Agency for Healthcare Research and Quality

Evidence Report/Technology Assessment

Number 55

# Diagnosis, Natural History, and Late Effects of Otitis Media with Effusion

Summary

## Overview

This evidence-based report reviews the evidence on the natural history of otitis media with effusion (OME), the impact of otitis media on long-term speech and language development and on hearing, and the operating characteristics of various methods of diagnosing otitis media with effusion. OME is defined as "fluid in the middle ear without signs or symptoms of ear infection." The evidence compiled in this report is intended to aid clinicians, health care provider organizations, and others to develop clinical practice guidelines or medical review criteria for OME. The report will also identify areas for future research.

## Reporting the Evidence

Based on degree of importance (including level of controversy) and feasibility of answering the question, the Technical Expert Panel limited the scope of this evidence report to four key questions:

1) The natural history of otitis media with effusion (OME)?
2) The long-term effects of early-life otitis media, defined as positive otitis media history at less than three years of age, on speech and language development?
3) The long-term effects of early-life otitis media on hearing?
4) The operating characteristics of various methods of diagnosing otitis media with effusion?

## Methodology

A 12-member Technical Expert Panel that consisted of clinical experts, a consumer, and a representative of a managed care organization convened to:

- advise the project in the ranking of proposed key questions and influencing factors
- guide the development of the scope and definition of OME
- advise in development of the search strategy, and
- review and comment on the plan of analysis.

The Technical Expert Panel and project staff developed a literature search strategy. Project staff searched MEDLINE® (1966-January 2000), the Cochrane Library (through January 2000), and EMBASE (1980-January 2000). Additional articles were identified by review of reference lists in proceedings, published articles, reports, and guidelines.

The MEDLINE® search strategy used both controlled vocabulary MeSH® (Medical Subject Headings) terms and keywords to ensure that all relevant citations were retrieved. The strategy included search terms for otitis media with effusion combined with search terms for natural history, speech and language development, hearing, and diagnosis.

The otitis media module included *otitis media, otitis media with effusion, suppurative otitis media, allergic otitis media, fluid ear, glue ear, middle-ear effusion, mucoid otitis media, nonsuppurative otitis media, secretory otitis media, and serous otitis media.*

The natural history terms included *natural course, natural history, placebo, placebos, resolution, self-limited, self limiting, and untreated,* as well as a variety of terms for spontaneous resolution.

The speech and language module included *speech and language, speech and language disorders, child language, communication, communication*

*disorders, language development and tests, voice, and voice disorders.*

The hearing module included *hearing and hearing disorders, hearing aids and tests*, and the text word *hearing.*

The diagnosis module used *diagnosis and diagnostic techniques and procedures*, as well as the text words *audiometry, diagnosis, diagnostic, otoscopy, and tympanometry*.

Two physicians or one physician and one health services researcher independently screened all titles and/or abstracts for potential inclusion, evaluated the quality of the articles, and abstracted data from full-length articles onto pre-designed forms. The selection criteria included human studies that addressed a key question about OME in children. Excluded were case reports, editorials, letters, reviews, practice guidelines, non-English language publications, and studies on patients with immunodeficiency disorders or craniofacial anomalies, including cleft palate.

For the natural history question, we used only prospective cohort(s) studies on untreated subjects from which outcome data were abstractable for children up through age 12 years. For the speech and language and hearing questions, we used only prospective cohort studies that fulfilled the following criteria: the degree of OME was determined during the first three years of life, upper age limit was 22 years, the degree of OM was graded in some way, and the outcome was measured when the child was older than age three years. For the diagnostic methods question, we used only prospective studies on children up through 12 years of age that fulfilled four criteria: the diagnostic procedure of interest was performed within 24 hours of the reference standard, was not an algorithm or combination of multiple diagnostic procedures, used one of the acceptable reference standards specified in the scope, and produced abstractable data.

The first step of all analyses was to obtain a distribution of studies stratified by the population characteristics, type of outcome measures, and non-treatment factors. This step provided us with an overview of the emphasis of past research in this area and an opportunity to identify gaps and areas for future research.

In strata with more than three studies, we performed a meta-analysis for a pooled random effects estimate of an outcome with 95% confidence intervals. In addition to deriving the pooled estimate, we evaluated the heterogeneity of the study outcomes. For the evaluation of diagnostic methods, we estimated the sensitivity, specificity, and positive and negative predictive values for each diagnostic procedure compared to a particular reference standard with three or more studies.

This evidence report was reviewed by the Technical Expert Panel as well as an 18-member peer review panel that consisted of content experts, consumers, representatives of managed care organizations, an expert in pediatric pharmacology, and methodologists. All comments received from these individuals were reviewed and acted upon appropriately.

# Findings

## Natural History of OME

- No meta-analyses for children under three years of age were possible, because we could identify only two studies each for the under six months and the three-months-to-three-years age groups. For the over-three-years age group, two sets of meta-analyses showed that 22.5 to 42.7 percent of ears with OME cumulatively resolved over a period of three months, depending on the definition of OME resolution. These estimates must be viewed with caution due to the clinical heterogeneity evident in the data synthesized and due to the weaknesses of design or documentation of the study cohorts. In particular, in most cases investigators did not document whether subjects had received medical or surgical treatment during the course of the study that could affect OME outcome or how compliance with non-treatment was established. Of those investigators who reported how many children received treatment, the majority did not stratify their findings by treatment status.
- A few of the studies analyzed OME resolution by influencing factors such as gender, care at home versus daycare, season, side of affected ear, race or ethnicity, or diagnostic instrument. Because of the paucity of such studies, quantitative synthesis was not possible, and we refrain from drawing any conclusions regarding the effect of these influencing factors on resolution.
- As measured by scoring of documentation in the published articles, the quality of 28 cohort studies on natural history was generally poor.

- Half of the studies that attempted to study the natural history of OME did not control for or did not document control of interventions, either medical or surgical, that might affect OME outcome during the study period. The majority of these studies did not stratify findings by intervention status.
- The interval between examinations for OME in these studies ranged from one day to three years. For studies with long follow-up intervals, it was not possible to determine whether the presence of OME was due to persistence or recurrence. The criteria for follow-up varied among studies. Most studies continued follow-up for the duration of the study period regardless of the OME status at a particular exam, but four cohorts discontinued follow-up of individuals who had type A or normal tympanograms at any exam.

## Early-life OM and Long-term Speech and Language Development

- Studies that addressed the effects of early-life otitis media on long-term speech and language development among children differed considerably with respect to risk factors studied, type of outcome measured, method of measurement, unit of measurement, age at outcome determination, and study design.
- The meta-analyses that could be conducted on long-term expressive language, receptive language, and cognitive verbal intelligence showed no effect of early otitis media as measured during the first three years of life. These findings may not be generalizable, since five of the six cohorts that were included in these three meta-analyses focused primarily on children from specific ethnic/racial groups or from particular socioeconomic groups. Furthermore, the results of these studies cannot be applied to children with craniofacial defects, primary mucosal disorders, immunodeficiency disorders, genetic conditions, or pre-existing developmental disorders, because children with these conditions were excluded from this analysis. In addition, only one of the studies included in these meta-analyses focused solely on persistent bilateral otitis media as opposed to unspecified unilateral or bilateral otitis media.

## Early-life OM and Long-term Hearing

- Few studies on the effects of early-life otitis media on long-term hearing used a prospective cohort study design.
- Of the eight cohort studies analyzed, one set of four studies reported percentage of conductive hearing loss at six to ten years of age. For this analysis, the threshold for conductive hearing loss was defined as greater than or equal to 20 dB at any frequency, with or without treatment of otitis media.
- The pooled risk of conductive hearing loss at six to ten years among 346 children who had a positive history of early-life OM was 22 percent (95% CI: 7% to 36%). In contrast, the pooled risk of conductive hearing loss at six to ten years of age among 237 children with no history of early-life OM was 6 percent (95% CI: 1% to 12%). The pooled rate difference of conductive hearing loss at six to ten years of age between children with a positive OM history and those with a negative OM history was 11 percent (95% CI: 3% to 19%). Neither the studies pooled for the rate difference nor the studies pooled for the risk ratio showed significant heterogeneity in the outcomes.
- The findings were based on four homogeneous, though very different populations, one from Finland, another from Sweden, one primarily of American Indian children, and another primarily of Eskimo children. The four studies also differed on the definition and collection of OM history and on exclusion factors.
- We found insufficient data to assess the impact of early-life OM on permanent (sensorineural) hearing loss.

## Diagnostic Methods for OME

- Based on our evaluation of 52 diagnostic studies, we were able to assess the ability of the following methods to diagnose middle-ear effusion in OME at a single point in time: acoustic reflectometry at ≤5 or >5 reflective units (RU); pneumatic otoscopy; portable tympanometry; professional tympanometry using acoustic reflex at 500 or 1000 Hz; professional tympanometry using static compensated acoustic admittance at 0.1, 0.2, and 0.3; professional tympanometry using B curve as abnormal; and professional tympanometry using B

or C2 curves as abnormal. All comparisons used myringotomy as the reference standard.

- Among the eight diagnostic methods, the receiver-operator characteristic points (plotting sensitivity against 1 minus specificity) showed that pneumatic otoscopy was closest to the optimal operating point where both sensitivity and specificity would be 100%. However, tester qualifications were reported inconsistently, and training was not specified. The pooled sensitivity was 94 percent (95% CI: 91%, 96%) and the pooled specificity was 80 percent (95% CI: 75%, 86%). These findings were based on 2,694 children from seven studies that reported a pooled prevalence of OME of 63 percent (95% CI: 58%, 67%). The prevalence rate ranged from 56 percent to 71 percent, which indicated significant heterogeneity among outcomes ($p<0.001$).

## Limitations of the Literature

- **Natural History of OME:** Literature on the natural history of otitis media with effusion was difficult to interpret because of its generally poor quality, the lack of control for therapeutic interventions, the inability to distinguish persistent from recurrent OME due to the length of follow-up intervals, and the varied criteria for continued follow-up from exam to exam. Differing definitions of OME resolution and diagnostic methods made comparison difficult. Few studies considered the child or the episode as the unit of analysis, included younger children, or assessed types of OME other than newly diagnosed OME of unknown duration. In addition, few studies addressed the possible effects of influencing factors on OME resolution.
- **Early-life OM and Long-term Speech and Language Development:** The literature on the long-term effects of early-life otitis media on speech and language development diverged considerably with respect to methodology. As a result, findings could not be combined easily.
- **Early-life OM and Long-term Hearing:** Although the literature on the long-term effects of early-life otitis media on hearing was abundant, few studies used a prospective cohort study design. Because of the limited nature of this evidence and because the rate of intervention is highly dependent on the threshold hearing level adopted, the findings of this analysis should be applied with caution.
- **Diagnostic Methods for OME:** Nine comparisons of diagnostic methods enabled derivations of pooled estimates of diagnostic accuracy. However, more comparisons could not be made, including those that would have evaluated clinical signs and/or symptoms, air and/or bone threshold audiometry, binaural micro-tympanoscopy, and non-pneumatic otoscopy. Diagnostic methods that use algorithms or aggregated scorings are important but are not included in this evidence assessment.

## Future Research

Future research on the natural history of otitis media with effusion must focus on improvement of study quality and establishing the effect of OME on long-term outcomes such as speech, language, and hearing. In particular, control of therapeutic interventions during the study and the distinction between OME persistence and recurrence need to be addressed. Adopting a less restrictive definition of non-intervention might simplify the analysis of studies of the natural history of OME. In addition, researchers, in conjunction with clinicians, should agree upon standard procedures for follow-up, including intervals of follow-up, definition of OME resolution, and diagnostic methods, so that resolution rates are indeed comparable. Future research must consider the child as the unit of analysis, since the outcomes of ultimate interest, such as speech, language, and hearing, are functional requirements of a child, not an ear. More research is needed on the role of influencing factors on the natural history of OME, so that the clinician on a particular day in a particular setting can make a better decision when assessing a particular child with particular characteristics.

Evaluation of long-term effects of early-life otitis media on speech, language, or hearing requires a coordinated systematic approach that uses a rational conceptual framework. Such an approach should address the risk factors, interventions, and outcome measures in an integrated fashion. The definition, classification, and type and unit of measure should be developed by a team of experts with the goal of standardizing definitions and approaches. Literature on findings should report both univariate and multivariate findings to enhance understanding of the patient and study characteristics and to allow pooling of data. An

integrated approach is also important for the evaluation of diagnostic methods. Such an approach will provide guidance for future studies. Future studies of diagnostic assessments of OME also should consider cost-effectiveness analysis, which can take into account the variable proficiency of clinicians in performing pneumatic otoscopy as well as the consequences of testing and patient preferences. Cost-effectiveness analysis will lead to a more informed decision on the best diagnostic method for OME.

## Availability of Full Report

The full report from which this summary was taken was prepared for AHRQ by the Southern California Evidence-based Practice Center/RAND under contract No. 290-97-0001. It is expected to be available in summer 2002. When available, printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 1-800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 55, *Diagnosis, Natural History, and Late Effects of Otitis Media with Effusion* (AHRQ Publication No. 02-E026). Internet users will be able to access the report online through AHRQ's World Wide Web site www.ahrq.gov.

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