A Multicenter Evaluation of How Many Infants With Permanent Hearing Loss Pass a Two-Stage Otoacoustic Emissions/Automated Auditory Brainstem Response Newborn Hearing Screening Protocol

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ABSTRACT. *Objective.* Ninety percent of all newborns in the United States are now screened for hearing loss before they leave the hospital. Many hospitals use a 2-stage protocol for newborn hearing screening in which all infants are screened first with otoacoustic emissions (OAE). No additional testing is done with infants who pass the OAE, but infants who fail the OAE next are screened with automated auditory brainstem response (A-ABR). Infants who fail the A-ABR screening are referred for diagnostic testing to determine whether they have permanent hearing loss (PHL). Those who pass the A-ABR are considered at low risk for hearing loss and are not tested further. The objective of this multicenter study was to determine whether a substantial number of infants who fail the initial OAE and pass the A-ABR have PHL at ~9 months of age.

Methods. Seven birthing centers with successful newborn hearing screening programs using a 2-stage OAE/A-ABR screening protocol participated. During the study period, 86 634 infants were screened for hearing loss at these sites. Of those infants who failed the OAE but passed the A-ABR in at least 1 ear, 1524 were enrolled in the study. Data about prenatal, neonatal, and socioeconomic factors, plus hearing loss risk indicators, were collected for all enrolled infants. When the infants were an average of 9.7 months of age, diagnostic audiologic evaluations were done for 64% of the enrolled infants (1432 ears from 973 infants).

Results. Twenty-one infants (30 ears) who had failed the OAE but passed the A-ABR during the newborn hearing screening were identified with permanent bilateral or unilateral hearing loss. Twenty-three (77%) of the ears had mild hearing loss (average of 1 kHz, 2 kHz, and 4 kHz ≤40-decibel hearing level). Nine (43%) infants had bilateral as opposed to unilateral loss, and 18 (86%) infants had sensorineural as opposed to permanent conductive hearing loss.

Conclusions. If all infants were screened for hearing loss using the 2-stage OAE/A-ABR newborn hearing screening protocol currently used in many hospitals, then ~23% of those with PHL at ~9 months of age would have passed the A-ABR. This happens in part because much of the A-ABR screening equipment in current use was designed to identify infants with moderate or greater hearing loss. Thus, program administrators should be certain that the screening program, equipment, and protocols are designed to identify the type of hearing loss targeted by their program. The results also show the need for continued surveillance of hearing status during childhood. *Pediatrics* 2005;116:663–672; *hearing loss, hearing screening, efficacy.*

ABBREVIATIONS. OAE, otoacoustic emissions; ABR, auditory brainstem response; TEOAE, transient evoked otoacoustic emissions; DPOAE, distortion product otoacoustic emissions; VRA, visual reinforcement audiometry; A-ABR, automated-auditory brainstem response; CDC, Centers for Disease Control and Prevention; RFP, request for proposals; PHL, permanent hearing loss; dB, decibel; nHL, normal hearing level; JCIH, Joint Committee on Infant Hearing; NCHAM, National Center for Hearing Assessment and Management.

Since 1993, the percentage of infants who have been screened for hearing loss in the United States has increased dramatically, from <5% in 1993 to >90% at the beginning of 2004.[1] This increase in newborn hearing screening resulted from several factors. First, largely as a result of the pioneering efforts of Dr Marion Downs,[2] the importance of newborn hearing screening became recognized as early as 1969, when the Joint Committee on Infant Hearing was established.[3] Second, identification of hearing loss in the neonatal period became possible by the late 1980s as a result of the revolutionary work of Dr David Kemp in the development of the otoacoustic emission (OAE) technology that could be applied to the screening of hearing in infants[4] and the development of automated procedures and equipment for

doing auditory brainstem response (ABR) testing.[5] With the availability of this technology, Surgeon General C. Everett Koop issued an ambitious challenge in 1988 that by the year 2000, 90% of all infants who were born with significant hearing loss would be identified by 12 months of age. This challenge was incorporated into the Healthy People 2000 National Health Promotion and Disease Prevention Objectives.[6] The Rhode Island Hearing Assessment Project demonstrated the feasibility of accomplishing that objective.[7] This project, begun in 1989, was the first large-scale newborn hearing screening program implemented in both a NICU and a well-infant nursery. A total of 1850 infants were screened using otoacoustic emissions, and almost 6 infants per 1000 were identified with congenital hearing loss. (The unusually high prevalence of hearing loss in this study is attributable in part to the sample's having significantly more infants from the NICU [16%] as would be the case in a general population sample.)

In March 1993, the National Institutes of Health held a Consensus Conference about early identification of hearing loss and recommended that all infants be screened for hearing loss during the first 6 months of life using a 2-stage screening protocol[8]: "The preferred model for screening should begin with an evoked otoacoustic emissions test and should be followed by an auditory brainstem response test for all infants who fail the evoked otoacoustic emissions test." In 1994, the Joint Committee on Infant Hearing recommended the universal detection of hearing loss by 3 months of age, with appropriate intervention beginning no later than 6 months of age.[9]

As hospitals implemented successful newborn hearing screening programs, there was growing interest in determining which screening protocols were most efficient. Shortly after the 1993 Consensus Conference, the National Institute on Deafness and Other Communication Disorders (NIDCD) provided funding for a large-scale, multisite study of the 3 physiologic measures used most frequently at that time for newborn hearing screening: transient evoked otoacoustic emissions (TEOAE), distortion product otoacoustic emissions (DPOAE), and ABR. This study's design and results were described as a landmark for newborn hearing screening.[10] Seven institutions participated in the study to examine the efficacy of TEOAE, DPOAE, and ABR methods in identifying infants with a hearing loss. A total of 7179 infants were recruited for the study, including graduates of the NICU and well infants with 1 or more risk factors for hearing loss. At 8 to 12 months corrected age, these infants were evaluated using visual reinforcement audiometry (VRA).[11] The results from this study showed both the feasibility of using each of those 3 physiologic measures for newborn hearing screening[12] and the appropriateness of using VRA to assess accurately the hearing status of infants.[13] In fact, on the basis of this study and others, VRA is now frequently referred to as the "gold standard" for assessing infants' hearing status.[14,15]

During this same period, the equipment for doing both OAE and ABR screening continued to evolve, and more hospitals began implementing screening programs using automated equipment, particularly the ABR. Currently, most ABR equipment used in newborn hearing screening programs is automated ABR (A-ABR), in which a statistical algorithm is used by the equipment to determine whether the infant passes or fails.

Because of concerns about high false-positive rates in many newborn hearing screening programs[16] and the associated problems caused by high percentages of infants being lost to follow-up,[17] many managers of newborn hearing screening programs began looking for ways to reduce the percentage of infants who failed the newborn hearing screening, without increasing the percentage of infants who had congenital hearing loss and passed the screening protocol. The 2-stage OAE/A-ABR was a likely solution because refer rates at time of hospital discharge from such programs were reported to be much lower than those in programs that used just OAE screening.[18,19] However, there was also concern that such programs might be reducing the refer rate at time of hospital discharge at the expense of missing infants with congenital hearing loss.

Responding to these concerns, the Centers for Disease Control and Prevention (CDC) issued a request for proposals (RFP) in January 2000 for a study that would test the efficacy of the 2-stage OAE/A-ABR newborn hearing screening protocol. The RFP stated, "Concerns have been raised about infants who fail OAE but pass ABR and are then dismissed from follow-up. These infants may have a mild loss that was missed by ABR." In response to this RFP, the study reported here was designed to determine how many infants who fail the OAE and pass the A-ABR in a 2-stage newborn hearing screening protocol have permanent hearing loss (PHL) when they are ~9 months of age.

METHODS

Study Population

A multicenter, prospective, cohort study was implemented with a geographically dispersed group of 7 birthing centers. To be considered for inclusion in the study, hospitals had to have at least 2000 births per year and have a successful program of universal newborn hearing screening using a 2-stage OAE/A-ABR protocol. "Successful" was defined as having operated a newborn hearing screening program for at least a 6-month period immediately before the initiation of the study with referral rates of <10% for OAE and 4% for A-ABR and existence of a tracking and follow-up system that had been successful in getting ≥85% of infants referred from screening to return for diagnostic evaluation. Also required was access to a facility where infants in the sample could be evaluated by experienced audiologists with demonstrated competence using VRA and other procedures in the diagnosis of hearing loss for infants who are younger than 1 year.[13] Each facility had to be willing to develop and use collaboratively a standardized VRA protocol. In addition, hospitals were selected so that the characteristics of the study's birth cohort would be similar in ethnic and socioeconomic characteristics to births in the United States.

Newborn hearing screening in the hospitals was done using either TEOAE screening equipment from Otodynamics LTD (www.otodynamics.com) or DPOAE screening equipment from Bio-logic Systems Corp (www.blsc.com/hearing/audx1.html). For A-ABR screening, all sites used the Algo Newborn Hearing Screener from Natus Medical, Inc (www.natus.com/products/a3.html) that uses a 35-decibel (dB) normal hearing level (nHL) click to screen for hearing.

Infants were recruited over a 21-month period (May 2001

through January 2003). Only infants from families whose primary language was English or Spanish were recruited and enrolled in the study. In addition, in 5 of the 7 sites, infants from the well-infant nursery and the NICU participated in the study, but in the remaining 2 sites, only infants from the well-infant nursery were included because these 2 hospitals used only a single screening technology (A-ABR) in their NICU.

To assist in interpreting the results, the study used a comparison group of infants who were born during the same time period in the same hospitals. These infants were referred for diagnostic follow-up because of their failing both the OAE and the A-ABR. The prevalence of PHL in this comparison group was used as a reference point to help interpret the significance of the number of infants with PHL identified in the study group. To the degree possible, co-investigators obtained the same demographic, prenatal, and neonatal data; risk indicators for hearing loss; and socioeconomic data for infants in the comparison group as were obtained for the study group. Audiologic diagnostic data were also obtained for each infant in the comparison group, although the diagnostic protocol for these infants was not always identical to that used for infants in the study group. For the 2 sites that enrolled study infants only in the well-infant nursery, the comparison group was also restricted to the well-infant nursery.

Infants who were in the study group and for whom 1 or both ears met the enrollment criteria were followed to obtain diagnostic evaluation data at ~9 months of age. When infants with 1 study ear returned for a diagnostic assessment, the presumably normal ear was often tested using the same protocol.

Design

Each infant who was born at 1 of the 7 sites during the enrollment period (May 2001 through January 2003), who failed the OAE but passed the subsequent A-ABR screening, and whose primary family language was English or Spanish was eligible to participate in the study ($n = 3462$). Mothers of these infants were given a brochure (in either English or Spanish) explaining the "Healthy Hearing Project" and were invited to participate. Mothers who agreed to participate signed an informed consent form and completed a general information form, which included demographic and socioeconomic information as well as information to facilitate follow-up contact. The infant's medical records were reviewed to obtain prenatal and neonatal data and data about the Joint Committee on Infant Hearing (JCIH) risk indicators for late-onset or progressive hearing loss.[20] Parents who enrolled were given a small gift or financial remuneration (~$10) as compensation for the time involved in enrolling the infant in the study. Study protocols and procedures for obtaining informed consent were approved by the Institutional Review Boards of all participating hospitals, the CDC, and the University of Hawaii.

After an enrolled infant was discharged from the hospital, parents received a postcard to thank them for their agreement to participate in the study. Every 2 months thereafter, parents received a postcard to remind them of their participation. The postcards also asked them short, simple questions about their child's developmental progress. Forwarding address corrections were requested from the post office. When the infants were ~7 months of age, the parents were contacted by telephone to schedule a time to bring the infant for a diagnostic audiologic evaluation. Parents were reimbursed for each diagnostic visit (generally $20 per visit) to pay for transportation and child care and to compensate them for their time.

Diagnostic Procedures

In the follow-up testing, the diagnostic protocol included the collection of data using at least VRA, tympanometry, and OAE. The VRA protocol required minimum behavioral response levels of 15-dB hearing level, using insert earphones, at 500 Hz, 1 kHz, 2 kHz, and 4 kHz. Tympanometry (a test of middle ear function) was obtained on each ear. OAE testing was conducted using either TEOAE or DPOAE. When appropriate, other diagnostic data were collected (eg, tone pip auditory brainstem response, bone conduction responses). Masking on the nontest ear was used when appropriate.

To ensure consistency and comparability across sites, detailed instructions were provided to each cooperating audiologist for conducting the audiologic evaluation. The project coordinator for diagnostic evaluations traveled to each site and confirmed that the

pediatric audiologists who would be conducting the audiologic evaluations had appropriate equipment and were able to implement correctly the agreed-on protocol. A standardized form for data collection was completed after each diagnostic evaluation. These forms were reviewed regularly by the research staff, and feedback was given as necessary to ensure that the protocol was being followed.

Infants were scheduled for the audiologic evaluations after they reached 7 months of adjusted age. For some infants, multiple testing sessions were necessary because of the difficulty in completing the entire protocol in a single session: 67.6% of the infants completed it in 1 session, 24.5% completed it in 2 sessions, and 7.9% completed it in 3 or more sessions.

Data Management

As each infant was enrolled, the general information and enrollment forms with a unique-site identifier but minus any personal identifying information were forwarded to the National Center for Hearing Assessment and Management (NCHAM) at Utah State University. Summary data were posted by NCHAM at least monthly on a password-protected web site. Contact information for each enrolled child was maintained by the respective sites and was updated with any address changes received from the post office. NCHAM notified sites monthly of any missing data for individual children, the date on which contact postcards were to be mailed, and the due dates for diagnostic assessments.

As diagnostic data were obtained, the study forms showing the results of the evaluation were also forwarded to NCHAM and linked via a study-generated identification number with the information about that infant. Procedures were also established for deactivating infants whose parents decided that they no longer wanted to participate in the study. For each such case, it was determined whether any data that were previously collected on the infant could still be used in the study. Information on the comparison group was also sent to NCHAM for data entry.

The information on the web site was updated regularly and could be accessed at any time by the investigators through the use of a password. Demographic and enrollment data were reviewed in monthly conference calls, which enabled the co-investigators to monitor the progress of the study.

Definition of Hearing Status

All co-investigators reviewed the diagnostic audiologic data for each child in the study group and agreed on the hearing status for that child according to 1 of the 7 groups outlined in Table 1. These definitions were used to determine how many infants in the study group passed the 2-stage hearing screening protocol but had PHL when they were tested at ~9 months of age. Although infants in the high-suspicion category were not hearing normally at the time of their initial diagnostic evaluation, these children were not available for a repeat audiologic evaluation to confirm their hearing status. In all of these cases, extensive efforts to have these "at risk for PHL" children return for additional evaluation were unsuccessful, and co-investigators agreed that there were not sufficient data to place them in the PHL category.

RESULTS

Information about the enrollment of study infants at each of the sites is shown in Table 2. During the enrollment period, 86 634 infants were born at the sites. Of those, 3462 (4.0%) failed the OAE and passed the A-ABR. Parents of 1524 (44%) of these infants agreed to participate in the study. The percentage of infants who failed the OAE and passed the A-ABR and were enrolled varied significantly between sites from a low of 18.3% to a high of 87.9%. This variation can be attributed to the following factors: two of the sites, comprising 33% of the 86 634 births, were located in the New York City area, and recruitment of parents in those sites was disrupted for several months after the terrorist attacks on the World Trade Center in September 2001. In addition, temporary workforce shortages significantly re-

TABLE 1.   Definitions Used to Determine Hearing Status

Category	Description
Not PHL	Using the "best" results from all assessments, MRL thresholds of ≤20 dB HL at 1 kHz, 2 kHz, and 4 kHz.
Probable Not PHL	MRL data not available at 1 kHz, 2 kHz, and 4 kHz, but all frequencies had MRLs ≤20 dB or OAEs within normal limits* or toneburst ABR data ≤25 dB nHL.
PHL Sensorineural	MRLs ≥25 dB at 1 kHz, 2 kHz, or 4 kHz (tested with good confidence) or ABR threshold ≥30 dB nHL and, if tested, OAEs below normal limits at the frequencies with elevated MRLs and normal middle ear functioning based on tympanometry or bone conduction.
Permanent Conductive	MRLs ≥25 dB at 1 kHz, 2 kHz, or 4 kHz (tested with good confidence) and, if tested, OAEs below normal limits and bone conduction thresholds ≤20 dB with an air/bone gap ≥15 dB at frequencies with MRLs ≥25 dB. Otitis media ruled out on the basis of clinical examination and tympanometry.
High increased suspicion of PHL	MRLs ≥25 dB at 1 kHz, 2 kHz, or 4 kHz but OAEs within normal limits for those frequencies or only fair confidence in VRA testing.
Some increased suspicion of PHL	MRLs ≥30 dB at 1 frequency or ≥25 dB at >1 frequency but abnormal tympanometry and no bone conduction or sound field thresholds ≥25 dB (with fair confidence) and normal tympanometry and OAEs below normal limits.
Not sufficient data to rule out PHL	Even though child returned for diagnostic evaluation, no MRLs or OAEs within normal limits for 1 kHz, 2 kHz, or 4 kHz and none of the above criteria for PHL were met.

MRL indicates minimum response level.
* Normal OAEs were defined as a signal to noise ratio of ≥3 dB for 1 kHz and ≥6 dB for 2 to 4 kHz.

TABLE 2.   Enrollment Summary for Participating Sites

	Enrollment Period	Births During Enrollment Period	No. of Infants				Referral Rate During Enrollment Period		Infants Recruited From
			Failed OAE Passed A-ABR	Total Enrolled	Not Recruited	Families Refused Enrollment	OAE	A-ABR	
Site 1	May 1, 2001, to Dec 31, 2002	16 608	1044 (6.3%)	191 (18.3%)	418 (40.0%)	435 (41.7%)	6.3%	0.8%	WB/NICU
Site 2	Jun 1, 2001, to Jan 31, 2003	9393	421 (4.5%)	370 (87.9%)	18 (4.3%)	33 (7.8%)	4.5%	0.9%	WB/NICU
Site 3	Sep 20, 2001, to Jan, 2003	4509	285 (6.3%)	84 (29.5%)	186 (65.3%)	15 (5.3%)	8.0%	1.0%	WB
Site 4	May 15, 2001, to Jan 31, 2003	9252	209 (2.3%)	147 (70.3%)	30 (14.4%)	32 (15.3%)	3.1%	0.8%	WB
Site 5	May 1, 2001, to Jan 31, 2003	24 032	456 (1.9%)	170 (37.3%)	11 (2.4%)	275 (60.3%)	2.4%	0.8%	WB/NICU
Site 6	May 1, 2001, to Jan 31, 2003	6217	433 (7.0%)	266 (61.4%)	50 (11.5%)	117 (27.0%)	9.6%	2.8%	WB/NICU
Site 7	May 1, 2001, to Jan 31, 2003	16 623	614 (3.7%)	296 (48.2%)	71 (11.6%)	247 (40.2%)	5.3%	1.2%	WB/NICU
Total		86 634	3462	1524	784	1154	4.8%	1.0%	
% of eligible				44.0	22.6	33.3			

WB = Well baby nursery; NICU = Neonatal intensive care unit

duced recruitment at many of the sites at various times. Finally, a significant number of families at all sites were not recruited because their primary language was not Spanish or English, their residence was so far from the hospital that it was not reasonable to expect them to return for diagnostic evaluations, or the infant was born on a day when so many births occurred that the staff did not have time to recruit families for the study. In addition, 33.3% of the invited families declined to participate. That this percentage ranged from a low of 5.3% to a high of 60.3% among sites suggests that it was at least partly related to the skill and enthusiasm with which the invitation was presented. On the basis of the demographic characteristics of the enrolled infants, the co-investigators did not have any reason to believe that the incidence of hearing loss would be higher or lower among those who were enrolled than those whose infants failed OAE and passed A-ABR but were not enrolled.

Twelve percent of the enrolled newborns were in the NICU for ≥3 days. The mean birth weight for the sample was 3323 g, 12.6% of the infants had low birth weight (≤2500 g), and 5.6% had very low birth weight (<1500 g). The ethnicity of the sample was similar to the US birth cohort for the year with the exception of having a lower percentage of Hispanics (13.4% in the sample compared with 17.9% in the national birth cohort) and more Asian and Pacific Islanders (7.0% in the sample compared with 1.7% of the national birth cohort). Of the families enrolled, 2.9% reported that they did not have health insurance. Annual household income was highly variable.

Table 3 shows the hearing status of the 973 (63.8%) of the 1524 enrolled infants who returned for diagnostic evaluation. This return rate is very close to the

TABLE 3. Hearing Status of Infants in the Study Group by Site

	No. of Infants With Data Diagnosis	% of Enrolled Infants With Data Diagnosis	Total Ears	Not PHL Ears	Probable Not PHL Ears	Ears With PHL		Ears With Increased Suspicion of PHL		Ears With "Not Sufficient Data"
						SNHL	PC	High	Some	
Site 1	81	42.4%	148	131	6	0	0	0	0	11
Site 2	299	80.8%	478	432	35	7	0	0	0	4
Site 3	42	50.0%	59	40	6	0	0	0	2	11
Site 4	109	74.1%	165	82	24	10	5	17	12	15
Site 5	86	50.6%	111	58	16	2	0	0	5	30
Site 6	184	69.2%	241	202	8	4	0	2	8	17
Site 7	172	58.1%	230	195	5	2	0	0	1	27
Total	973	63.8%	1432	1140	100	25	5	19	28	115
			100%	79.6%	7.0%	1.7%	0.3%	1.3%	2.0%	8.0%

PC indicates permanent conductive; SNHL, sensorineural hearing loss.

return rate of 64% in the earlier NIDCD multicenter study on the efficacy of screening technologies used in newborn hearing screening.[13] Reasons for not returning included that the family had moved and the current address could not be found, refused to make an appointment, did not return telephone calls or respond to letters, and/or repeatedly failed to keep appointments. Because some of the infants in the study group failed OAE and passed A-ABR in only 1 ear, 1432 ears were evaluated.

On the basis of the definitions given earlier in Table 1, hearing status was determined for 1317 (92.0%) ears of the infants who returned for audiologic follow-up. Of those who returned, 30 of the ears (21 infants) had PHL. For an additional 19 ears (1.3% of the sample), the available data raised suspicion about the possibility of PHL. However, sufficient data were not obtained to meet the strict inclusion criteria for PHL outlined in Table 1. For some infants (8.0% of the total study group; $n = 115$), there were insufficient diagnostic data to reach a conclusion about hearing status. In all cases, this was because the parents could not be reached after the initial evaluations or decided not to return for additional diagnostic evaluations.

As shown in Table 4, infants with PHL who failed the newborn hearing screening OAE but passed A-ABR were identified in 5 of the 7 participating sites (the prevalence of PHL among those who received diagnostic testing at each site that identified infants ranged from 0.006% to 0.092%). That sites 2 and 4 identified 15 of the 21 infants raises questions about whether the quality with which the research or diagnostic procedures were implemented might have affected the number of infants who were identified with PHL. The quality of implementation at each site was evaluated by examining the variables shown in Table 4. As can be seen, the sites that identified most of the infants with PHL (2 and 4) were the best implemented sites (average rankings across the 4 variables of 1.3 and 2.8, respectively), and the sites that identified no infants with PHL (1 and 3) ranked relatively low on these variables (average rankings of 5.8 and 4.8, respectively).

Table 5 provides additional information about the 21 infants in the study group who passed the second stage of the OAE/A-ABR screening protocol and were identified with PHL at ~9 months of age. In most ears ($n = 23$), the hearing loss was mild, with more infants having unilateral ($n = 12$) than bilateral ($n = 9$) hearing loss. Although most of the infants ($n = 18$) received a diagnosis of a sensorineural hearing loss, 3 of the 21 infants had a permanent conductive hearing loss caused by a physical abnormality of the external or middle ear instead of a problem with the cochlea or auditory nerve. Eight of these infants with hearing loss had 1 or more risk indicators for late-onset or progressive hearing loss as specified by the JCIH.[20]

The following reference points were used to evaluate the clinical significance of identifying 21 infants with PHL in the study group:

- The incidence of PHL among infants in the same birth cohort of 86 634 infants who failed both the initial OAE and the A-ABR (hereafter referred to as the comparison group)
- Some infants in the study group had 1 ear that met the criteria for inclusion in the study group and the other ear passed the initial OAE screen; if the

TABLE 4. Indicators of Implementation Quality at Each Site

	No. of Study Group Infants With PHL	Average "Rank" for Implementation Quality of Site	Births During Enrollment Period	% and No. of Eligible Infants Enrolled	% and No. of Refusals During Recruitment	% Returning for Diagnostic Evaluations	% With "Not Sufficient Data"
Site 1	0	5.8	16 608	18.3/191	41.7/435	42.4	7.4
Site 2	5	1.3	9393	87.9/370	7.8/33	80.8	0.8
Site 3	0	4.8	4509	29.5/84	5.3/15	50.0	18.6
Site 4	10	2.8	9252	70.3/147	15.3/32	74.1	9.1
Site 5	2	6.0	24 032	37.3/170	60.3/275	50.6	27.0
Site 6	3	3.0	6217	61.4/266	27.0/117	69.2	7.1
Site 7	1	4.5	16 623	48.2/296	40.2/247	58.1	11.7

TABLE 5. Characteristics of Infants With PHL in Study Group

Patient	Site	ID	Ear	MRL at 0.5 kHz	MRL at 1 kHz	MRL at 2 kHz	MRL at 4 kHz	Mean MRL (1 kHz, 2 kHz, and 4 kHz)	Type of Hearing Loss	Hearing Status of "Other" Ear	No. of Days in NICU	Gender	Annual Household Income	Mother's Ethnicity	Health Insurance	Gestational Age	Birth Weight, g	JCIH Risk Indicators for Late-Onset PHL
1	2	053	R	25	25	30	35	30	Mild SN		0	M	$35 000	White	Private Insurance	38	3150	
			L	20	25	30	35	30	Mild SN									
2	2	091	R	20	25	35	35	32	Mild SN		64	M	$35 000	Black	Private HMO	27	645	Yes
			L	20	35	35	35	35	Mild SN									
3	2	130	L	25	30	35	45	35	Mild SN	PHL	5	F	$45 000	White	Private Insurance	38	3160	Yes
4	2	131	L	30	35	40	45	40	Mild SN	PHL	42	M	$45 000	White	Private Insurance	27	1450	
5	2	148	R	25	30	35	35	33	Mild SN	nh	37	M	$25 000	White	Medicaid	28	1205	Yes
6	4	005	R	45	40	40	60	47	Moderate PC		0	M	$15 000	Asian	Private Insurance	39	2942	
			L	35	35	30	35	33	Mild PC									
7	4	020	L	35	20	25	20	22	Mild SN	nh	0	F	$50 000+	White	Private Insurance	40	2940	
8	4	027	R	20	30	20	40	30	Mild PC		0	M	$25 000	Asian	Private Insurance	40	3456	
			L	40	20	50	60	43	Mild PC									
9	4	029	R	20	20	40	45	35	Mild SN	nh	0	F	$50 000+	Mixed	Private HMO	40	3136	Yes
10	4	055	R	25	25	20	30	25	Mild SN	nh	0	M	$50 000+	Mixed	Private HMO	37	4060	
11	4	066	R	30	40	15	40	32	Mild PC	nh	0	M	$45 000	Pacific Islander	Private HMO	39	2892	Yes
12	4	089	R	C	35	30	35	33	Mild SN	nh	0	M	$15 000	Mixed	Medicaid	37	3535	Yes
13	4	122	R	40	40	45	40	42	Moderate SN		0	F	$7500	Asian	Private Insurance	38	2368	
			L	40	40	45	40	42	Moderate SN									
14	4	126	R	15	20	25	30	25	Mild SN		0	F	$25 000	Asian	Medicaid	42	3379	
			L	20	20	15	30	22	Mild SN									
15	4	138	R	20	30	20	30	27	Mild SN		0	M	$50 000+	Mixed	Private HMO	38	2832	
			L	40	40	30	30	33	Mild SN									
16	5	046	R	55	65	65	65	65	Severe SN	nh	0	M	$45 000	White	Private HMO	40	3288	
17	5	065	R	91+	D	91+	91+	91+	Profound SN	PHL	5	F	$50 000+	Black	Private HMO	36	2126	Yes
18	6	002	R	25	25	20	20	22	Mild SN		0	M	<$5000	White	Medicaid	37	2830	
			L	25	25	30	25	27	Mild SN									
19	6	003	L	45	45	60	55	53	Moderate SN	nh	0	M	<$5000	White	Medicaid	37	3040	
20	6	072	L	50	40	30	40	37	Mild SN	nh	40	M	$50 000+	White	Private Insurance	40	2942	Yes
21	7	258	R	30	45	30	50	42	Moderate SN		0	M	$35 000	White	Private Insurance	36	2892	
			L	40	35	40	40	38	Mild SN									

R indicates right; L, left; M, male; F, female; C, could not test; D, did not test.

2-stage OAE/A-ABR protocol is "missing" ears with hearing loss, then one would expect the incidence of PHL to be much higher among "failed" ears than among "passed" ears

• The percentage of the 21 infants who had PHL and might have been identified at a reasonably early age because their opposite ear failed the A-ABR or because they had a risk indicator that might have led to subsequent audiologic monitoring

Results for each of these reference points are summarized below.

Incidence of PHL Among Comparison Group Infants

Of the 86 634 infants in the birth cohort from which infants were recruited for this study, 704 were referred for a diagnostic audiologic evaluation because they failed the OAE and failed the A-ABR screening. As shown in Table 6, follow-up diagnostic results were obtained on 604 (85.8%) of these infants as part of the procedures for the newborn hearing screening program at the study sites. Of the 604 infants, 158 (243 ears) were identified with PHL (an incidence of 1.82 infants with PHL per 1000). Thus, the total number of infants from this birth cohort who were identified with PHL was 179 (158 who failed OAE and failed A-ABR, plus the 21 infants in the study group who failed OAE and passed A-ABR). Infants who had PHL but who passed the A-ABR and would not normally have been referred for diagnostic evaluation represent 11.7% of all hearing loss identified in the birth cohort (an incidence of 0.24 infants per 1000).

For accurately estimating the percentage of all infants who have PHL and would be expected to pass the OAE/A-ABR screening protocol as implemented in these hospitals, an adjustment must be made for the fact that only 44% of the 3462 eligible infants (those who failed OAE and passed A-ABR) in the birth cohort were recruited and scheduled to return for a diagnostic assessment at 8 to 12 months of age. In the comparison group, 100% of the infants who failed OAE and failed A-ABR were asked to return for a diagnostic evaluation. In other words, the 21 infants with PHL in the study group are from a subset of 1524 of 3462, or 44%, of the eligible infants. Thus, the best estimate of the prevalence per 1000 of PHL among infants who failed OAE and passed A-ABR is 21 infants divided by 39 119 (which is 44% of 86 634). This yields an estimate of 0.54 infants with PHL per 1000 in the study group, which is 22.8% of the infants with PHL in the birth cohort.

It could also be argued that the best estimate of the number of infants who have PHL and fail newborn hearing screening OAE and pass A-ABR would require making an adjustment for the fact that there were likely some infants who have PHL among the 36% of the study group (551 infants) and did not return for a diagnostic evaluation. However, because it is unclear whether the incidence of PHL in this nonreturning group would be lower or higher than the returning group, it was decided not to make any adjustment because of the lack of complete diagnostic data. (For example, the incidence in the returning group likely would be higher if parents in this group had some "cues" from the infant that he or she was not hearing correctly, and thus they were more likely to return for a diagnostic evaluation. The incidence in the nonreturning group would be higher if factors that contribute to not returning (eg, poor health of the child, low socioeconomic status of family) are also predictive of the child's having PHL.) This means that the estimate given above is a conservative estimate of the percentage of children who have PHL and fail the OAE and pass the A-ABR in the newborn hearing screening program.

Incidence of PHL Among Nonstudy Ears of Enrolled Infants

A substantial number of infants were enrolled in the study group because 1 ear failed the OAE and passed the A-ABR in the hospital screening (the study group ear). However, the opposite ear for these infants passed the OAE and was generally not screened with A-ABR before discharge. When these infants returned for their diagnostic audiologic evaluation, the ear that passed the initial OAE was sometimes evaluated. Table 7 shows that none of these 496 ears that passed the hospital-based OAE was diagnosed with PHL. It is important to note that 17 of these ears were categorized as having increased suspicion of PHL. These ears were not categorized as having PHL because all of the losses could have been caused by otitis media and it was not possible to obtain additional diagnostic data for these children.

Identification by Risk Factor or Follow-up of Contralateral Ear

The clinical significance of finding that 21 infants who failed the OAE in the hospital but passed the

TABLE 6. Comparison Group Infants With PHL by Site

	Total Births During Enrollment	Total Infants With PHL	Referred for Diagnosis	Completed Diagnosis	Total Ears With PHL	Infants From	Prevalence of Infants With PHL (Per 1000)*
Site 1	16 608	18	1.2% (199)	82.4% (164)	26	WB/NICU	1.08
Site 2	9393	19	1.5% (140)	95.7% (134)	33	WB/NICU	2.02
Site 3	4509	4	0.2% (9)	88.9% (8)	6	WB	0.89
Site 4	9252	16	0.3% (28)	96.4% (27)	27	WB	1.73
Site 5	24 032	42	0.8% (193)	87.6% (169)	63	WB/NICU	1.75
Site 6	6217	17	0.7% (41)	65.9% (27)	27	WB/NICU	2.73
Site 7	16 623	42	0.6% (94)	79.8% (75)	61	WB/NICU	2.53
Total	86 634	158	704 (0.8%)	604 (85.8%)	243		1.82

* Prevalence is for this study only because infants from the NICU in hospitals 3 and 4 were not included as either sample or comparison infants.

TABLE 7. Hearing Status of "TEOAE-Passed" Ears of Study Group Infants

	Total Ears	Not PHL	PHL		Increased Suspicion of PHL		Probable Not PHL	Not Sufficient Data
			SNHL	PC	High	Some		
Site 1	13	11	0	0	0	0	0	2
Site 2	112	107	0	0	1	0	3	1
Site 3	25	3	0	0	1	0	15	6
Site 4	53	19	0	0	2	6	15	11
Site 5	53	30	0	0	1	2	5	15
Site 6	127	60	0	0	3	1	38	25
Site 7	113	30	0	0	0	0	22	61
Total	496 (100%)	260 (52.4%)	0 (0.0%)	0 (0.0%)	8 (1.6%)	9 (1.8%)	98 (19.8%)	121 (24.4%)

TABLE 8. Degree of PHL* in Study Group and Comparison Group Infants

	Mild (25–40 dB)	Moderate (41–70 dB)	Severe Through Profound (≥71 dB)	Total Infants With PHL
Study group	15 (71.4%)	5 (23.8%)	1 (4.8%)	21 (100.0%)
Comparison group	31 (19.6%)	64 (40.5%)	63 (39.9%)	158 (100.0%)
Total	46 (25.7%)	69 (38.5%)	64 (35.8%)	179 (100.0%)

* For the poorer ear.

A-ABR were identified later with PHL depends in part on how likely it is that these infants' PHL would have been identified at an early age by other means. As shown in Table 5, 8 of the 21 infants with PHL had 1 or more of the risk indicators for late-onset or progressive loss specified by the JCIH.[20] If the infants with risk factors were receiving audiologic monitoring every 6 months as currently recommended by the JCIH,[20] then their PHL likely would have been identified at an early age. However, the expense of doing such frequent audiologic monitoring is substantial, and very few infants with these risk indicators currently receive such monitoring in the United States.[21]

One additional infant from the study group who received a diagnosis of PHL probably would have been identified early because the other ear failed the OAE and failed the A-ABR. Thus, under the protocol being used in the participating hospital, this infant would have been called back for a diagnostic evaluation, although the ear that qualified him for inclusion in the study passed the A-ABR. In summary, 43% of the 21 infants who have PHL and were not identified by the 2-stage OAE/A-ABR screening protocol had a risk factor for late-onset or progressive hearing loss or would have been followed because the other ear failed the initial A-ABR.

Degree of PHL for Infants in Study and Comparison Group Infant

Table 8 shows the distribution of degree of PHL for infants in the study and comparison groups. As can be seen, infants who have hearing loss and fail the OAE but pass the A-ABR are most likely to have mild PHL, but this is not the case with infants who fail OAE and fail A-ABR.

DISCUSSION

Data from this study demonstrate that a substantial number of infants who have PHL when they are ~9 months of age will not be identified by a 2-stage OAE/A-ABR newborn hearing screening protocol in which infants who fail an initial OAE but pass a subsequent A-ABR are not followed after discharge. It is estimated that ~23% of all infants with PHL ≥25 dB will not be identified because they pass the A-ABR. The majority of infants who are not identified will have mild hearing loss (>70% in this study), but the exact proportion of the PHL that is congenital as opposed to late-onset hearing loss is unknown. Given that many of these infants do not exhibit indicators for late-onset or progressive loss as specified by the JCIH and that almost all of the infants who were not identified by the 2-stage protocol have mild hearing loss, it is likely that many of these infants had congenital hearing loss. Although this hypothesis needs additional evaluation, it is consistent with the conclusions from the study by Norton et al[11], in which only 1 of 56 ears with PHL at 8 to 12 months of age was thought to have late-onset hearing loss.[22]

Several issues need to be considered in evaluating the importance of the fact that 21 infants who failed the OAE and passed the A-ABR were found to have PHL at ~9 months of age. First, when universal newborn hearing screening programs were being implemented in the early 1990s, the primary goal was to identify infants with congenital moderate or greater bilateral hearing loss. Consequently, newborn hearing screening equipment (particularly A-ABR equipment) was developed with this objective in mind. In the past decade, there has been increasing interest in identifying milder forms of congenital hearing loss,[23,24] but the same equipment is still being used in most newborn hearing screening programs. Therefore, it is important to emphasize that this study provides data about the percentage of infants who have PHL (primarily mild PHL) and are not identified using the 2-stage OAE/A-ABR protocol, which was implemented with equipment that was designed to identify moderate and greater degrees of hearing loss.

Second, there is still debate about what should be done to intervene with infants who have elevated hearing thresholds on the order of 25 to 30 dB.[25] The purpose of this study, as outlined by the CDC, was to

identify how many infants with PHL ≥25 dB were not identified by the 2-stage OAE/A-ABR protocol for newborn hearing screening. This study did not address whether or which type of audiologic, medical, or educational follow-up interventions should be implemented with infants who have mild PHL.

Third, it would be inappropriate to conclude that a 2-stage (OAE/A-ABR) screening protocol should never be used because 23% of the infants with PHL by ~9 months of age are not identified with such a protocol. The appropriate protocol in a specific setting depends on many variables. For example, many factors can contribute to infants with PHL being "missed" in a newborn hearing screening program. One such factor is when hospitals experience difficulty getting parents to return for additional screening and diagnostic evaluation after the infant has been discharged from the hospital.[16,17,21] In such situations, many infants who have PHL and fail an initial screening in the hospital may still be missed because they do not return for additional screening and diagnostic tests. For example, consider a screening protocol that has perfect sensitivity and refers 10% of those screened. If 50% of those who fail the screen are lost to follow-up, then at least 50% of those with PHL will be "missed." Compare those results with a screening protocol that refers 1% of those screened but has only 75% sensitivity (similar to what was found in this study if all of the losses identified at 9 months of age were congenital). In this case, follow-up success probably could be improved substantially because more resources could be devoted to the much smaller number of infants who must be followed. Thus, in situations in which "loss to follow-up" is a serious problem, it is likely that a smaller number of infants with PHL might be "missed" by the protocol with a much lower refer rate, although it also has substantially lower sensitivity.

Fourth, the specific application of the 2-stage protocol in this study was one in which the A-ABR equipment being used was based on a click stimulus of 35 dB nHL. A 2-stage OAE/A-ABR protocol in which the stimulus used for A-ABR is set at a lower level, such as 25 dB nHL or 30 dB nHL, could be implemented. Although this probably would result in higher refer rates at the time of hospital discharge, there likely would be fewer infants who pass the A-ABR screening and are later identified with PHL.

Fifth, it is important to note that this study was not designed to determine the percentage of infants who pass OAE-based hospital screening and are found to have hearing loss at ~9 months of age. At first glance, the data in Table 7 for the "passed" ears seem to provide data about this issue. However, the sample size is too small to be confident that there would be no infants who pass the hospital-based OAE screening and would receive a diagnosis of PHL when they are ~9 months of age. For answering this important question, a study of similar magnitude in which infants who pass the hospital-based OAE screening are followed would be needed.

Finally, the study design specified by the CDC does not permit definitive conclusions with regard to how many of the 21 infants had congenital as opposed to late-onset PHL. That 8 of the 21 infants had 1 or more risk indicators associated with late-onset or progressive PHL is consistent with the hypothesis that some but not all of these infants with PHL had late-onset loss. Had a diagnostic ABR been done for each enrolled infant before hospital discharge, it would have been possible to estimate with more confidence the proportion of the 21 infants who had late-onset instead of congenital PHL. Resource limitations precluded this possibility. The National Institute on Deafness and Other Communication Disorders study[22] concluded that only 1 of 56 ears with PHL had late-onset loss that was missed by the procedures for newborn hearing screening used in that study. Considering all of the available data, although it is impossible to state the exact proportion, it is likely that a number of the study group infants with PHL at ~9 months of age had congenital hearing loss.

CONCLUSIONS

Results of this study lead to a number of important recommendations for screening hearing of infants and young children. First, screening for PHL should extend into early childhood. Likely settings for such screening include physicians' offices and early childhood programs. All programs that provide services to young children (eg, Head Start, early intervention, child care, community health clinics) should be vigilant in monitoring for delayed language development and possible hearing loss. Recent advances in screening technology make such screening feasible. Such continuous hearing screening is important because even a perfect newborn hearing screening program will never identify late-onset PHL or identify fluctuating hearing loss as a result of otitis media. Regardless of the results of newborn hearing screening, audiologic assessment is particularly important for infants and toddlers who are enrolled in an early intervention program because of speech and/or language delays.

Second, it is critically important to continue to emphasize to families and physicians that passing a hospital-based hearing screening test does not eliminate the need to monitor systematically and consistently language development and to conduct additional hearing screening. Parents are the front-line defense and at every opportunity should be provided with understandable information regarding language milestones and anticipatory guidance. Regardless of the results of the infant hearing screening, the medical home[26] of young children must always be vigilant in monitoring language development and hearing status.

Third, it is important for hearing screening programs to use equipment that is designed specifically for the level of hearing loss targeted for identification by the program. Programs that aim to identify infants with mild and unilateral hearing loss must use different stimulus levels (which may require different equipment) than they would use if their aim were to identify only moderate and greater hearing loss. One of the most important issues to be addressed is

the actual stimulus level at the tympanic membrane being used by the hearing screening equipment. In OAE screening devices, the sound pressure level of the test stimulus is monitored in the ear canal; thus, the intensity level of the evoking signal (clicks or tones) can be held constant for each infant regardless of differences in ear canal size. However, although the A-ABR screening device used by all sites in this study delivered a 35-dB nHL click stimulus, the actual sound pressure level present at the eardrum probably varied significantly from infant to infant depending on the physical volume of the closed ear canal, as shown by Stevens et al.[27] This variable could explain why some infants with mild degrees of hearing loss (and greater) may pass A-ABR screening while failing OAE. Furthermore, whenever a stimulus level is specified in dB nHL, the reference is the adult ear. Thus, a stimulus level of 35 dB nHL does not mean that a 35-dB hearing loss (or worse) will be detected in an infant. It is also important to remember that there are presently no agreed-on standards (American National Standards Institute or International Standards Organization) for calibrating OAE or ABR test equipment.

Fourth, the relative advantages and disadvantages of a 2-stage (OAE/A-ABR) protocol for newborn hearing screening need to be considered carefully for individual circumstances. In locations where getting infants to return for outpatient screening and testing is very difficult, the substantially lower refer rate that likely will be achieved by using both OAE and A-ABR has significant advantages.

Finally, the results of this study emphasize the need for better information about the incidence, causes, and correlates of late-onset hearing loss. Much of what is thought to be known about late-onset hearing loss is based on very small samples of data and on anecdotal reports. Although it is likely that many of the infants in the study group who were identified later with PHL had congenital hearing loss, the exact proportion is not known because of the gaps in our knowledge about late-onset hearing loss.

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