Tympanic Membrane Abnormalities and Hearing Levels at the Ages of 5 and 6 Years in Relation to Persistent Otitis Media and Tympanostomy Tube Insertion in the First 3 Years of Life: A Prospective Study Incorporating a Randomized Clinical Trial

Lindsay C. Johnston, MD*‡; Heidi M. Feldman, MD, PhD*‡; Jack L. Paradise, MD*‡; Beverly S. Bernard, RN, BS‡; D. Kathleen Colborn, BS‡; Margaretha L. Casselbrant, MD, PhD§‖; and Janine E. Janosky, PhD¶

ABSTRACT. *Objective.* **One current practice guideline recommends myringotomy with tympanostomy tube insertion (M&T) for young children in whom middle-ear effusion (MEE) has persisted for 3 months, and another recommends the procedure after MEE has persisted for 4 to 6 months provided that a bilateral hearing loss of ≥20 dB is present. Sequelae of M&T are not uncommon, but the extent to which these sequelae are attributable to M&T itself or to the middle-ear disease that prompted the procedure or to both has not been clear. Our objective in the present study was to examine the prevalence of various tympanic membrane (TM) abnormalities in otherwise healthy children at the age of 5 years and hearing levels at the age of 6 years in relation to persistent MEE and M&T in the children's first 3 years of life.**

Methods. **In a prospective study of child development in relation to early-life otitis media, we randomly assigned 429 children who met specified criteria regarding the persistence of MEE in their first 3 years of life to undergo M&T either promptly (the "early-treatment" group) or after a defined extended period if MEE remained present (the "late-treatment" group). We also followed a representative sample of 241 children who ranged from having no MEE to having MEE whose cumulative duration fell just short of meeting randomization criteria for the clinical trial (the "nontrial" group). Most of the children in each group underwent both otomicroscopic examination at the age of 5 years and audiometric testing at the age of 6 years, at times when they were free of MEE. Among these children, M&T had been performed in 82.3% of those in the early-treatment group, 38.1% of those in the late-treatment group, and 3.0% of those in the nontrial group.**

Results. **At the age of 5 years, we found 1 or more types of TM abnormality in 1 or both ears in 70.7%, 42.5%, and 9.5% of the children in the early-treatment, late-treatment, and nontrial groups, respectively. Within the 3 groups, however, among children who received tubes, the proportions who had an abnormality of some type were similar, namely, 82.6%, 80.4%, and 83.3%, respectively. The corresponding proportions among children who had not received tubes were 15.4%, 19.3%, and 7.2%, respectively. Segmental atrophy and tympanosclerosis were the most common abnormalities found. At the age of 6 years, mean pure-tone average audiometric thresholds in the early-treatment, late-treatment, and nontrial groups, respectively, were 6.18 dB, 5.49 dB, and 4.63 dB in left ears and 6.17 dB, 6.02 dB, and 4.32 dB in right ears. The thresholds in the early- and late-treatment groups did not differ significantly, but the thresholds in the early- and late-treatment groups were each significantly higher than in the nontrial group. Within the early- and late-treatment groups, we found no significant relation between hearing levels and the presence or type of TM abnormalities.**

Conclusion. **In otherwise healthy children who have persistent MEE during their first 3 years of life, ready resort to M&T results in far more TM abnormalities at age 5 than does selective management in which most children do not receive the procedure. With these differing approaches, however, hearing levels at age 6 do not differ. Regardless of whether children with persistent early-life MEE receive M&T, they have more TM abnormalities at age 5 and negligibly poorer hearing at age 6 than do children who had less or no otitis media. Longer term otologic and audiologic outcomes of persistent early-life MEE and of M&T remain to be determined. In view of 1) the present findings and the remaining uncertainties concerning sequelae, 2) the fact that M&T involves certain immediate risks—albeit minimal—and substantial cost, and 3) previously reported findings in the study's randomized clinical trial that show no developmental advantage at ages 3 and 4 years accruing from children's having received prompt M&T, a prolonged period of watchful waiting seems desirable in otherwise healthy children who are younger than 3 years and have persistent, asymptomatic MEE that is not complicated by sensorineural or severe conductive hearing loss, balance dysfunction, or severe TM retraction.** *Pediatrics* **2004; 114:e58–e67. URL: http://www.pediatrics.org/cgi/content/full/114/1/e58;** ***otitis media with effusion, middle-ear effusion, myringotomy, tympanostomy tube insertion, audiometric testing, tympanic membrane abnormality, tympanosclerosis, segmental atrophy, retraction pocket, hearing levels.***

From the *Department of Pediatrics, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; ‡Department of Pediatrics, Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania; §Department of Otolaryngology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; ‖Department of Otolaryngology, Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania; and the ¶Department of Family Medicine and Clinical Epidemiology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.

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Reprint requests to (J.L.P.) Children's Hospital of Pittsburgh, 3705 Fifth Ave, Pittsburgh, PA 15213-2583. E-mail: jpar@pitt.edu

ABBREVIATIONS. M&T, myringotomy with tympanostomy tube insertion; MEE, middle-ear effusion; TM, tympanic membrane; HL, hearing level; PTA, pure-tone average.

Otitis media is, next to the common cold, the most commonly diagnosed illness in US children,[1] and myringotomy with tympanostomy tube insertion (M&T) is the most common surgical operation among US children beyond the newborn period.[2] Current practice guidelines recommend M&T for young children in whom middle-ear effusion (MEE) has persisted for 3 months,[3] or for 4 to 6 months provided that a bilateral hearing loss of ≥20 dB is present.[4] The recommendation stems from concern that prolonged middle-ear inflammation might result in untoward otologic or audiologic sequelae[5] and that the conductive hearing loss that accompanies MEE might result in later impairments of cognition, language, speech, or psychosocial development.[4]

On the other hand, sequelae once tympanostomy tubes have been extruded are not uncommon. These sequelae include residual perforation of the tympanic membrane (TM), tympanosclerosis, segmental atrophy, retraction or retraction pocket, cholesteatoma, and hearing loss.[6,7] The extent to which these sequelae are attributable to M&T itself or to the middle-ear disease that prompted the procedure or to both has not been clear. Also unclear and the subject of controversy has been the extent to which the untoward sequelae of M&T might be offset by possible benefits in regard to children's later development.[8]

In 1991, we began a prospective study, the main objective of which was to clarify relations between persistent MEE in children's first 3 years of life and their later cognitive, language, speech, and psychosocial development. Findings to date in such children indicate that prompt insertion of tympanostomy tubes does not measurably improve their outcomes in those developmental domains at 3 and 4 years of age[9,10] or their intelligence, receptive language, and auditory processing at 6 years of age.[11] In the present report, we address a secondary objective of the study, namely, to delineate possible later otologic and audiologic consequences of persistent MEE and of M&T.

METHODS

Subjects and General Procedures

Details concerning study procedures have been described previously.[9,12–14] In brief, we enrolled 6350 healthy infants from 2 to 61 days of age at 8 practice sites (2 urban hospital outpatient departments and 2 small-town/rural and 4 suburban private pediatric group practices) in the Greater Pittsburgh area between June 1991 and December 1995. The study was approved by the institutional review boards of Children's Hospital of Pittsburgh and Mercy Hospital of Pittsburgh, and written informed consent was obtained from 1 or both parents of each enrolled infant. We evaluated children's middle-ear status at least monthly until they were 3 years of age, using pneumatic otoscopy supplemented in most instances by tympanometry. We regularly monitored the validity of study clinicians' otoscopic observations and found satisfactory levels of interobserver agreement, and we prescribed antimicrobial drugs for episodes of otitis media according to a specified protocol. In the clinical trial component of the study, we randomly assigned 429 children who met specified minimum criteria regarding the presence of persistent MEE to undergo M&T either promptly (the "early-treatment" group) or after a defined extended period if their MEE persisted (the "late-treatment" group).[9] The criteria for entering the clinical trial consisted of MEE that persisted continuously for 90 days in the case of bilateral effusion or 135 days in the case of unilateral effusion or intermittently for specified proportions of longer periods, eg, bilaterally during at least 67% of the preceding 180-day period or unilaterally during at least 67% of the preceding 270-day period. (Additional details concerning intermittent MEE criteria are listed in Appendix 2 of the electronic version of reference 9 and are available from the authors.) Children who were assigned to the early-treatment group were scheduled to undergo M&T as soon as practicable. Children who were assigned to the late-treatment group were to undergo the operation 6 months later if bilateral effusion remained present or 9 months later if unilateral effusion remained present. When effusion was unilateral, a tube was placed only in the affected ear.

Of the 402 randomized children who were followed up to 3 years of age and who underwent developmental testing, 37% were randomized on the basis of bilateral MEE (18% continuous, 19% discontinuous); of the children who were randomized on the basis of unilateral MEE, bilateral MEE had been present during >25% of the immediately preceding 6-month period in 73%.[9] The 402 children underwent 765 audiometric examinations before randomization and 952 examinations after randomization. On the basis of data obtained in study children who had no MEE, abnormal hearing was defined as an auditory brainstem response >20 dB hearing level (HL) or a pure-tone average (PTA) >25 dB HL up to 10 months of age, >20 dB HL from ages 10 through 23 months, and >15 dB HL from 2 years of age onward. Both before and after randomization, hearing acuity was abnormal as so defined in approximately one half of instances when children had unilateral MEE and in approximately three quarters of instances when children had bilateral MEE.[9]

In children who underwent surgery, Armstrong-type tympanostomy tubes were inserted in the anterosuperior portion of the pars tensa and allowed to remain in place until they were extruded spontaneously. As anticipated from the known effects of tube insertion in resolving MEE and maintaining middle-ear ventilation,[4] after assignment of the children there were large differences in the cumulative duration of MEE between the early-treatment group and the late-treatment group (two thirds of whom never actually underwent tube insertion). For example, during the first 12 months after randomization, 43.3% of the children in the late-treatment group had MEE for >50% of the days, compared with 14.4% of the children in the early-treatment group. Corresponding values for the first 24 months postrandomization were 27.4% and 14.1%.[9]

We also followed a sociodemographically representative sample of 241 children who represented a spectrum of MEE experience from having no MEE to having MEE whose cumulative duration fell just short of meeting our criteria for enrollment in the randomized clinical trial (the "nontrial" group, termed "associational" in previous reports). In the nontrial group, the estimated duration of MEE ranged from none to 65.6% of the first year of life and 44.8% of the first 3 years of life. In 69.3% of these children, the estimated proportion of time with MEE in the first 3 years of life was <20%.

Children in the early-treatment group, the late-treatment group, and the nontrial group were scheduled to undergo otomicroscopic examination at ~5 years of age and audiometric examination in conjunction with comprehensive developmental evaluation at ~6 years of age, at times when they were free of MEE. Children who were found to have MEE when they presented for these examinations were rescheduled for a later visit or, if unable to return for either examination, were excluded from the present analysis.

Otomicroscopic Examination

Otomicroscopic examinations were performed by 1 of the authors (M.L.C.), an experienced pediatric otolaryngologist who was unaware of the children's histories and study status, using a Zeiss Model 12935 binocular otomicroscope. For each ear, the presence or absence and, if present, the estimated extent of specific TM abnormalities were recorded, along with a hand-drawn sketch, on a standardized form. The abnormalities considered were tympanosclerosis (whitish calcific plaques on the TM), fibrosis (fibrotic scarring of the TM), segmental atrophy (localized area of thinning of the TM with or without atelectasis), retraction pocket (sharply

demarcated area of atelectasis in the TM with visible edges), perforation, and cholesteatoma.

Audiometric Testing

Pneumatic otoscopic examination, tympanometric testing, and audiometric testing were performed in conjunction with developmental testing scheduled to be performed at the age of 6 years. All audiometric testing was conducted in an acoustically shielded sound suite (Acoustic Systems, Austin, TX, or Industrial Acoustic Company, Bronx, NY) using a GSI 16 (Grason-Stadler Inc, Milford, NH) or Beltone 2000 (Beltone Electronics Corp, Rockford, IL) audiometer. PTA audiometric thresholds were calculated from individual thresholds at 500, 1000, 2000, and 4000 Hz. Audiologists were unaware of children's otoscopic diagnoses.

Statistical Analysis

We used χ^2 or Fisher exact tests to test for differences between proportions of children in different groups. For continuous outcomes, we used analysis of variance to test for differences between mean group values. To test for differences between mean hearing threshold levels, we performed a repeated measures analysis of variance including Scheffe post hoc procedures, following statistically significant omnibus tests. For this analysis, because the necessary assumption of sphericity was violated, we used the Greenhouse-Geisser conservative test. We used linear regression analysis to adjust for potentially confounding variables. All statistical analyses were performed as nondirectional, and statistical significance was set at $P < .05$.

RESULTS

Study Population

A total of 395 (92.1%) of the 429 randomized children and 233 (96.7%) of the 241 nontrial children underwent audiometric examination in conjunction with developmental evaluation at 6 years of age, but only 281 (65.5%) of the randomized children and 200 (83.0%) of the nontrial children had also undergone otomicroscopic examination at 5 years of age and thus could be included in the present analysis. The proportion of nontrial children included (83.0%) was significantly higher than the corresponding proportions of children in the early-treatment group (147 of 216 [68.1%]) or in the late-treatment group 134 of 213 [62.9%]; $P < .001$). (The numbers included in the present analysis were reduced in part because 35 children—7 in the nontrial group, 13 in the early-treatment group, and 15 in the late-treatment group—were excluded because of the presence of MEE at the time of either examination.) Figure 1 shows the numbers of children who were enrolled in the study, randomized, and followed up, respectively, and the numbers included the present analysis, and Table 1 shows selected demographic and clinical characteristics of the included children. Within each of the 3 groups, none of the differences in these characteristics between the children who were included and the children who were not included were statistically significant, with 1 exception: in the late-treatment group, a higher proportion of the children who were not included than of the children who were included had met randomization criteria within the first year of life (58.2% vs 35.0%; $P = .003$).

Within the present study population, higher proportions of children in the trial group than in the nontrial group were black and from urban practice sites; higher proportions also had Medicaid health insurance, and their mothers had lower levels of education (all $P < .001$). These differences reflected the strong direct relation previously noted in study participants as a whole between otitis media prevalence and low socioeconomic status.[12] Within the clinical trial, except for the difference in the numbers and distributions of children who received tubes and the resultant differences subsequently in the proportions of days with MEE, none of the differences between the early- and late-treatment groups were statistically significant. M&T had been performed in 121 (82.3%) of the children in the early-treatment group, 51 (38.1%) of the children in the late-treatment group, and 6 (3.0%) of the children in the nontrial group. In 33 of the children (21 in the early-treatment group, 10 in the late-treatment group, and 2 in the nontrial group), the procedure had been performed 2 or more times. Within the present study population, nonperformance of M&T in both the early- and the late-treatment groups was attributable in most instances to spontaneous resolution of MEE, but in a few instances in which MEE persisted, to parental refusal of the procedure.

Otomicroscopic Findings

Tables 2 and 3 show the proportions of TM abnormalities found on otomicroscopic examination at the age of ~5 years in children and in ears, respectively. One or more types of TM abnormality were found in 1 or both ears in 70.7% of the children in the early-treatment group, 42.5% of the children in the late-treatment group, and 9.5% of the children in the nontrial group ($P < .001$). More or less paralleling these differences were differences between the 3 groups regarding children who had 2 or more abnormalities (60.5%, 29.9%, and 3.9%, respectively; $P < .001$). Within the 3 groups, however, among children who received tubes, the proportions who had any abnormality were similar, namely, 82.6%, 80.4%, and 83.3%, respectively ($P = .94$). The corresponding proportions among children who had not received tubes were 15.4%, 19.3%, and 7.2%, respectively ($P = .011$). Segmental atrophy and tympanosclerosis were the most common abnormalities found, present in 74.7% and 40.4%, respectively, of children who had received tubes but in only 3.0% and 0.6%, respectively, of children who had not received tubes. The proportions of ears affected by the various abnormalities were parallel to but somewhat lower than the corresponding proportions of affected children, reflecting that abnormalities were not always found bilaterally. In the ears with segmental atrophy, the estimated proportion of TM area affected was <20% in 81.9%, 20% to 50% in 16.9%, and >50% in 1.2%. In the ears with tympanosclerosis, the estimated proportion of TM area affected was <20% in 49.5%, 20% to 50% in 45.9%, and >50% in 4.6%.

Within the clinical trial as a whole, the tube-versus-no-tube risk ratio in ears for segmental atrophy was 17.42 (95% confidence interval: 10.2–29.8) and for tympanosclerosis was 24.5 (95% confidence interval: 10.1–59.5). Fibrosis, retraction pocket, and perforation were found relatively infrequently; retraction pocket and perforation were found only in ears that had received tubes. Cholesteatoma was not found. In

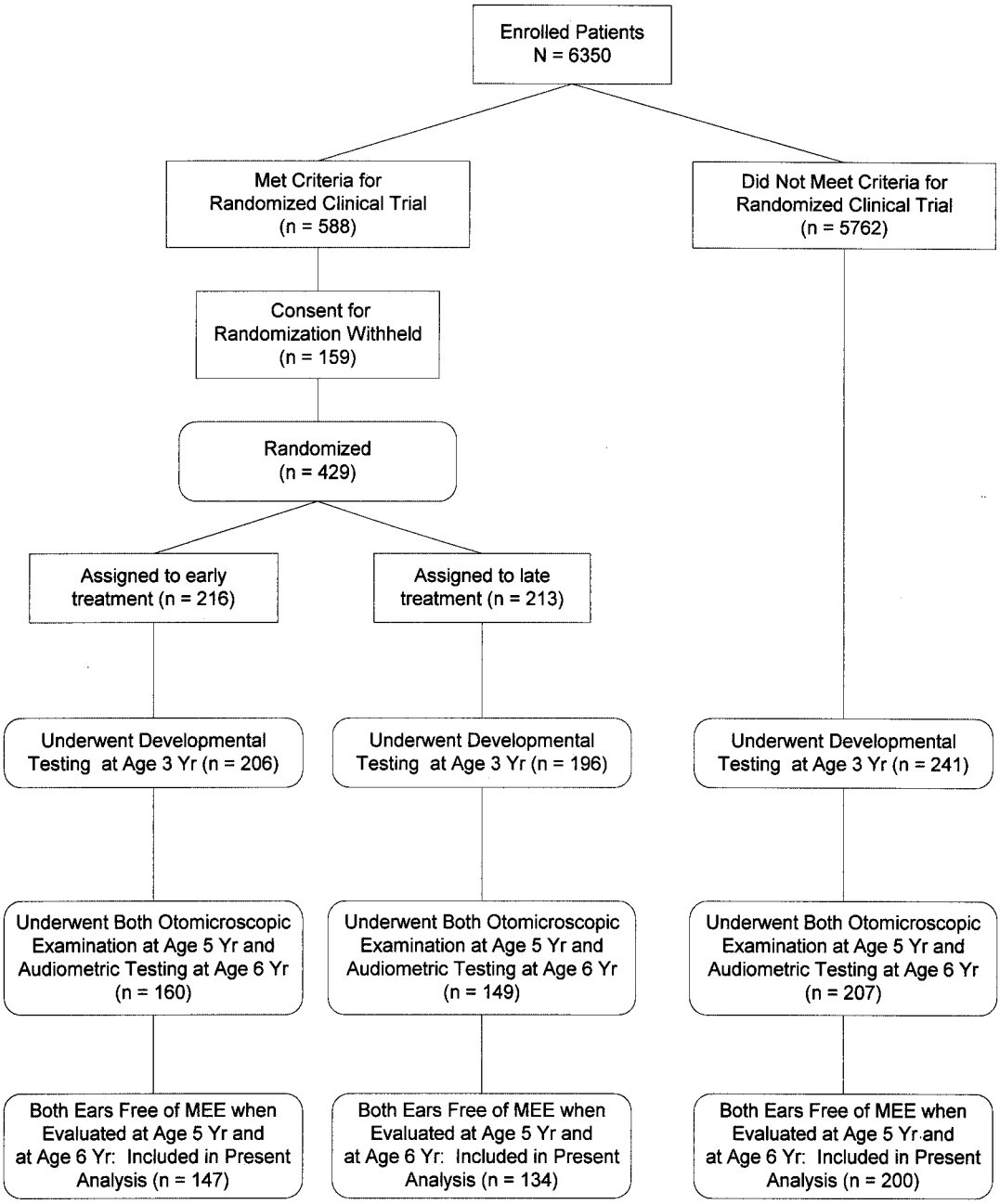

Fig 1. Flow diagram showing the numbers of children who were enrolled, randomized, and followed up and the numbers who received both otomicroscopic examination at age 5 and audiometric testing at age 6 and were included in the present analysis.

the nontrial group, of the 14 children who had not received tubes but who had TM abnormalities (17 ears), 12 had had percentages of time with MEE during their first and/or second year of life ranging from 22.6% to 56.6%. Of the remaining 2 children, both of whom had had relatively small percentages of time with MEE during only their first year of life (9.3% and 6.7%, respectively), 1 had atrophy and 1 had fibrosis, in each case involving an estimated 5% of 1 TM.

Among children in the study population as a whole who had undergone M&T, the proportion who had any TM abnormality was higher in those whose only or initial procedure was performed before the age of 24 months than in those in whom the procedure was performed at a later age (86.3% vs 67.9%; $P = .027$). The proportion of children with any abnormality did not differ significantly as between those who had undergone only 1 procedure and those who had undergone 2 or more procedures.

Audiometric Findings

Tables 4 and 5 show children's mean PTA audiometric thresholds and mean thresholds at 500, 1000, 2000, 4000, and 8000 Hz in the left and right ears, respectively, at the age of 6 years. In the randomized clinical trial, mean thresholds in the early-treatment group were generally slightly higher (ie, less favorable) than in the late-treatment group, but the differences were not statistically significant ($P = .13$ for left

TABLE 1. Selected Characteristics of Study Participants According to Study Component and Treatment Group

	Study Component		
	Randomized Clinical Trial		Nontrial Group (n = 200)
	Early-Treatment Group (n = 147)	Late-Treatment Group (n = 134)	
Practice site			
Urban	80 (54.4)	69 (51.5)	51 (25.5)
Small town/rural	48 (32.7)	43 (32.1)	76 (38.0)
Suburban	19 (12.9)	22 (16.4)	73 (36.5)
Gender			
Male	75 (51.0)	77 (57.5)	101 (50.5)
Female	72 (49.0)	57 (42.5)	99 (49.5)
Race			
Black	56 (38.1)	57 (42.5)	35 (17.5)
White	86 (58.5)	74 (55.2)	162 (81.0)
Other	5 (3.4)	3 (2.2)	3 (1.5)
Maternal level of education			
Less than high school graduate	18 (12.2)	22 (16.4)	18 (9.0)
High school graduate	115 (78.2)	100 (74.6)	136 (68.0)
College graduate	14 (9.5)	12 (9.0)	46 (23.0)
Health insurance status			
Medicaid	96 (65.3)	91 (67.9)	68 (34.0)
Private	51 (34.7)	43 (32.1)	132 (66.0)
Age at which randomization criteria were met (month of life)			
3–6	3 (2.0)	1 (0.7)	N/A
7–12	54 (36.7)	46 (34.3)	N/A
13–18	48 (32.7)	49 (36.6)	N/A
19–24	27 (18.4)	21 (15.7)	N/A
25–30	11 (7.5)	9 (6.7)	N/A
31–36	4 (2.7)	8 (6.0)	N/A
Age at receiving M&T (month of life)			
Not received	26 (17.7)	83 (61.9)	194 (97.0)
3–6	0 (0)	0 (0)	0 (0)
7–12	31 (21.1)	3 (2.2)	1 (0.5)
13–18	47 (32.0)	12 (9.0)	3 (1.5)
19–24	24 (16.3)	15 (11.2)	1 (0.5)
25–30	12 (8.2)	9 (6.7)	0 (0)
31–36	6 (4.1)	2 (1.5)	0 (0)
≥37	1 (0.7)	10 (7.5)	1 (0.5)
Mean percentage of days with MEE (months of life)			
3–12	48.7	49.9	21.5
13–24	40.7	50.5	14.7
25–36	23.6	27.5	10.3

Data are n (%) of children. N/A indicates not applicable.

ears, .80 for right ears). On the other hand, the thresholds in the early- and late-treatment groups were each significantly higher than in the nontrial group (early-treatment vs nontrial, $P < .001$ for left and right ears; late-treatment vs nontrial, $P = .04$ and $< .001$ for left and right ears, respectively).

Tables 6 and 7 show audiometric thresholds in the left and right ears, respectively, in the randomized children at the age of 6 years in relation to TM abnormalities found in the same children at the age of 5 years. Within the early- and late-treatment groups, respectively, we found no significant relation between HLs and the presence or type of TM abnormalities, except for the combination of tympanosclerosis and segmental atrophy compared with no abnormality in right ears ($P = .02$).

DISCUSSION

The objective of the present study was to delineate possible later otologic and audiologic consequences of persistent early-life MEE and of M&T, drawing on data derived from children who were enrolled in a larger study whose main outcome measures concerned children's later development. In the larger study, children with persistent MEE in the first 3 years of life were entered into a randomized clinical trial of prompt M&T versus delayed M&T if MEE persisted,[9] and a representative sample of children who failed to meet criteria for the clinical trial was also followed.[14] Among the children in those study components who served as subjects of the present report, M&T had been performed in 82.3% of the children in the trial's early-treatment group, 38.1% of those in the trial's late-treatment group, and 3.0% of those in the nontrial group.

We found that, within the clinical trial, TM abnormalities were more prevalent at age 5 in the early-treatment than in the late-treatment group and that the difference was attributable to the higher rate of performance of M&T in the early-treatment group.

TABLE 2. TM Abnormalities in Children at the Age of 5 Years by Study Component, Treatment Group, and Receipt or Nonreceipt of M&T

TM Status	Study Component								
	Randomized Clinical Trial						Nontrial Group		
	Early-Treatment Group			Late-Treatment Group					
	Tubes (n = 121)	No Tubes (n = 26)	Total (n = 147)	Tubes (n = 51)	No Tubes (n = 83)	Total (n = 134)	Tubes (n = 6)	No Tubes (n = 194)	Total (n = 200)
Any abnormality	100 (82.6)	4 (15.4)§	104 (70.7)§	41 (80.4)§	16 (19.3)§	57 (42.5)	5 (83.3)§	14 (7.2)§	19 (9.5)
Tympanosclerosis only	4 (3.3)	0 (0)	4 (2.7)	3 (5.9)	1 (1.2)	4 (3.0)	0 (0)	1 (0.5)	1 (0.5)
Fibrosis only	0 (0)	1 (3.8)	1 (0.7)	1 (2.0)	9 (10.8)	10 (7.5)	0 (0)	8 (4.1)	8 (4.0)
Segmental atrophy only	46 (38.0)	2 (7.7)	48 (32.7)	12 (23.5)	4 (4.8)	16 (11.9)	4 (66.7)	3 (1.5)	7 (3.5)
Tympanosclerosis + segmental atrophy	31 (25.6)	0 (0)	31 (21.1)	19 (37.3)	0 (0)	19 (14.2)	1 (16.7)	1 (0.5)	2 (1.0)
Other combinations of above*	12 (9.9)	1 (3.8)	13 (8.8)	3 (5.9)	2 (2.4)	5 (3.7)	0 (0)	1 (0.5)	1 (0.5)
Retraction pocket with other abnormality†	1 (0.8)	0 (0)	1 (0.7)	1 (2.0)	0 (0)	1 (0.7)	0 (0)	0 (0)	0 (0)
Perforation with other abnormality‡	6 (5.0)	0 (0)	6 (4.1)	2 (3.9)	0 (0)	2 (1.5)	0 (0)	0 (0)	0 (0)
No abnormality	21 (17.4)	22 (84.6)	43 (29.3)	10 (19.6)	67 (80.7)	77 (57.5)	1 (16.7)	180 (92.8)	181 (90.5)

Data are n (%) of children.
* Tympanosclerosis + fibrosis (n = 4); tympanosclerosis + fibrosis + segmental atrophy (n = 6); fibrosis + segmental atrophy (n = 9).
† With tympanosclerosis + segmental atrophy (n = 1); with segmental atrophy only (n = 1).
‡ With tympanosclerosis only (n = 2); with tympanosclerosis + fibrosis + segmental atrophy (n = 2); with tympanosclerosis + segmental atrophy (n = 1); with fibrosis + segmental atrophy (n = 1); with segmental atrophy only (n = 2).
§ Because of rounding, the percentage does not equal the sum of the percentages of the listed types of abnormality.

TABLE 3. TM Abnormalities in Individual Ears of Children at the Age of 5 Years by Study Component, Treatment Group, and Receipt or Nonreceipt of M&T

TM Status/Type of Abnormality	Study Component								
	Randomized Clinical Trial						Nontrial Group		
	Early-Treatment Group			Late-Treatment Group					
	Tubes (n = 242)	No Tubes (n = 52)	Total (n = 294)	Tubes (n = 102)	No Tubes (n = 166)	Total (n = 268)	Tubes (n = 12)	No Tubes (n = 388)	Total (n = 400)
Any abnormality	180 (74.4)	5 (9.6)§	185 (62.9)§	72 (70.6)	16 (12.7)§	93 (34.7)	9 (75.0)	17 (4.4)	26 (6.5)§
Tympanosclerosis only	10 (4.1)	0 (0)	10 (3.4)	10 (9.8)	1 (0.6)	11 (4.1)	0 (0)	2 (0.5)	2 (0.5)
Fibrosis only	3 (1.2)	2 (3.8)	5 (1.7)	4 (3.9)	11 (6.6)	15 (5.6)	0 (0)	9 (2.3)	9 (2.3)
Segmental atrophy only	97 (40.1)	2 (3.8)	99 (33.7)	31 (30.4)	7 (4.2)	38 (14.2)	8 (66.7)	5 (1.3)	13 (3.3)
Tympanosclerosis + segmental atrophy	51 (21.1)	0 (0)	51 (17.3)	23 (22.5)	0 (0)	23 (8.6)	1 (8.3)	1 (0.3)	2 (0.5)
Other combinations of above*	12 (5.0)	1 (1.9)	13 (4.4)	1 (1.0)	2 (1.2)	3 (1.1)	0 (0)	0 (0)	0 (0)
Retraction pocket with other abnormality†	1 (0.4)	0 (0)	1 (0.3)	1 (1.0)	0 (0)	1 (0.4)	0 (0)	0 (0)	0 (0)
Perforation with or without other abnormality‡	6 (2.5)	0 (0)	6 (2.0)	2 (2.0)	0 (0)	2 (0.7)	0 (0)	0 (0)	0 (0)
No abnormality	62 (25.6)	47 (90.4)	109 (37.1)	30 (29.4)	150 (87.3)	175 (65.3)	3 (25.0)	371 (95.6)	374 (93.5)

Data are n (%) of ears.
* Tympanosclerosis + fibrosis (n = 4); tympanosclerosis + fibrosis + segmental atrophy (n = 2); fibrosis + segmental atrophy (n = 10).
† With tympanosclerosis + segmental atrophy (n = 1); with segmental atrophy only (n = 1).
‡ Perforation only (n = 1); with tympanosclerosis only (n = 3); with fibrosis only (n = 2); with segmental atrophy only (n = 2).
§ Because of rounding, the percentage does not equal the sum of the percentages of the listed types of abnormality.

TABLE 4. Mean Hearing Threshold Levels in Children's Left Ears in Relation to Study Component and Treatment Group

Study Component and Assignment	4-Frequency PTA*	Frequency (Hz)				
		500	1000	2000	4000	8000
Randomized clinical trial						
Early-treatment group (n = 147)	6.2 (4.1)	9.0 (5.8)	6.3 (4.9)	4.7 (4.5)	4.8 (4.8)	12.0 (6.6)
Late-treatment group (n = 134)	5.5 (3.4)	8.6 (4.7)	5.6 (4.3)	3.9 (4.0)	3.8 (4.3)	10.3 (5.8)
Nontrial group (n = 200)	4.6 (3.8)	7.5 (5.6)	4.6 (4.5)	3.3 (4.3)	3.1 (4.5)	8.2 (5.3)

Data are mean (standard deviation [SD]) threshold, dB HL.
* The 4 frequencies were 500, 1000, 2000, and 4000 Hz.

TABLE 5. Mean Hearing Threshold Levels in Children's Right Ears in Relation to Study Component and Treatment Group

Study Component and Treatment Group	4-Frequency PTA*	Frequency (Hz)				
		500	1000	2000	4000	8000
Randomized clinical trial						
Early-treatment group (n = 147)	6.2 (4.1)	9.7 (6.6)	6.4 (5.7)	4.0 (4.2)	4.6 (4.4)	11.8 (6.2)
Late-treatment group (n = 134)	6.0 (5.5)	10.0 (6.5)	6.1 (6.9)	3.7 (5.6)	4.3 (6.0)	9.9 (5.7)
Nontrial group (n = 200)	4.3 (3.4)	7.5 (5.4)	4.0 (4.1)	3.0 (3.8)	2.8 (4.1)	8.3 (5.9)

Data are mean (SD) threshold, dB HL.
* The 4 frequencies were 500, 1000, 2000, and 4000 Hz.

TABLE 6. Mean Hearing Threshold Levels in Left Ears in Randomized Children in Relation to Presence and Type of TM Abnormalities

TM Status/Type of Abnormality*	4-Frequency PTA†	Frequency (Hz)				
		500	1000	2000	4000	8000
No abnormality (n = 149)	5.4 (3.7)	8.3 (5.3)	5.4 (4.7)	4.1 (4.0)	4.0 (4.3)	10.5 (6.4)
Tympanosclerosis only (n = 9)	8.2 (2.8)	11.1 (3.3)	8.9 (3.3)	5.6 (3.9)	7.2 (5.7)	14.4 (3.9)
Fibrosis only (n = 10)	5.1 (3.6)	8.0 (4.8)	5.5 (3.7)	3.5 (4.7)	3.5 (4.1)	13.0 (5.4)
Segmental atrophy only (n = 69)	5.9 (4.0)	8.7 (5.5)	5.9 (5.0)	4.4 (4.2)	4.5 (4.5)	10.3 (5.3)
Tympanosclerosis + segmental atrophy (n = 35)	7.3 (3.8)	10.7 (5.3)	7.7 (4.3)	5.3 (5.3)	5.3 (4.8)	14.4 (6.9)
Fibrosis + segmental atrophy (n = 4)	6.9 (4.4)	6.3 (4.8)	7.5 (2.9)	6.3 (6.3)	7.5 (6.5)	18.3 (5.8)

Data are mean (SD) threshold, dB HL.
* Not including ears with tympanosclerosis + fibrosis (n = 3), tympanosclerosis + fibrosis + segmental atrophy (n = 1), and perforation (n = 3).
† The 4 frequencies were 500, 1000, 2000, and 4000 Hz.

TABLE 7. Mean Hearing Threshold Levels in Right Ears in Randomized Children in Relation to Presence and Type of TM Abnormalities

TM Status/Type of Abnormality*	4-Frequency PTA†	Frequency (Hz)				
		500	1000	2000	4000	8000
No Abnormality (n = 135)	5.1 (3.0)	8.4 (4.5)	5.2 (4.1)	3.2 (3.5)	3.8 (4.1)	9.6 (5.3)
Tympanosclerosis only (n = 12)	7.9 (8.1)	14.2 (15.2)	7.9 (12.3)	3.8 (4.3)	5.8 (4.7)	14.6 (6.2)
Fibrosis only (n = 10)	7.5 (3.4)	12.5 (4.3)	8.0 (6.3)	6.0 (3.9)	3.5 (3.4)	12.5 (5.4)
Segmental atrophy only (n = 70)	5.7 (3.6)	9.2 (4.9)	6.1 (5.2)	3.6 (3.9)	4.1 (4.0)	11.4 (6.8)
Tympanosclerosis + segmental atrophy (n = 39)	8.1 (8.8)‡	11.9 (9.6)	8.5 (10.3)	5.5 (9.0)	6.4 (9.3)	12.4 (6.7)
Fibrosis + segmental atrophy (n = 6)	7.9 (4.4)	11.7 (2.6)	8.3 (5.2)	5.8 (5.8)	5.8 (5.8)	10.0 (3.2)

Data are mean (SD) threshold, dB HL.
* Not including ears with tympanosclerosis + fibrosis (n = 1), tympanosclerosis + fibrosis + segmental atrophy (n = 1), retraction pocket (n = 2), and perforation (n = 5).
† The 4 frequencies were 500, 1000, 2000, and 4000 Hz.
‡ P = .02 for comparison with no abnormality.

However, regardless of whether children in the clinical trial in either treatment group received M&T, they had more TM abnormalities at 5 years of age than did children in the nontrial group, suggesting that the more extreme histories of otitis media in the trial children had also contributed to their more frequent development of TM abnormalities. HLs at 6 years of age in all groups were well within the normal range. Thresholds were slightly higher (ie, poorer) in children in the trial group than in children in the nontrial group. However, HLs in the early- and late-treatment groups did not differ and were largely unrelated to the presence or type of TM abnormality. Together, these findings suggest that tube insertion and the resulting TM abnormalities had not themselves affected children's HLs at age 6. The slightly less favorable HLs in children in the clinical trial than in nontrial children may have been attributable either to the trial children's greater extent of antecedent otitis media or in some way to sociode-

mographic or other, indeterminate factors that may have differed as between trial children and nontrial children.

Comparison With Previous Research and Interpretation of Findings

Design Issues

The present study of consequences of persistent MEE and of M&T differs from previous studies in a number of respects. Notably, previous studies included no comparison group of children with indifferent or no histories of otitis media,[6,15–25] or they considered consequences of M&T that had been performed after the first 3 years of life or at unspecified ages,[6,7,15–23,26] or they had smaller sample sizes,[6,15,16,18,20–24,26] or they used retrospective or nonrandom designs,[6,17,19,23,26] or all or many of the subjects had undergone associated adenoidectomy and/or tonsillectomy,[6,15,18–21,23,24] or methods of treatment for episodes of otitis media were not specified,[6,15–22,24–27] or examiners at follow-up were not noted to have been blinded to children's original form of treatment,[6,15–22,24,26] or otoscopy rather than otomicroscopy was used for follow-up examination,[18,20,22,23,26] or the method of examination used was not specified,[16,19,22,23] or HLs at follow-up were not measured.[19,21,22,26]

We believe the present study to be unique in combining the following features: children were monitored closely from early infancy, antimicrobial treatment for episodes of otitis media was standardized, children who had persistent MEE during the first 3 years of life were compared with a representative group of children who had lesser or no histories of otitis media, the sequelae studied were of disease and treatment occurring mainly during children's first 3 years of life, and all follow-up examinations used otomicroscopy and were conducted by 1 experienced pediatric otolaryngologist who was unaware of children's history and study group assignment.

TM Abnormalities

In the present study, segmental TM atrophy was found in 74.7% of the ears of children who had received M&T, a value considerably greater than the prevalence of 24.6% reported in the meta-analysis by Kay et al.[7] This apparently higher prevalence must take into account that, in most instances in the present study, relatively small proportions of the TM area were involved, findings that may have been overlooked or disregarded in earlier studies. The difference may also reflect that M&T was performed at younger ages than in most previous studies and the possibility that, in younger children, the TM is more susceptible to damage from trauma. Indeed, we found higher rates of TM abnormalities in the children whose only or initial M&T was performed before 24 months of age than in those in whom the procedure was performed at older ages. In contrast, tympanosclerosis in the present study was found in 40.4% of the ears of children who had received tubes, a value relatively close to the prevalence of 31.7% reported by Kay et al.[7]

Fibrosis of the TM as described in the present study was probably the equivalent of the finding described by earlier authors as thickening or minor scarring,[18–20] a condition considered to constitute an intermediate stage in the development of tympanosclerosis.[19] In 2 previous studies of children with persistent MEE, the prevalence of thickening or minor scarring (as differentiated from tympanosclerosis) in ears that had received tubes was 12.7%[18] and 14%,[20] respectively. In 1 of the studies, the prevalence in unoperated ears was 7.5%, a value high enough to suggest to the authors that the scarring had been caused by the underlying disease.[20] Findings in the present study are consistent with that observation. We found higher rates of TM abnormalities among children in the early- and late-treatment groups who had not undergone M&T (15.4% and 19.3%, respectively) than among children in the nontrial group who had not undergone M&T (7.2%; $P = .011$), and we found that, in children in the nontrial group who had not undergone M&T, abnormalities were essentially limited to children who had had substantial periods of MEE. These findings provide additional support for the proposition that TM damage may result not only from tube insertion but also (albeit to a lesser degree) from long-standing or recurrent middle-ear inflammation.

Retraction pocket in the present study was found in 1.1% of children who had received tubes (0.6% of ears), and perforation was found in 4.5% of such children (2.2% of ears). These values are in keeping with those reported previously.[7] Retraction of the TM not extreme enough to be considered a retraction pocket was not systematically recorded in the present study, but in a study by Valtonen et al[27] of children 5 years after M&T had been performed between 5 and 16 months of age, retraction of the pars flaccida was recorded in 7.1% and of the pars tensa in 9.6% of the children. In most instances, the retraction was of mild degree. Notably, some of these children had received M&T because of recurrent acute otitis media rather than persistent MEE, and repeat M&T had been performed on 1 or more occasions in 37% of the children. That cholesteatoma, found in the meta-analysis by Kay et al[7] to have been present in 0.8% of 8321 ears that had undergone M&T, was not found in the present study may have been attributable to the present study's close follow-up and assiduous treatment of infection, but the number or children in the present study was not large enough to permit definitive comparison.

HLs

In the present study, mean HLs were slightly less favorable in children in the clinical trial than in nontrial children. However, the difference was not clinically significant, as the mean thresholds in trial children were well within the normal range. As discussed earlier, the factor or factors underlying this between-group difference remain uncertain. No previous study, to our knowledge, that was both prospective and controlled has compared HLs in children who were previously affected with persistent MEE with levels in children who had lesser or no

histories of otitis media. However, previous prospective studies limited to children with persistent MEE, in keeping with findings in children in the clinical trial in the present study, have found no significant differences between HLs in ears that had received tubes and ears that had not, despite the more frequent TM abnormalities in the ears that had received tubes.[6,15,18,21]

Limitations of the Present Study

Four limitations of the present study concern follow-up details and the cross-sectional nature of the observations. First, the proportion of participants who underwent otomicroscopic examination at age 5 was somewhat smaller than the proportion who received audiometric testing at age 6. (This was mainly because, given the study's main focus on developmental outcomes, we arranged to conduct developmental evaluations and the associated audiometric testing on weekends when requested to do so by parents, whereas we had not offered that option for the otomicroscopic examinations.) However, there were no significant differences in demographics or in the proportion of time with MEE in the first 3 years of life between the children who were included in the present analysis and those who, for one reason or another, were not included. Second, the otomicroscopic and audiometric findings were recorded at the ages (approximately) of 5 and 6 years, respectively; changes in either category of findings might have occurred during the 1-year interval. Third, it seems possible, if not likely, that TM abnormalities found at age 5 in children who have received tubes might either improve or become more extensive and/or more prevalent as the children grow older. Previous reports have described both improvement[6,15,28] and worsening[21,25,28] over time. Particularly concerning is the recent report by Daly et al,[25] from a long-term prospective study of children who have received tubes, of increasing prevalence over time of TM atrophy, retraction, and retraction pocket. In their series, only 22 of 165 ears examined 8 years after undergoing M&T had no TM abnormalities. Fourth, it seems possible that changes in HLs might also eventuate as children grow older. In the 5-year follow-up study by Valtonen et al[27] cited earlier, retraction of the pars tensa was associated with mild conductive hearing loss, but tympanosclerosis and atrophy were not.

Clinical Implications

The findings of the present study indicate that, in otherwise healthy children who were younger than 3 years and had persistent MEE within the durations that we studied, TM abnormalities at the age of 5 years are much more common in those who had received tympanostomy tubes than in those who were treated nonsurgically. This difference, however, is not associated with differences in HLs at the age of 6 years, and its clinical significance must be considered, for the most part, questionable. It may well be the case that, with the exception of perforation, TM changes such as those that we found will prove ultimately to be innocuous. Nonetheless, for a number of reasons beyond the relatively infrequent occurrence of perforation as a sequela of tube insertion, prudence seems to suggest a more conservative approach to managing persistent MEE in otherwise well young children than is called for in current practice guidelines.[3,4] First, as noted earlier, it seems possible that in children who have received tubes, middle ear and/or auditory status may worsen with time. In that regard, it seems worth noting that, as tympanostomy tube insertion in its present form was first introduced in the 1950s,[29] no recipients of tubes during early childhood have as yet reached advanced age. Second, other components of our study have found in children who have received tubes no measurable developmental advantage at either 3 or 4 years of age or, to the extent analyzed, at 6 years of age. Third, surgery involves immediate risks—albeit minimal—and substantial cost, as well as the chance, so long as tubes remain in place, that episodes of tube otorrhea will occur.[30] What seems called for instead is individualized management, with M&T reserved for children who have persistent MEE and 1 or more additional indications for surgery. Such children would comprise those who have inordinately recurring episodes of acute otitis media; who are discomfited by the attendant conductive hearing loss or have, in addition, appreciable sensorineural hearing loss; who have a related symptom, such as otalgia, tinnitus, or disturbance of balance; or whose TM shows a deep retraction pocket. In such children, M&T is clearly the treatment of choice. Additional findings as the present study progresses may further clarify the later consequences both of asymptomatic early-life MEE and of the use of M&T in its management.

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