery (**Table 7**), but there are no trials of wick efficacy. Consequently, the benefit of a wick is questioned by some clinicians, especially in managing uncomplicated AOE. However, following first principles, should anatomy (narrow or edematous canal) make delivery of the topical medicine problematic, the use of a wick seems prudent. A wick is unnecessary once the ear canal edema subsides, which may occur within 24 hours<sup>53</sup> or a few days of topical therapy. The wick may fall out spontaneously, may be removed by the patient if so instructed by the clinician, or may be removed by a clinician at a scheduled follow-up visit. The addition of systemic antibiotics may be considered in cases with severe external auditory canal edema in which adequate aural toilet, the placement of a wick, or both, is not possible or practical.

**STATEMENT 7. NONINTACT TYMPANIC MEMBRANE: When the patient has a known or suspected perforation of the tympanic membrane, including a tympanostomy tube, the clinician should prescribe a non-ototoxic topical preparation.** *Recommendation based on reasoning from first principles and on exceptional circumstances in which validating studies cannot be performed and there is a preponderance of benefit over harm.*

#### Action Statement Profile

- Aggregate evidence quality: Grade D, reasoning from first principles, and Grade X, exceptional situations in which validating studies cannot be performed
- Level of confidence in evidence: Moderate, because of extrapolation of data from animal studies and little direct evidence in patients with AOE
- Benefit: Reduce the possibility of hearing loss and balance disturbance
- Risk, harm, cost: Eardrops without ototoxicity may be more costly
- Benefits-harms assessment: Preponderance of benefit over harm
- Value judgments: Importance of avoiding iatrogenic hearing loss from a potentially ototoxic topical

preparation when non-ototoxic alternatives are available; placing safety above direct cost

- Intentional vagueness: None
- Role of patient preferences: None
- Exceptions: None
- Policy level: Recommendation
- Differences of opinion: None

#### Supporting Text

The purpose of this statement is to apprise clinicians of the importance of obtaining a history of tympanic membrane perforation and/or tympanostomy tube placement. Clinicians are also advised to carefully evaluate the patient for presence of nonintact tympanic membrane either due to tympanostomy tube or tympanic membrane perforation.

Special consideration must be given to the individual with known or suspected perforation of the tympanic membrane or history of tympanostomy tubes. The external auditory canal, including the tympanic membrane, is lined with keratinizing squamous epithelium, but the middle ear is lined with mucosa. This mucosa forms the lateral portion of the round window membrane, which separates the middle-ear space from the fluids of the inner ear. Antibiotics placed into the middle ear can cross the round window membrane and reach the inner ear. Ototoxic antibiotics delivered into the middle ear space of experimental animals, including primates, consistently cause severe hearing loss and ototoxic injury to the organ of Corti.<sup>149-151</sup>

Clinical experience with topical ototoxic antibiotics in patients with tympanic membrane perforation suggests that hearing loss does not occur after a single short course of therapy<sup>152,153</sup>; however, severe hearing loss has been observed after prolonged or repetitive administration of topical drops.<sup>153-155</sup> The validity of these and other clinical reports is limited by retrospective design, incomplete follow-up, and inconsistent audiologic testing. Given the ethical limitations of randomizing patients with a nonintact tympanic membrane to an ototoxic drug, it is unlikely that definitive evidence (validating studies) is forthcoming.

Careful examination of the tympanic membrane will reveal a perforation in some cases of AOE. The ear canal and auricle may be so tender or swollen, however, that the tympanic membrane cannot be visualized without undue pain or discomfort. If swelling or discomfort do not preclude its use, tympanometry can sometimes be helpful in establishing the presence of an intact tympanic membrane. When tympanometry shows a normal type A tracing (peaked curve with normal pressure), the tympanic membrane is assumed to be intact, unless there is a reason to believe it is not (eg, an indwelling tympanostomy tube).

A perforation may be suspected if the patient has a positive prior history, unless the most recent examination preceding the episode of AOE has verified that the perforation has closed. Children with tympanostomy tubes are a special instance within this category. Most tympanostomy tubes remain in the tympanic membrane for at least 6 to 12 months; therefore, a patent tube should be assumed to be present within the tympanic membrane of any individual who had it placed less than a year ago,

unless tube extrusion and subsequent closure of the tympanic membrane have been documented. Children with tubes inserted more than 1 year ago should also have the tympanic membrane carefully assessed, since in some cases the tube may remain functional for 3 years or longer. Individuals who taste substances, presumably medicines, placed into their ear or who can expel air out of their ear canal by pinched nose blowing can be assumed to have a perforation.

If the tympanic membrane is known or suspected to be nonintact, topical drops that contain alcohol, have a low pH (most acidifying/antiseptic agents), or both should be avoided because of pain and potential ototoxicity. Substances with ototoxic potential (eg, aminoglycosides, 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.<sup>156</sup> In the United Kingdom, the Committee for Safety of Medicines and the Medicines Control Agency cautions practitioners that the potential for ototoxicity exists when aminoglycoside eardrops are prescribed for patients with ear drum perforations.<sup>157</sup>

The only topical antimicrobials approved by the FDA (December 2005) for middle ear use are quinolone drops. Quinolone otic drops have a superior safety profile and a broad antimicrobial spectrum, some are available as low cost generic preparations, and their convenient dosing schedule is tolerated by most patients.<sup>158</sup> Moreover, there is an explicit warning by the manufacturer that neomycin/polymyxin B/hydrocortisone not be used with a nonintact tympanic membrane:

**WARNINGS.** Neomycin can induce permanent sensorineural hearing loss due to cochlear damage, mainly destruction of hair cells in the organ of Corti. The risk is greater with prolonged use. Therapy should be limited to 10 consecutive days (see PRECAUTIONS-General). Patients being treated with eardrops containing neomycin should be under close clinical observation. **CORTISPORIN<sup>®</sup> Otic Suspension should not be used in any patient with a perforated tympanic membrane.**<sup>159</sup> (emphasis added)

AOE can be secondary to AOM. For example, mucopurulent exudate from the middle ear flowing through an acute tympanic membrane perforation can infect the tissues of the ear canal, creating a secondary otitis externa. Less commonly, AOE will develop independently in an ear with AOM. When AOM exists together with AOE, the AOM should be treated as an independent disease process according to the current guidelines.<sup>54</sup>

**STATEMENT 8. OUTCOME ASSESSMENT: The clinician should reassess the patient who fails to respond to the initial therapeutic option within 48 to 72 hours to confirm the diagnosis of diffuse AOE and to exclude other causes of illness. *Recommendation based on observational studies and a preponderance of benefit over harm.***

### Action Statement Profile

- Aggregate evidence quality: Grade C, outcomes from individual treatment arms of randomized controlled trials of efficacy of topical therapy for AOE
- Level of confidence in evidence: Medium, because most randomized trials have been conducted in specialist settings and the generalizability to primary care settings is unknown
- Benefit: Identify misdiagnosis and potential complications from delayed management; reduce pain
- Risks, harms, costs: Cost of reevaluation by clinician
- Benefits-harms assessment: Preponderance of benefit over harm
- Value judgments: None
- Intentional vagueness: Time frame of 48 to 72 hours is specified since there are no data to substantiate a more precise estimate of time to improvement
- Role of patient preferences: None
- Exceptions: None
- Policy level: Recommendation
- Differences of opinion: None

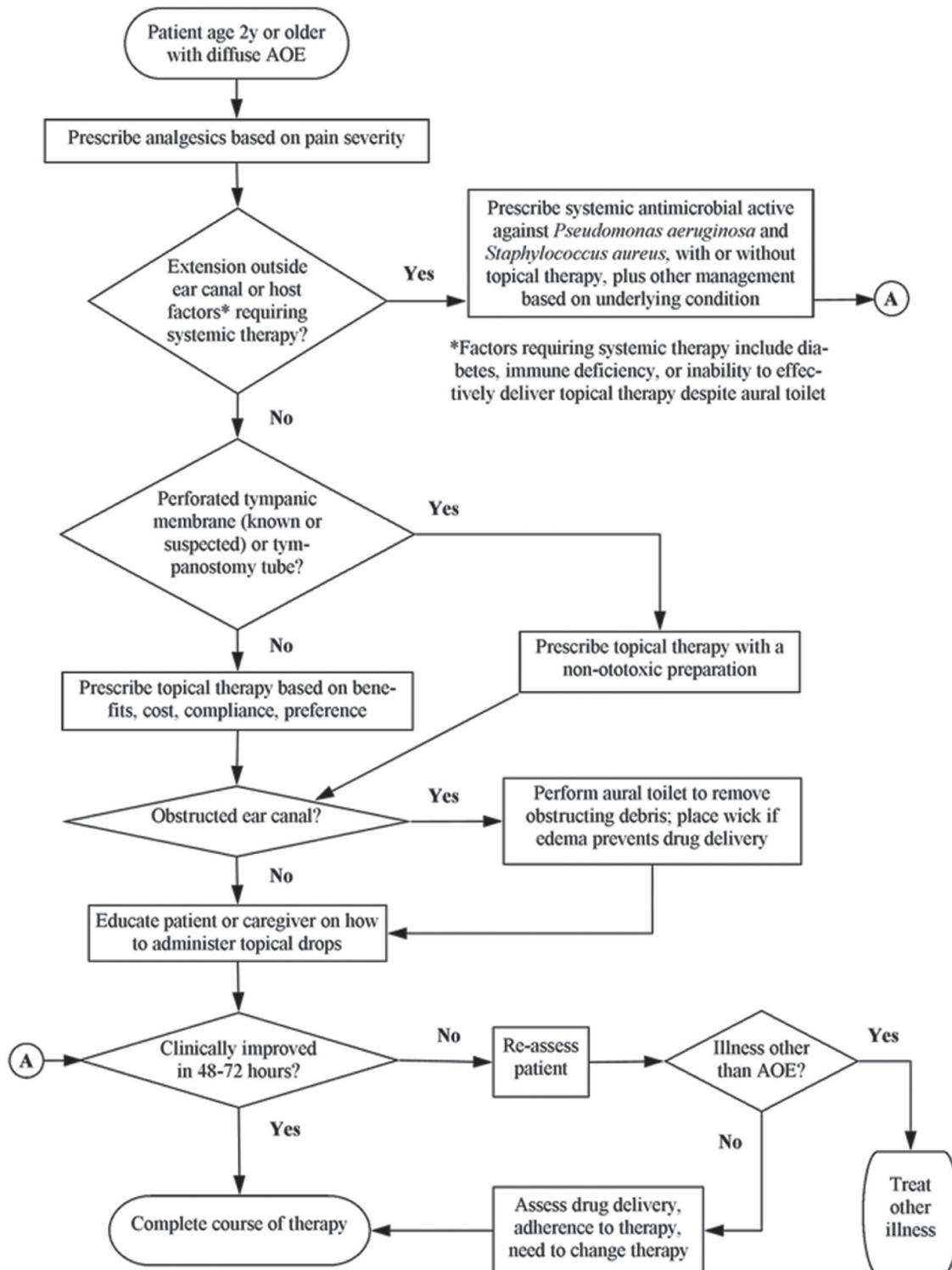
### Supporting Text

The purpose of this statement is to ensure that patients without an appropriate response to treatment are reassessed to confirm the original diagnosis and to institute additional therapy, such as aural toilet, as needed.

### Assessing Initial Treatment Response

Appropriate treatment of uncomplicated AOE should be followed by symptom improvement (otalgia, itching, fullness) within 48 to 72 hours (**Figure 1**), although symptom resolution may take up to 2 weeks. In clinical trials that evaluate patient outcomes of topical treatment using symptom diaries, significant decreases in patient-reported ear pain are generally seen after 1 day of treatment, and most pain resolves within 4 to 7 days.<sup>100,123,136</sup> One prospective cohort study<sup>41</sup> that explored the relationship of patient-reported satisfaction with clinical outcomes showed that symptom relief was the factor most highly associated with patient satisfaction.

A Cochrane review in 2010 evaluated these same data and recommended follow-up in 2 weeks if any symptoms persist at that point.<sup>110</sup> That review focused on complete resolution of symptoms (defining treatment failure), which could take up to 2 weeks to determine as some patients who ultimately respond to therapy will still have symptoms beyond 1 week. The symptoms diary data in the 2003 van Balen study showed, however, that most patients show rapid improvement (within 72 hours) even if complete resolution may take a week or more.<sup>100</sup> This panel found the data compelling that improvement should occur rapidly and felt that reassessment is warranted for those patients without signs of early improvement. Early reassessment for those failing to show signs of improvement affords an opportunity to reassess the ear to determine the need for aural toilet or wicking, reconsider the diagnosis, and reevaluate need for pain management even if no change in prescribed therapy is indicated



**Figure 1.** Flow chart for managing acute otitis externa.

at that time. Follow-up is also warranted if symptoms fail to resolve completely by 2 weeks after initiation of therapy.

Initial treatment failure of diffuse AOE may be caused by an obstructed ear canal, poor adherence to therapy, misdiagnosis, microbiologic factors, host factors, or contact sensitivity to eardrops. If topical antimicrobial therapy was prescribed,

the clinician should reassess the patency of the ear canal to ensure that edema or debris are not impeding drug delivery. Any obstruction should be addressed with aural toilet, wick placement, or both (see Statement 7), or, if the obstruction cannot be relieved, systemic therapy is begun with an oral antibiotic that covers *P aeruginosa* and *S aureus*.

The clinician should also assess adherence with therapy, including successful physical placement of topical medication into the ear canal by the patient or proxy. Patients tend to over-administer ear drops when pain is greatest and to underadminister as symptoms resolve.<sup>41,143</sup>

### Excluding Other Causes of Illness

Alternative causes of ear pain and associated otorrhea should be considered if the patient fails to respond to treatment, although the need for specialist referral is uncommon (3%) when AOE is treated appropriately.<sup>160</sup> Fungi may be present as a co-pathogen in some patients with AOE and can cause persistent infection from overgrowth in the ear canal if the flora is altered after topical antibacterial therapy.<sup>3</sup> A culture of the ear canal can identify fungi, resistant bacteria, or unusual causes of infection that require targeted topical or systemic therapy.

Initial treatment failures that are not related to drug delivery or microbiologic factors may reflect comorbidity or misdiagnosis.<sup>39,161</sup> Persistent symptoms can be caused by dermatologic disorders that include dermatitis (atopic, seborrheic, or contact), psoriasis, dermatomycosis, or acne that involves the external auditory canal. The ear canal and tympanic membrane should be reexamined to detect an unrecognized foreign body, perforated tympanic membrane, or middle ear disease. Patients with severe refractory symptoms should be reassessed for malignant otitis externa or carcinoma of the external auditory canal, especially if granulation tissue is present.<sup>53,162</sup>

Allergic contact dermatitis of the external auditory canal can result in refractory AOE in some patients, especially in cases with prolonged use of antimicrobial otic drops. In susceptible individuals with a predisposition to allergy, an initial sensitization phase occurs over a period of 10 to 14 days. Subsequent delayed-type hypersensitivity reactions to topical antiseptic otic preparations result in erythema, pruritus, skin inflammation, edema of the external auditory canal, and persistent otorrhea; blisters and vesicles may be present in severe cases. This allergic reaction can extend beyond the ear canal to involve the skin around the ear and the neck wherever contact is made. After a patient has been sensitized, subsequent exposure to the antigen leads to a more pronounced inflammatory response that begins shortly after reexposure.

Neomycin-containing eardrops are most commonly noted to cause contact sensitivity, which has a 13% to 30% prevalence on patch testing of patients with chronic otitis externa.<sup>161,163,164</sup> Contact sensitivity of the ear canal may also result from other topical antimicrobials (bacitracin, quinolones, gentian violet, polymyxin B sulfate), topical steroid preparations (hydrocortisone, triamcinolone), or topical anesthetics (benzocaine alone or combined with dibucaine and tetracaine [caine mix]). Preservatives and vehicles in topical otic medications associated with at least a 1% incidence of contact sensitivity include propylene glycol, thimerosal, benzalkonium chloride, benzethonium chloride, and methyl-p-oxybenzoate. Fragrance additives also commonly cause allergic contact dermatitis. Lastly, contact sensitivity may be caused by silicone ear plugs or by

hearing aid molds that contain silicone or methyl-methacrylate.<sup>161,163,164</sup> In patients with suspected allergic contact dermatitis, patch testing to an appropriate panel of antigens is useful in identifying contributing agents.

### Implementation Considerations

The complete guideline is published as a supplement to *Otolaryngology Head & Neck Surgery* to facilitate reference and distribution. A full-text version of the guideline will also be accessible free of charge at the [www.entnet.org](http://www.entnet.org), the AAO-HNSF website. A podcast discussing the updated guideline and its key action statements will also be made available. The guideline will be presented to members at AAO-HNSF Annual Meeting & OTO EXPO as a miniseminar following publication. Existing brochures and publications by the AAO-HNSF will be updated to reflect the guideline recommendations.

Anticipated barriers to applying the recommendations in the guideline include (1) difficulty of changing ingrained clinician habits toward prescribing ineffective systemic therapy for AOE, (2) inability or unwillingness of some clinicians to perform aural toilet or insert a wick into the ear canal, and (3) cost of some topical medications, especially the quinolone products recommended for use with a nonintact tympanic membrane. The first two can be addressed with educational events and workshops at continuing medical education events. The issue of cost should become less problematic in the next few years as additional generic versions of the quinolone otic drops become available. For example, subsequent to the first publication of this guideline in 2006, a generic version of ofloxacin otic solution has become available at reasonable cost.

The impact of the guideline on clinical practice will be assessed by monitoring physician performance on the AOE quality measures included within the Centers for Medicare & Medicaid Services (CMS) Physician Quality Reporting System (PQRS). The AOE quality measures were developed by the American Medical Association's convened Physician Consortium for Performance Improvement (PCPI) in conjunction with the AAO-HNSF; two are available for PQRS reporting in 2013. The two measures assess the prescribing of systemic and topical antimicrobials. In addition, the AAO-HNSF will continue to promote adherence to the guideline's recommendations through its quality improvement activities. This includes participation in the ABIM Foundation's *Choosing Wisely*® campaign. The AAO-HNSF's first list of 5 things physicians and patients should question included an item to not prescribe systemic antimicrobials for diffuse, uncomplicated AOE (see Statement 4).<sup>165</sup>

### Research Needs

1. RCTs of absolute and comparative clinical efficacy of ototopical therapy of uncomplicated AOE in primary care settings, including the impact of aural toilet on outcomes
2. Clinical trials to determine the efficacy of topical steroids for relief of pain caused by AOE

3. Observational studies or clinical trials to determine if water precautions are necessary, or beneficial, during treatment of an active AOE episode
4. Observational studies or clinical trials to determine optimal time to discontinue water precautions for AOE
5. Increased ability to distinguish treatment failure from topical sensitivity when a patient with AOE fails to respond to topical therapy
6. High-quality randomized trials of comparative clinical efficacy for AOE that use an appropriate randomization scheme, use an explicit double-blind protocol, and fully describe dropouts and withdrawals
7. High-quality randomized trials assessing the benefit of systemic antimicrobial therapy versus topical therapy in patients stratified by severity of signs and symptoms
8. High-quality randomized trials of comparative clinical efficacy for AOE that provide clinical outcomes early in the course of therapy (eg, after 2-4 days of therapy) and compare time to symptom resolution in addition to categorical responses (eg, cure, improvement, failure) for specific days
9. Comparative clinical trials of “home therapies” (eg, vinegar, alcohol) versus antimicrobials for treating AOE
10. Define the optimal duration of topical therapy for AOE and the role of patient preferences
11. Define with greater precision the indications for aural toilet and wick placement
12. Determine the efficacy of aural toilet as an independent factor when treating AOE
13. Comparative clinical trials of wick versus no wick when administering topical therapy
14. Comparative clinical trials of suction or active debridement of the ear canal versus dry mopping
15. Define the best methods of teaching clinicians, especially those in primary care settings, how to safely and effectively perform aural toilet and wick insertion
16. Determine the optimal method to assess tympanic membrane integrity in patients with AOE (eg, what is the utility of tympanometry)
17. Development of medicated wicks that gradually release drug into the ear canal
18. Continued monitoring of bacteriology and antibiotic resistance patterns in AOE

## Disclaimer

This clinical practice guideline is provided for information and education purposes only. It is not intended as a sole source of guidance in managing patients with AOE. Rather, it is designed to assist clinicians by providing an evidence-based framework for decision-making strategies. This guideline is not intended to replace clinical judgment or establish a protocol for all individuals with this condition and may not provide the only appropriate approach to diagnosis and management.

As medical knowledge expands and technology advances, clinical indicators and guidelines are promoted as conditional and provisional proposals of what is recommended under specific conditions, but they are not absolute. Guidelines are not mandates; these do not and should not purport to be a legal standard of care. The responsible physician, in light of all the circumstances presented by the individual patient, must determine the appropriate treatment. Adherence to these guidelines will not ensure successful patient outcomes in every situation. The AAO-HNSF emphasizes that these clinical guidelines should not be deemed inclusive of all proper treatment decisions or methods of care nor exclusive of other treatment decisions or methods of care reasonably directed to obtaining the same results.

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## Disclosures

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