ARTICLE

Bacterial Meningitis Among Children With Cochlear Implants Beyond 24 Months After Implantation

Krista R. Biernath, MD[a], Jennita Reefhuis, PhD[a], Cynthia G. Whitney, MD[b], Eric A. Mann, MD, PhD[c], Pamela Costa, MA[a], John Eichwald, MA[a], Coleen Boyle, PhD[a]

[a]National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, Georgia; [b]National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; [c]Food and Drug Administration, Rockville, Maryland

The authors have indicated they have no financial relationships relevant to this article to disclose.

ABSTRACT

BACKGROUND. More than 11 000 children in the United States with severe-to-profound hearing loss have cochlear implants. A 2002 investigation involving pediatric cochlear implant recipients identified meningitis episodes from January 1, 1997, through September 15, 2002. The incidence of pneumococcal meningitis in the cohort was 138.2 cases per 100 000 person-years, >30 times higher than that for children in the general US population. Children with implants with positioners were at higher risk than children with other implant models. This higher risk of bacterial meningitis continued for up to 24 months after implantation.

OBJECTIVE. To evaluate additional reported cases to determine whether the increased rate of bacterial meningitis among children with cochlear implants extended beyond 24 months after implantation.

METHODS. Our study population consisted of the cohort of children identified through the 2002 investigation; it included 4265 children who received cochlear implants in the United States between January 1, 1997, and August 6, 2002, and who were <6 years of age at the time of implantation. We calculated updated incidence rates and incidence according to time since implantation.

RESULTS. We identified 12 new episodes of meningitis for 12 children. Eleven of the children had implants with positioners; 2 children died. Six episodes occurred >24 months after implantation. When cases identified in the 2002 and 2004 investigations were combined, the incidence rate of ≥24-months postimplantation bacterial meningitis among children with positioners was 450 cases per 100 000 person-years, compared with no cases among children without positioners.

CONCLUSIONS. Our updated findings support continued monitoring and prompt treatment of bacterial infections by health care providers and parents of children with cochlear implants. This vigilance remains important beyond 2 years after implantation, particularly among children with positioners. The vaccination recommendations for all children with implants, with and without positioners, and all potential recipients of implants continue to apply.

www.pediatrics.org/cgi/doi/10.1542/peds.2005-0824

doi:10.1542/peds.2005-0824

Key Words
hearing loss, intervention, meningitis, bacterial infections

Abbreviations
FDA—Food and Drug Administration
CDC—Centers for Disease Control and Prevention
CSF—cerebrospinal fluid

Accepted for publication Jun 8, 2005

Address correspondence to Krista R. Biernath, MD, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, 1600 Clifton Rd, MS E-88, Atlanta, GA 30333. E-mail: kbiernath@cdc.gov

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

CURRENTLY >11 000 CHILDREN in the United States with severe-to-profound hearing loss have a cochlear implant (James K. Kane, PhD, E-mail communication, 2005), a surgically implanted device that includes an electrode array that is inserted into the cochlea. In 2002, the US Food and Drug Administration (FDA) received reports of bacterial meningitis among children and adults who had received cochlear implants. In an investigation that identified meningitis episodes from January 1, 1997, through September 15, 2002, Reefhuis et al[1] described an incidence of pneumococcal meningitis in a cohort of pediatric cochlear implant recipients of 138.2 cases per 100 000 person-years, 30 times higher than that for children in the general US population. Children with implants with a positioner were at higher risk than were children with other types of implant models. A positioner is a small Silastic wedge inserted next to the implanted electrode in certain earlier device models, to facilitate transmission of electrical signals by pushing the electrode against the medial wall of the cochlea. Implant models with a positioner were available from 1999 until July 2002, at which time they were removed voluntarily from the market by the manufacturer. The 2002 investigation found that the rate of bacterial meningitis decreased rapidly in the first few months after implantation for children with cochlear implants with and without positioners. However, the rate for those with implants with positioners remained higher, compared with those with implants without positioners, for up to 24 months after implantation.[1]

Because of on-going reports of new cases, the Centers for Disease Control and Prevention (CDC) and the FDA updated the 2002 investigation through December 1, 2004. The focus of the 2002 and 2004 investigations was young children, because they account for the majority of known cases and represent the population that will receive most cochlear implants in the future. The purpose of the 2004 investigation was to evaluate the additional cases to determine whether the increased rate of bacterial meningitis among children with positioners extended beyond 24 months after implantation.

METHODS

The methods used in this investigation were similar to those used in the 2002 cohort study. Our study population consisted of the cohort of children identified during the 2002 investigation. This cohort included children who received a cochlear implant in the United States during the period from January 1, 1997, through August 6, 2002, and who were <6 years of age at the time of the implantation. In addition to 4264 children included in the original cohort, 1 additional child was identified as being eligible for the cohort after meningitis occurred, which resulted in a total cohort of 4265 children. The 2004 investigation included episodes that were identified from September 16, 2002, through December 1, 2004, by the FDA Adverse Event Reporting System. (Case reports were also requested through CDC surveillance programs, state health departments, and contacts with the 3 manufacturers of FDA-approved cochlear implants, but no additional cases were identified through these means.) Information on new cases was abstracted from medical records of hospitalizations for treatment of meningitis. Classification of bacterial meningitis cases and the definition of the use of a positioner were based on criteria from the previous study.[1] Briefly, cases of definite meningitis included those with a bacterial pathogen isolated from cerebrospinal fluid (CSF) or from blood with CSF findings suggesting bacterial meningitis. Cases of probable meningitis included those with abnormal CSF findings suggesting bacterial meningitis and evidence of bacteria in CSF (with antigen testing, Gram staining, or polymerase chain reaction testing). Possible meningitis was defined as abnormal CSF findings with no evidence of a nonbacterial cause or death after an unexplained illness with consistent symptoms. The use of a positioner was defined as use of an implant model that included the electrode positioner as well as a standard component (AB-5100H and AB-5100H-11; Advanced Bionics, Sylmar, CA).

We estimated the updated incidence of meningitis in the study population by using the sum of new and original cases of meningitis as the numerator and the number of person-years between implantation and the diagnosis of meningitis or between implantation and December 1, 2004, as the denominator. We calculated updated, stratified, incidence rates for type of implant and time since implantation. Incidence according to time since implantation was limited to children who received implants after the devices with the positioner became available in 1999.

RESULTS

Our cohort consisted of 3436 children with implants without positioners and 829 children with implants with positioners who received their implants between 1997 and August 6, 2002. The times since implantation for the cohort are depicted in Fig 1. The median time since implantation for children with implants without positioners was 59 months, compared with 42 months for children with positioners. At the time of the 2004 investigation, 67% of children with models without positioners had had their implants in place for ≥48 months, compared with 27% of children with models with positioners. A total of 12 new episodes of postimplantation bacterial meningitis were identified for 12 children (Table 1). Of the 12 children, 11 had implant models that included a positioner. Two of the twelve children died. Six children had factors other than an implant that might have predisposed them to meningitis; 2 children had radiographic evidence of inner ear malformations, 1 of the 2 children had a CSF leak, 3 children had ≥1 cases

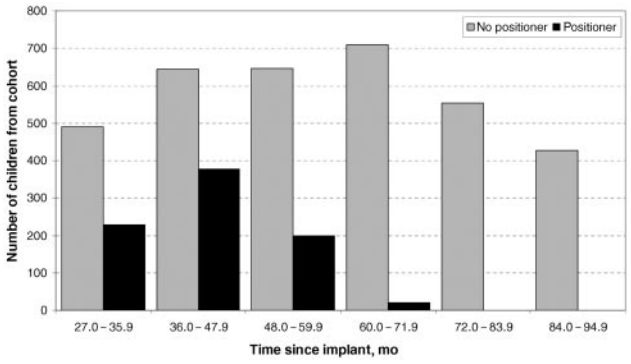

FIGURE 1
Distribution of times between implant date and December 1, 2004, for children in the United States who received cochlear implants, with or without positioners, before 6 years of age.

of meningitis before implantation, 1 child had a history of recurrent otitis media, 1 child had pressure-equalizing tubes, and 5 children had signs of acute otitis media at the time of presentation. The time between implantation and occurrence of meningitis was ≥24 months for 6 of the 12 episodes of meningitis; all 6 children had cochlear implant models with positioners.

Of the 12 episodes, 10 were cases of definite bacterial meningitis, 1 met the definition of probable meningitis, and 1 was classified as possible meningitis. *Streptococcus pneumoniae* accounted for 9 of the 10 episodes of definite bacterial meningitis; 1 of the 10 episodes was caused by group A *Streptococcus*. The 1 case of probable meningitis demonstrated Gram-positive cocci in the CSF examination, which suggested pneumococcal meningitis. Records for 4 of the 9 children with bacterial meningitis caused by *S pneumoniae* indicated partial pneumococcal immunization according to the current schedule,[2] 1 child was described as having received no pneumococcal immunization, and no records were available for the remaining 4 children.

When cases from the 2002 and 2004 investigations were combined, there was a total of 41 episodes of postimplantation bacterial meningitis among 38 children. Twenty-seven (71%) of those 38 children had implants with positioners. The updated incidence for all cases of meningitis in the cohort was 189 cases per 100 000 person-years (95% confidence interval: 155–288 cases per 100 000 person-years). Meningitis caused by *S pneumoniae* accounted for 120 cases per 100 000 person-years (95% confidence interval: 77–178 cases per 100 000 person-years).

The time from implantation to meningitis was ≥24 months in 8 (20%) of 41 episodes; 7 of those 8 children had cochlear implants with positioners. The incidence rate of ≥24-month postimplantation meningitis for children with positioners was 450 cases per 100 000 person-years (95% confidence interval: 165–980 cases per 100 000 person-years), compared with none for those without positioners. For this same time period, the incidence rate of meningitis caused by *S pneumoniae* for children with cochlear implants with positioners was 214 cases per 100 000 person-years (95% confidence interval: 44–627 cases per 100 000 person-years).

When the analysis was restricted to children who received implants between 1999 and 2002 (the time period the positioners were on the market), the incidence of bacterial meningitis between 0 and 63 months after implantation was higher among children with implants with positioners (915 cases per 100 000 person-years; 95% confidence interval: 603–1331 cases per 100 000 person-years) than among those with implant models without positioners (83 cases per 100 000 person-years; 95% confidence interval: 36–164 cases per 100 000 person-years). The incidence of meningitis among children with implants with and without positioners decreased sharply in the first few months after implantation (Table 2). However, the rate remained elevated for up to 48 months after implantation for children with cochlear implants with positioners, compared with the rate for children with implants without positioners. No cases of bacterial meningitis have been diagnosed among the 214 children who received their implants >4 years before December 1, 2004.

DISCUSSION

Our results suggest a continued high rate of meningitis among children with cochlear implants, especially those with implants with positioners. Since September 15, 2002, 12 additional episodes of bacterial meningitis were reported for 12 children from a cohort of 4265 children with cochlear implants. Although the overall incidence rates of meningitis were similar to those reported in the earlier cohort study, we found that the rate of meningitis decreased as the time after implantation increased. This decrease may reflect the decreased rate of bacterial meningitis seen in the general US population as children grow older.[3] However, the rate of bacterial meningitis among children with cochlear implants with positioners, although decreasing, continued to remain higher than that for the general population. The rate of pneumococcal meningitis among children with implants with positioners 24 to 47 months after implantation was 214 cases per 100 000 person-years, compared with the rate among children 24 to 59 months of age in the general population of 0.3 cases per 100 000 population (on average, in 2002 and 2003) (Cynthia G. Whitney, MD, E-mail communication, 2005). A more accurate comparison might be with the incidence of bacterial meningitis in the population of deaf or hard-of-hearing children without cochlear implants. However, such data are currently unavailable. During the study period, no cases of bacterial meningitis were reported among 214 children (both with and without positioners) who were monitored for >4 years, although the majority of children

TABLE 1 **Episodes of Postimplantation Bacterial Meningitis Occurring Between September 15, 2002, and December 1, 2004, and Predisposing Factors Among Children Who Received Cochlear Implants in the United States Between 1997 and 2002**

Patient No.	Time From Implantation to Meningitis, mo	Age at Time of Meningitis, mo	Gender	Causative Bacteria	Implant Model at Time of Episode	Radiographic Evidence of Inner Ear Malformation	CSF Leak or Gusher	Ventriculoperitoneal Shunt or Previous Meningitis	History of Recurrent Otitis Media	History of Tympanostomy Tubes After Implantation	Signs of Acute Otitis Media at Time of Meningitis Hospitalization
1	5	21	M	*Streptococcus pneumoniae*	AB-5100H-11	Not noted	Not noted	Not noted	No	Not noted	No
2[a]	9	47	M	*S pneumoniae*	AB-5100H-11	Not noted	Not noted	Yes[b]	Yes	Yes	Yes
3	10	48	M	*S pneumoniae*	AB-5100H-11	Yes[c]	Yes	Not noted	No	Not noted	Yes
4[a]	13	58	M	*S pneumoniae*	C40+HGB	Not noted	No	Yes[b]	No	No	No
5	17	49	M	*S pneumoniae*	AB-5100H-11	Not noted	Not noted	Not noted	Not noted	No	Yes
6	20	59	M	*S pneumoniae*	AB-5100H-11	Not noted	Not noted	Yes[b]	Not noted	Not noted	Yes
7[a,d]	25	52	M	Group A *Streptococcus*	AB-5100H-11	Not noted	No	No	No	No	No
8	28	48	F	Unknown	AB-5100H-11	Yes[e]	Not noted	Not noted	Not noted	Not noted	Yes
9	28	68	M	Unknown	AB-5100H	Not noted	Not noted	Not noted	Not noted	Not noted	No
10	35	70	M	*S pneumoniae*	AB-5100H	Not noted	Not noted	Not noted	Not noted	Not noted	Not noted
11[a,d]	36	103	F	*S pneumoniae*	AB-5100H-11	Not noted	No	No	No	No	No
12	40	79	F	*S pneumoniae*	AB-5100H	Not noted	Not noted	Not noted	Not noted	Not noted	No

This table includes only cases reported between September 16, 2002, and December 1, 2004.

[a] Risk factor data for patients 2, 4, 7, and 11 were coded as "yes" or "no." Risk factor data for all other patients were coded as "yes," "no," or "not noted." Because fewer information sources were used for this update, compared with the 2002 investigation, notation of uncertainty was made where possible.

[b] Meningitis before implantation.

[c] Cochlea had ~2 turns present.

[d] The child died at the time of the meningitis hospitalization.

[e] Cochlear hypoplasia with semicircular canal dysplasia.

TABLE 2 **Incidence Rates of Bacterial Meningitis Among Children With Cochlear Implants With and Without Positioners and Comparison of Time to Meningitis After Cochlear Implant Surgery (United States, 1999–2004)**

Time,[a] mo	Positioner		No Positioner		Incidence Rate Ratio (95% CI)[b]
	No. of Cases	Incidence Rate, Cases per 100 000 Person-y (95% CI)[b]	No. of Cases	Incidence Rate, Cases per 100 000 Person-y (95% CI)[b]	
0.0–0.9	4	5825 (1587–14 913)	3	1529 (315–4466)	3.8 (0.6–26.0)
1.0–2.9	5	3667 (1191–8558)	0	0 (0–941)	Undefined (2.6–∞)[c]
3.0–5.9	2	982 (119–3547)	0	0 (0–627)	Undefined (0.5–∞)[c]
6.0–11.9	6	1478 (543–3218)	2	170 (21–614)	8.7 (1.6–88.1)
12.0–23.9	4	497 (135–1273)	3	128 (26–373)	3.9 (0.7–26.6)
24.0–35.9	4	535 (146–1371)	0	0 (0–167)	Undefined (1.9–∞)[c]
36.0–47.9	3	458 (56–1654)	0	0 (0–229)	Undefined (0.7–∞)[c]

[a] No cases were observed for the period of 48 to 63 months after implantation.

[b] Confidence intervals (CIs) for incidence rates and incidence rate ratios were calculated with the exact method, under the assumption that the number of cases was a Poisson random variable.

[c] In cases where the incidence rate ratio was undefined, lower limits for the 95% confidence intervals were calculated with exact methods. The upper limit for these intervals was infinity.

with implants with positioners (583 of the 829 children) had had their implants for <4 years.

In the 2002 investigation, cases were ascertained through several sources, including contact with all parents. For the 2004 investigation, we did not contact parents but relied on reports to the FDA, CDC, and state health departments; therefore, case ascertainment might have been less complete. However, manufacturers are directed explicitly to report all cases of meningitis to the FDA, regardless of whether the device is perceived to have any causal relationship to the infection. Moreover, publication of the first article might have made parents and medical professionals more aware of the association between cochlear implants and meningitis, thus increasing the likelihood of these events being reported.

In this investigation, we reported our findings on the immunization status of the children identified as having bacterial meningitis after implantation. We relied on inpatient meningitis hospitalization records; therefore, our information on timing and number of doses of vaccines might be incomplete. In addition, given the retrospective nature of the study, we were unable to evaluate the serotype of the pneumococcal cases, because the isolates had been discarded. Therefore, it is not known whether these children were fully immunized against *S pneumoniae*.

At the time of the publication of results from the 2002 investigation, explantation (removal) of the positioner was not recommended as a means of preventing meningitis. This update reopens the discussion regarding whether explantation would be prudent. The benefit of explantation of the positioner (with or without replacement of the active electrode) in reducing the risk of meningitis is not known and likely would depend on the underlying pathophysiologic features of the disease process. Explantation of the positioner might be expected to reduce risk if infections resulted from a foreign body reaction or from bacteria from the middle ear entering the cochlea via the potential space between the electrode and positioner components.[4] However, the risk of bacterial meningitis for all types of implants is reported to be highest immediately after implantation, which suggests a risk associated with the surgery itself.[1] For instance, if increased risk stems from cochlear trauma produced by the positioner (either acute fracture or pressure-induced resorption of the osseous spiral lamina over time),[5] then the potential benefit of elective removal is less clear. Furthermore, inner ear malformations alone are associated with an increased risk of meningitis.[6] Therefore, in some cases in which the child has both an inner ear malformation and a cochlear implant, the cochlear implant may have no role or only a partial role in the pathogenesis of the disease. Regardless of the possible mechanism, the meningitis risk associated with reopening the cochleostomy and adequately resealing the void created by the positioner at the cochleostomy site must be considered in any decision related to elective removal of the positioner. One child (patient 3) in the study cohort with both a CSF leak and a congenital cochlear abnormality underwent removal of the positioner after the episode of postimplantation bacterial meningitis and then experienced an episode of suspected meningitis ~40 days after explantation. (This episode of suspected meningitis did not meet our case definition and therefore was not reported in the results.) Of note, ~150 cases of cochlear implant removal and reimplantation have been reported in the literature; the procedures were performed most commonly because of surgical wound breakdown and infection, device failure, or electrode misplacement but not meningitis.[7] Therefore, current data are insufficient to support a recommendation for elective explantation of the positioner after an episode of bacterial meningitis.

Since our initial cohort study in 2002, many children have received cochlear implants, although none has received the implant model with the positioner. Our updated findings support continued vigilance for symptoms of meningitis, as well as acute otitis media,[8] by health care providers and parents of all children with cochlear implants. This vigilance is important in the 2-year period

after implantation and >2 years after implantation, particularly among children with implants with positioners. In addition, the recommendation that all children with implants with and without positioners and all potential recipients of implants receive pneumococcal and *Haemophilus influenzae* type b vaccinations continues to apply for young children.[2,9] In addition, given the possibility that meningitis could have occurred through entry of bacteria into the inner ear through the cochleostomy, it would seem prudent to heed recommendations for meticulous intraoperative packing around the electrode at this site with soft tissue (eg, fascia, pericranium, or muscle).[10] Although the results of these studies are not generalizable to older children and adults, no significant difference in the risk of meningitis has been found across age categories for young children with cochlear implants.[1] Therefore, health care providers, parents of older children, and adults with implants should also be vigilant for symptoms of illness and should be aware of the immunization recommendations.

ACKNOWLEDGMENTS

We are indebted to L. Gelling, T. Hadley, S. Huang, C. Light, H. Marx, Jr., S. Rainey, A. Reingold, R. Rolfs, B. Schulz, D. Vugia, G. Watkins, and B. Zhu for their assistance; to L. Hershey, S. Holloway, M. Johnson, M. Messer, L. Peterson, and H. Thomas for their technical support; and to O. Devine, M. Honein, J. Kane, J. Moran, and D. Tavris for their scientific expertise.

REFERENCES

1. Reefhuis J, Honein MA, Whitney CG, et al. Risk of bacterial meningitis in children with cochlear implants. *N Engl J Med.* 2003;349:435–445
2. Centers for Disease Control and Prevention. Recommended childhood and adolescent immunization schedule: United States, 2005. *MMWR Morb Mortal Wkly Rep.* 2005;53:Q1–Q3
3. Schuchat A, Robinson K, Wenger JD, et al. Bacterial meningitis in the United States in 1995: Active Surveillance Team. *N Engl J Med.* 1997;337:970–976
4. Arnold W, Bredberg G, Gstottner W, et al. Meningitis following cochlear implantation: pathomechanisms, clinical symptoms, conservative and surgical treatments. *ORL J Otorhinolaryngol Relat Spec.* 2002;64:382–389
5. Cohen NL. Surgical techniques to avoid complications of cochlear implants in children. *Adv Otorhinolaryngol.* 1997;52:161–163
6. Ohlms LA, Edwards MS, Mason EO, Igarashi M, Alford BR, Smith RJ. Recurrent meningitis and Mondini dysplasia. *Arch Otolaryngol Head Neck Surg.* 1990;116:608–612
7. Woolford TJ, Saeed SR, Boyd P, Hartley C, Ramsden RT. Cochlear reimplantation. *Ann Otol Rhinol Laryngol Suppl.* 1995;166:449–453
8. Whitney CG. Cochlear implants and meningitis in children. *Pediatr Infect Dis J.* 2004;23:767–768
9. Centers for Disease Control and Prevention. Pneumococcal vaccination for cochlear implant candidates and recipients: updated recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep.* 2003;52:739–740
10. Cohen NL, Roland JT Jr, Marrinan M. Meningitis in cochlear implant recipients: the North American experience. *Otol Neurotol.* 2004;25:275–281

Bacterial Meningitis Among Children With Cochlear Implants Beyond 24 Months After Implantation

Krista R. Biernath, Jennita Reefhuis, Cynthia G. Whitney, Eric A. Mann, Pamela Costa, John Eichwald and Coleen Boyle

Pediatrics 2006;117;284-289; originally published online Jan 3, 2006;
DOI: 10.1542/peds.2005-0824