Chapter 5. Future Research

General Issues

The need for future research on otitis media with effusion (OME) and otitis media (OM) can be substantiated only by the demonstration of a negative effect of OM on important outcomes such as speech, language, and hearing. The available data do not provide such evidence in the case of speech and language and, suggest, at most, a possible effect of early-life OM on long-term hearing, based on evidence that may not be generalizable. Thus, future research must still establish the effect of early-life OM on speech, language, and hearing. Such future research will benefit by addressing the following general issues, which affect study quality and outcomes assessment. The definitions of OME and OM and of relevant interventions, influencing factors, and outcomes should be standardized.

A common, testable framework, with flexibility for competing hypotheses, that links predisposing factors to OME and OM and then OME or OM to outcomes such as long-term speech and language development and hearing, should be adopted. This framework should include hypotheses on the role of child characteristics, environmental and social influences such as socioeconomic status, and medical factors such as interventions, on outcomes.

Agreement on appropriate follow-up intervals to provide valid estimates of duration or frequency of OME and OM is needed to help in comparing results from different studies.

Additional areas where future research should focus include potential gaps in practice and newer outcome measures. Such outcome measures include general health status and quality issues such as satisfaction with treatment.

Natural History

Future research on the natural history of OME 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 intervention during the study and the distinction between OME persistence and recurrence need to be addressed. Considering the difficulties of conducting a natural history study on OME, a less restrictive definition of nonintervention might be considered. Even with a less restrictive definition of nonintervention, studies should consider presenting data that has been stratified by the level of intervention each child receives during the study period. For example, if a child is allowed to have antibiotics, the exact circumstances when antibiotics may be given should be determined a priori, the number of episodes of such antibiotic administration should be noted, and the outcome measures reported should be stratified by intervention level. However, with a less restrictive definition of nonintervention, the researcher runs the risk of conducting a study with little meaning or applicability to natural history.

Researchers and clinicians should agree upon standard procedures for follow-up, including intervals of follow-up, so that resolution rates are indeed comparable. As the study by Moller and Tos (1990) demonstrated, even daily exams did not necessarily lead to a greater distinction between persistence of OME and recurrence; thus, we do not expect this to be an easy issue to resolve. The issue of assessment of OME duration or recurrence is as important as the issue of diagnosis of OME at a single point in time.

Researchers need to agree upon a definition of OME resolution and the diagnostic methods with which to make that determination. The latter will require further research into the operating characteristics of OME diagnostic methods, as we have reported in this evidence report. Further enhancements in diagnostic methods must also be achieved. Although perhaps more relevant to studies on outcomes other than resolution, more research is needed that views the child as the unit of analysis, since the actual outcomes of concern, such as speech, language, and hearing, are functional requirements of a child, not an ear.

Further research on the role of influencing factors, such as socioeconomic status, on the natural history of OME may help the clinician in a particular setting make a better decision when assessing a child with particular characteristics. Among the influencing factors the technical expert panel thought were potentially important, the only factors addressed were age, gender, daycare setting, season, and racial/ethnic origin, and those were addressed by only a few studies. Study findings will be useful when they are generalizable, either because of their similarity to the population served by a particular clinician or because they address children with characteristics similar to a specific child the clinician is assessing. However, the issue of OME resolution is relevant only if OME has an impact on outcomes of relevance, such as long-term speech, language, or hearing.

Effects of Early-life OM on Long-term Speech and Language Development

For evaluation of long-term effects of early-life otitis media on speech and language development, a coordinated uniform approach that uses a rational conceptual framework is recommended. Such an approach should address the risk factors, such as socioeconomic status, interventions, and outcome measures in an integrated fashion. Conceptual frameworks include the Global Language Model, the Interactive Language and Attention Model, and a transactional model (Vernon-Feagans, 1999; Roberts and Wallace, 1997). The Global Language Model hypothesizes that mild to moderate hearing loss that results from otitis media is the actual causal factor that leads to speech and language deficits. The Interactive Language and Attention Model also hypothesizes an important role for hearing loss. However, this model also distinguishes between early and later developmental effects and the timing of hearing loss in the life of the child and places greater emphasis on risk and protective factors that may interact with hearing loss as well as directly affecting speech and language development. The transactional model ascribes an important role to differences in parent or caregiver response to children with and without chronic otitis media on long-term effects.

Generalizability of study findings will be enhanced in future research if details of risk or influencing factors and interventions are well planned and documented. Included in this assessment of risk factors should be the issue of hearing loss (both conductive and sensorineural) associated with otitis media as a possible cause of long-term speech and language deficits.

For future systematic reviews, we propose the consideration of an “individual-level-data meta-analysis” method (Mathew and Nordstrom, 1999; Stewart and Clarke, 1995; Stewart and Parmar, 1993) to study the long-term effects on outcomes such as speech, language, or hearing, with many of the suggestions for improvement of study quality noted above. This approach would call for the collaboration of investigators from various institutions who have been following cohorts of children prospectively to contribute data on individual members of their cohorts. Eligible cohorts are identified based on *a priori* criteria. Risk factors, interventions,

and outcomes of interest are also defined *a priori*. The unique feature of "individual-level-data meta-analysis" is the ability it confers to retrieve a uniform set of data directly on risk factor, intervention, and outcome data, case by case. This case-specific data set could then be analyzed using meta-regression or other multivariate techniques. A meta-analysis of updated individual patient data has been found to provide the least biased and most reliable means of addressing questions that have not been satisfactorily resolved by individual studies (Stewart and Parmar, 1993). However, the quality of data and the ability for cohort investigators to collect and share relevant data are important factors in the success of this approach (Steward and Clarke, 1995).

In all aspects of analysis, definitions, classifications, and types and units of measure should be developed by a team of experts prior to the start of a study. A consensus on the definitions and classification of otitis media and on relevant outcome measures will allow for comparisons among cohorts. We realize the lack of knowledge as to what specific aspects of speech and language development might be affected by early otitis media. Nevertheless, we would encourage experts to develop a uniform panel of tests that would measure the broad array of possible aspects of speech and language development hypothesized to be affected and could be consistently applied in research studies by all investigators. Literature on findings should report univariate as well as multivariate analysis findings to allow pooling of data. Many studies reported correlation coefficients or regression coefficients, which are difficult to interpret and to use in quantitative synthesis.

Several prospective studies on the effect of early otitis media on long-term speech and language development are ongoing (Paradise, Dollaghan, Campbell et al., 2000; Feldman, Dollaghan, Campbell et al., 1999; Paradise, Rockette, Colborn et al., 1997; Roberts, Burchinal, Zeisel et al., 1998; Roberts, Burchinal, Jackson et al., 2000). Whether these studies answer more definitively the questions regarding the effect of otitis media on long-term speech and language and delineate areas, apart from the general research issues noted above, for further prospective studies on speech and language will be better assessed when the results of these studies are reported in the peer-reviewed literature.

Effects of Early-life OM on Long-term Hearing

Future research should attempt to confirm whether early-life otitis media leads to more permanent hearing loss than intermittent and transient conductive hearing loss. The importance of hearing loss, whether intermittent and transient or permanent and long-standing, associated with early-life otitis media, should be addressed as noted in the section above on the effect of early otitis media on speech and language development. Similar methodological recommendations, including the "individual-level-data meta-analysis" approach, apply to research on long-term hearing effects and speech and language effects of early otitis media. If OM does affect long-term hearing, the effect of OM treatment on long-term hearing and its cost-effectiveness are of great importance and must be addressed in future prospective studies.

Diagnostic Methods for OME

Future research on the diagnosis of OME will need to start with the definition of OME. The difficulty in reaching a consensus on the definition of OME was seen in our discussion of this issue with our technical expert panel. The technical experts agreed that OME was defined as "fluid in the middle ear without signs or symptoms of ear infection," as proposed by the 1994

OME guideline (Stool, Berg, Berman et al., 1994). However, they could not agree on which signs or symptoms should be absent, i.e. what signs or symptoms differentiated OME from acute otitis media. Without such agreement, we believe little progress can be made in improving the diagnosis of OME.

Limiting the assessment of OME diagnostic methods to those that address middle-ear effusion specifically, as we did, will require further expert consensus on important conceptual issues. One issue that was brought to our attention by one of our technical experts and that was discussed in depth by our technical expert panel was whether diagnosis of middle-ear effusion in the child with OME was different than in the child with acute otitis media. For example, since the child with acute otitis media is in discomfort, whatever the symptoms that are ascribed to acute otitis media, that child will be more difficult to examine for the presence of middle-ear effusion than a child with OME, who by definition is asymptomatic. After much discussion, our panel decided that the diagnosis of middle-ear effusion was different in the context of these two clinical conditions; however, we are aware that other experts may not agree with this opinion. Future systematic reviews will require studies of much higher quality than are currently available. In addition, future studies must provide details on the characteristics of the children studied and the study setting so that the generalizability of the findings can be assessed. Studies confined to children with known middle-ear effusions in tertiary care settings may be easier to conduct, but the clinician in general practice is faced with children whose middle-ear status is unknown at the time of presentation. Future research must provide information that is applicable to the child with unknown middle-ear status in the primary care setting.

Pneumatic otoscopy might appear to be less costly and more easily employed by the typical clinician than other diagnostic options such as tympanometry and acoustic reflectometry. Nevertheless, future studies on the diagnostic assessment of OME 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 (Sox, Stern, Owen et al., 1989). Cost-effectiveness analysis will enable more informed decisions on the best diagnostic method for OME. The assessment of more complex diagnostic methods such as combination tests or algorithms would also benefit from cost-effectiveness analysis. Such analysis should be undertaken in the future.