Hearing loss during bacterial meningitis

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Abstract

Objective—To determine the natural history and pathogenesis of hearing loss in children with acute bacterial meningitis.

Design—Multicentre prospective study.

Setting—21 hospitals in the south and west of England and South Wales.

Subjects—124 children between the ages of 4 weeks and 16 years with newly diagnosed bacterial meningitis.

Methods—Children underwent repeated audiological assessment with the first tests being performed within six hours of diagnosis. By using a combination of otoacoustic emissions, auditory brainstem responses, and tympanometry the differences between cochlear, neural, and conductive defects were distinguished.

Results—Ninety two children (74%) had meningococcal and 18 (15%) had pneumococcal meningitis. All cases of hearing loss were apparent at the time of the first assessment. Three children (2.4%, 95% confidence interval (CI) 0.5 to 6.9%) had permanent sensorineural hearing loss. Thirteen children (10.5%) had reversible hearing loss of whom nine had an impairment that resolved within 48 hours of diagnosis. It is believed that this 'fleeting' hearing loss has not been reported previously. The cochlea was identified as the site of the lesion in both the permanent sensorineural and reversible impairments. Hearing loss was more common in children who had been ill for more than 24 hours (relative risk 2.72; 95% CI 0.93 to 7.98).

Conclusions—Sensorineural hearing loss developed during the earliest stages of meningitis. Permanent deafness was rare but 10% of the patients had a rapidly reversible cochlear dysfunction. This may have progressed to permanent deafness if the patients had not been treated promptly.

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Deafness is the commonest serious complication of bacterial meningitis in childhood. In developed countries, approximately 10% of survivors are left with permanent sensorineural hearing loss.[1][2] Other children experience a transient loss of hearing.[2–6] Both types of hearing impairment are thought to develop during the first few days of the illness.[5–7] The pathological processes involved in postmeningitic hearing loss are uncertain. Postmortem reports[8][9] and some clinical studies[3–5] have sug-

gested that either the auditory nerves or the cochlea are damaged. However, there is also some evidence that lesions of the brainstem or higher centres are responsible.[10–12]

To find out more about the pathophysiology and natural history of postmeningitic hearing loss, we conducted a multicentre prospective study in which children with newly diagnosed bacterial meningitis underwent repeated audiological assessment. A battery of hearing tests was used, including the recently developed technique of otoacoustic emissions (OAEs). OAEs are minute sounds produced by the cochlea that can be recorded from nearly all normal ears.[13][14] Because the measurement of OAEs is quick, objective, and non-invasive, we were able to obtain sequential recordings when more conventional techniques would have been impossible. Also, because OAEs are abolished by lesions of the cochlea but preserved in retrocochlear (neural) deafness,[14] we were able to identify the site of the lesion in postmeningitic deafness.

Methods

PATIENTS

Between November 1993 and April 1995, children between the ages of 4 weeks and 16 years were recruited from 21 hospitals in the south and west of England and South Wales. We asked to be informed of all cases of bacterial meningitis within one hour of diagnosis. A working diagnosis was usually made on the basis of cerebrospinal fluid microscopy. Children with clinical signs of bacterial meningitis but who were deemed too ill to undergo lumbar puncture were also recruited. To be included in the analysis children were required to have either specific bacteria identified on microscopy or culture of cerebrospinal fluid, or to have convincing meningism plus at least one other sign of bacterial infection (cerebrospinal fluid neutrophil pleocytosis, positive blood culture, or petechiae indicative of meningococcal infection). Children were treated with intravenous cefotaxime, ceftriaxone, or a combination of penicillin and chloramphenicol, according to local policy. Dexamethasone was given at a dosage of 0.6 mg/kg/day in some centres. Informed consent was obtained before enrolling children into the study. Ethical approval had been granted by all participating centres.

HEARING TESTS

Recordings of transient evoked OAEs were attempted as soon as possible after diagnosis, and repeated at 6–12, 12–24, and 36–48 hours. OAEs were also recorded at discharge from hospital. The QuickScreen programme on the ILO88 System (Otodynamics, Hatfield) was

Table 1 Details of children with persistent sensorineural hearing loss

Patient No	Sex	Age (years)	Pathogen	Previous audiological history	Hearing loss at discharge	Follow up (time/outcome)
1	Male	0.1	Group B streptococcus	Not tested. Reacted to sound	Bilateral profound (> 100 dB HL)	18 months/continuing profound loss
2	Male	1.4	*S pneumoniae*	Normal	Bilateral severe (70 dB HL)	18 months/profound loss, awaiting cochlear implant
3	Male	9.1	*N meningitidis*★	Normal	Right severe (70 dB HL), left profound (110 dB)	9 months/continuing severe to profound losses

★ Case diagnosed on basis of cerebrospinal fluid pleocytosis plus petechial rash.

used as previously described.[15] The programme delivers a click stimulus to a loudspeaker that is contained within a loosely sealed aural probe. Acoustic responses are detected by a microphone that is also housed within the probe. The responses to 260 clicks are averaged and displayed by the system's software. In children where a convincing OAE was seen at an earlier stage the test was terminated after a minimum of 60 responses. The presence of an OAE was confirmed both visually and objectively using our previously validated screening criterion (pass = signal-to-noise ratio ≥ 3 dB on one or more bandwidths).[15] If OAEs were absent, the entire test procedure was repeated to exclude methodological failure. All OAEs were recorded and analysed by one experienced user (MPR).

Auditory brainstem responses were used to measure hearing thresholds shortly before discharge from hospital. Whenever possible, brainstem responses were also measured earlier to confirm hearing impairments detected by OAEs. Responses were recorded on a Sapphire 2A EP System (Medelec, Old Woking) and wave V thresholds were estimated to the nearest 10 dB hearing level (HL) using a conventional technique.[16] Hearing loss was classified according to previously used criteria[3] adapted for use with the above protocol. Absent wave V at 30 or 40 dB HL represented mild hearing loss. Thresholds of 50 to 60 dB represented moderate; 70 to 90 dB, severe; and over 90 dB, profound hearing losses. All children were examined otoscopically and by tympanometry at discharge, or earlier if they had absent OAEs. A type B tympanogram was taken to be indicative of a middle ear effusion.[17]

Hearing impairments were classified as conductive if the child had a brainstem threshold ≥ 30 dB HL, absent OAEs, and a type B tympanogram. Children with a raised threshold and normal tympanometry were classified as having a cochlear hearing loss if OAEs were absent, or a retrocochlear hearing loss if OAEs were preserved.

We performed audiological follow up using OAEs, brainstem responses, and tympanometry on children who had hearing loss of any degree at the time of discharge from hospital. These children were tested at one, three, and nine months after diagnosis. All children enrolled in the study were referred for local audiological follow up. We were informed of the results of these assessments.

ANALYSIS
The incidence of the various types of hearing loss is expressed as a proportion with an exact 95% confidence interval (CI). Potential clinical, microbiological, and biochemical risk factors for sensorineural hearing loss are expressed as a relative risk with the 95% CI. The same method is used to compare subgroups within the population.

Results
During the 18 month study period, 133 children with a working diagnosis of acute bacterial meningitis were enrolled. Nine patients did not fulfil the inclusion criteria, so the results from 124 children are presented. We estimate that this represents 83% of eligible children admitted to the participating centres. The patients' ages ranged from 0.1 to 15.6 years (median 2.1 years). There were no fatalities in this series.

Meningococcal meningitis was diagnosed in 92 children (74%). Fifty two of these children had *Neisseria meningitidis* isolated by microscopy or culture of cerebrospinal fluid. Twenty six patients had cerebrospinal fluid pleocytosis plus positive meningococcal blood cultures or petechiae, and 14 children who did not undergo lumbar puncture had meningism and evidence of meningococcal disease. *Streptococcus pneumoniae* was isolated from the cerebrospinal fluid of 18 patients (15%). There was one case each of meningitis due to *Haemophilus influenzae* type b, *Listeria monocytogenes*, and group B streptococcus. In the remaining 11 cases (8%), all of whom had a cerebrospinal fluid neutrophil pleocytosis, the pathogen was unknown. Thirty four children had received parenteral penicillin before admission. This included 24 of the 26 patients with cerebrospinal fluid pleocytosis and signs of meningococcal disease.

The first audiological tests were performed within six hours of diagnosis in 83 children (67%). All but five had the first test performed

Table 2 Details of children with severe reversible hearing loss

Patient No	Sex	Age (years)	Pathogen	Time after diagnosis until:	
				Hearing loss detected by OAE	Recovery of normal hearing
4	Male	0.3	*N meningitidis*★	3 hours†	5 days
5	Female	0.4	*N meningitidis*	12 hours†	40 hours
6	Female	0.4	*N meningitidis*★	8 hours†	20 hours
7	Male	0.4	*N meningitidis*	2 hours	42 hours
8	Female	0.4	*S pneumoniae*	3 hours	3 days
9	Male	0.8	*N meningitidis*★	7 hours†	18 hours
10	Female	0.9	*N meningitidis*	2 hours†	42 hours
11	Female	2.5	*N meningitidis*	2 hours	5 days
12	Male	3.8	*N meningitidis*	8 hours	44 hours
13	Male	4.2	*N meningitidis*★	5 hours†	21 hours
14	Male	7.4	*N meningitidis*★	12 hours	42 hours
15	Male	10.5	*N meningitidis*	1 hour‡	48 hours
16	Male	12.1	*N meningitidis*	2 hours‡	14 hours

★ Case diagnosed in absence of positive cerebrospinal fluid microscopy or culture.
Notes: † Moderate or severe hearing loss confirmed by auditory brainstem responses;
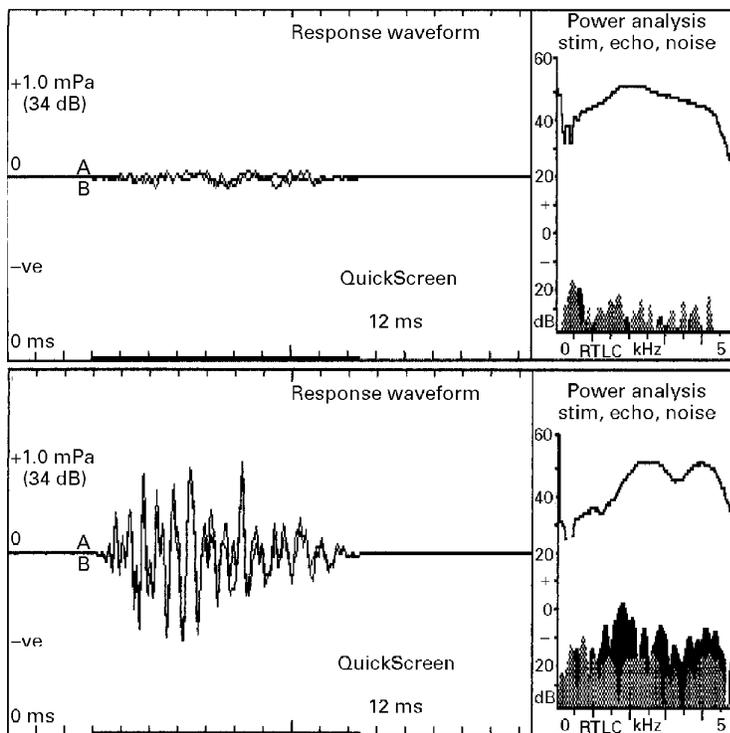‡ complained of hearing loss at presentation.

Figure 1   OAE recordings from a child with fleeting hearing loss. Left hand panel of each recording ('response waveform') is a visual representation of the soundwaves produced by the ear. Right hand panel ('power analysis') is a fast Fourier transformation of the response showing strength of signal (black) and an estimate of noise (hatched) across the auditory frequencies. In the upper recording, taken at two hours after diagnosis, there is no emission. Lower recording shows strong OAE at 42 hours.

within 24 hours. Twenty one children (17%) had hearing impairments detected at the time of their first OAE recordings. No children developed hearing loss at a later stage. The 21 children with evidence of hearing loss will be described according to their audiological diagnosis at discharge.

Three children (2.4%, 95% CI 0.5 to 6.9%) have persistent sensorineural hearing loss. The absence of OAEs in these children indicates cochlear damage. Their histories are summarised in table 1. Child number 3 complained of hearing loss at presentation.

Thirteen children had evidence of hearing impairment at the time of their first assessments but normal auditory function at discharge (table 2). The incidence of reversible hearing loss is therefore 10.5% (95% CI 5.7 to

Table 3   Potential risk factors for sensorineural hearing loss

| Characteristic | Sensorineural hearing | | Relative risk (95% CI) |
	Present (n=16)*	Absent (n=108)*	
Clinical:			
Age ≤ 12 months	8 (50)	33 (31)	2.02 (0.82 to 5.00)
History > 24 hours	12 (75)	53 (49)	2.72 (0.93 to 7.98)
Coma†	1 (6)	6 (6)	1.11 (0.17 to 7.24)
Seizures	2 (13)	13 (12)	1.04 (0.26 to 4.13)
Neurological signs‡	1 (6)	8 (7)	0.85 (0.12 to 6.08)
Cerebrospinal fluid			
S pneumoniae	2 (13)	16 (15)	0.84 (0.21 to 3.39)
N meningitidis	13 (81)	79 (73)	1.51 (0.46 to 4.96)
Glucose ≤ 1 mmol/l	8 (50)	32 (30)	1.57 (0.62 to 3.98)
Protein > 0.3 g/l	1 (6)	15 (14)	0.38 (0.05 to 2.76)
White cell count > 1.0×10⁹/l	5 (31)	43 (40)	0.49 (0.18 to 1.32)

* Values are number (%).
† Grade ≥ III on 0-IV scale.[18]
‡ Hemiplegia, cranial nerve palsy, or ataxia.

17.3%). All these children had absent OAEs and normal tympanograms, indicating cochlear dysfunction. In eight cases the hearing loss was bilateral. Nine children regained normal hearing within 48 hours of diagnosis. An example of this 'fleeting' hearing loss is shown in fig 1.

The prevalence of potential risk factors for hearing impairment is shown in table 3. For the sake of clarity, the data presented are for permanent and reversible sensorineural hearing loss combined. Independent analysis of each type of impairment produced similar results. No definite risk factors for sensorineural hearing loss were identified as the 95% CI for each relative risk included 1.0. Nevertheless, there did appear to be a trend towards a higher incidence of deafness in children who had been ill for over 24 hours before diagnosis (relative risk 2.72; 95% CI 0.93 to 7.98). The relationship between duration of symptoms and audiological outcome is demonstrated further in fig 2.

Thirty nine children in this study received dexamethasone as part of their treatment. In 29 patients the drug was given before, or concurrently with, the first dose of antibiotics. Dexamethasone was given within four hours of the diagnosis in eight others. In this non-randomised study the use of dexamethasone did not appear to affect audiological outcome. The relative risk of permanent or transient sensorineural hearing loss after steroid treatment was 1.70 (95% CI 0.68 to 4.23).

Five children (4.0%, 95% CI 1.3 to 9.2%), had absent OAEs in association with otoscopic
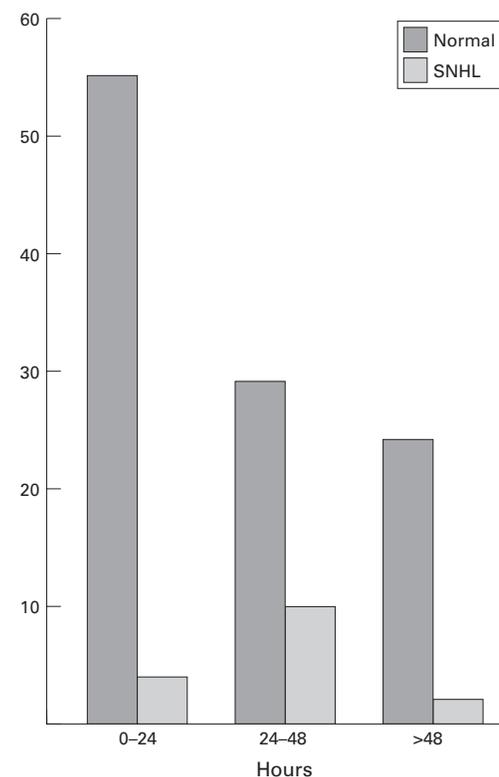

Figure 2   Duration of symptoms and number of children with normal hearing and permanent or reversible sensorineural hearing loss (SNHL).

and tympanometric evidence of middle ear effusions. All had mild to moderate hearing loss confirmed by auditory brainstem responses. These conductive impairments have persisted in four of the five children.

All children with hearing loss at discharge were followed up for at least nine months. Follow up data is also available for 104 (90%) of the remaining 116 children. Three of these children have mild to moderate conductive defects that were not present in hospital. The others have normal hearing.

Discussion

This study provides further evidence that hearing loss develops early in the course of bacterial meningitis. All children with hearing impairment had absent OAEs at the time of their first assessment. In most cases this was within six hours of diagnosis. Furthermore, three children actually complained of deafness at presentation. These findings extend the work of others who have detected sensorineural hearing loss within 24 to 48 hours of admission to hospital.[5–7] As most children with hearing loss had been unwell for between 24 and 48 hours, our data suggest that hearing loss commences during the first two days of the illness.

Until now, the cause of postmeningitic hearing loss has been uncertain. Lesions of the cochlea, auditory nerves, brainstem, and higher centres have all been proposed.[2 3 8–12] In our study, all children with sensorineural hearing loss failed to produce OAEs. Because the production of emissions is independent of the nervous system,[14] this observation suggests that the cochlea is the site of the lesion in postmeningitic deafness.

The cochlea has also been identified as the site of the auditory lesion in animal experiments. In the guinea pig, appropriate bacterial toxins have been shown to damage the organ of Corti.[19] In other experiments, bacteria and inflammatory cells have been seen in the cochlear aqueduct and the inner ear.[20 21] The cochlear aqueduct, which links the scala tympani to the subarachnoid space, has also been proposed as a route of bacterial invasion in children.[3 8 9] Indeed, the fact that the aqueduct is more likely to be patent in infancy than in adulthood[22] may explain the higher incidence of postmeningitic hearing loss in childhood.

The most striking finding of this study was that 10% of the subjects had a rapidly reversible hearing loss. All these children had evidence of hearing loss at admission but regained normal hearing within five days of diagnosis. Indeed, most cases had resolved within 48 hours. We do not believe that this 'fleeting' hearing loss has been reported before. Previous reports of reversible hearing loss have described children who have an impairment in hospital but then regain normal hearing over the following weeks or months.[3 6–11]

In our study, all children with reversible hearing loss had absent OAEs and normal tympanograms. This indicates cochlear dysfunction. We can only postulate as to the mechanism of this. It may result from the effects of bacterial toxins or inflammatory mediators on the hair cells of the organ of Corti.[19 23] Alternatively, the endocochlear potential could be disrupted by the same mechanisms.[24] Other possibilities include a metabolic defect secondary to low cerebrospinal fluid glucose,[9] and the effect of changes in intracranial pressure transmitted through the cochlear aqueduct. The latter mechanism is supported by case reports of patients who have lost hearing after lumbar puncture.[25] However, this finding has only been reported in adults, most of whom have undergone invasive procedures such as myelography or spinal anaesthesia. The fluid shift after diagnostic lumbar puncture with a paediatric needle is likely to be much less. Furthermore, three of our patients had evidence of hearing loss before lumbar puncture and one did not undergo the procedure. We do not therefore believe that fleeting hearing loss is caused by lumbar puncture. This conclusion is supported by the recent finding that large changes in intracranial pressure do not abolish OAEs in children.[26]

It is tempting to propose that fleeting hearing loss would progress to permanent deafness if the meningitis had not been treated. This hypothesis is supported by the work of Bhatt *et al* who found that rabbits always showed signs of hearing loss 12 hours after the intrathecal injection of live pneumococci.[21] Untreated animals progressed to permanent deafness whereas animals given antibiotics 12 hours after the induction of meningitis usually regained normal hearing.[27]

In a recent meta-analysis, the incidence of deafness in children surviving bacterial meningitis was reported to be 10.5% (95% CI 8.6 to 12.7%).[1] The incidence of permanent deafness in our study, at 2.4%, was much less. We are confident that this figure is accurate because all our patients underwent thorough audiological testing and we studied over 80% of eligible patients in the study area. Our inclusion criteria could be criticised because 51 patients did not have a bacterium isolated from the cerebrospinal fluid. However, the exclusion of these children does not alter the incidence figures for permanent and reversible sensorineural hearing loss.

How, then, can we account for the low incidence of postmeningitic hearing loss in this study? In most previous studies, *H influenzae* type b was the leading cause of meningitis.[1] After the introduction of *H influenzae* type b vaccination, this form of meningitis is now rare. Consequently, nearly three quarters of our cases were caused by the meningococcus. However, this change in epidemiology is unlikely to explain the rarity of deafness in our study because the incidence of hearing loss after meningococcal meningitis (1.1%) was also much lower than expected. The use of steroids cannot explain the reduction in deafness either. Dexamethasone has been shown to significantly reduce the incidence of deafness in some studies,[28 29] but in our population the children treated with steroids actually had a higher incidence of hearing loss (relative risk 1.70).

Key messages
- Sensorineural deafness is one of the most important complications of bacterial meningitis
- Hearing loss develops during the acute stage of meningitis
- The inner ear is the site of the auditory lesion in meningitis
- Many children have a reversible loss of hearing during the first two days of the illness.
- Early diagnosis and prompt treatment may be associated with a lower incidence of hearing loss

Another possibility is that the children in this study were less likely to become deaf because they were treated quickly. Half the children had been unwell for less than 24 hours before admission to hospital. In previous reports the average duration of symptoms has been around two days.[5 7 28] The relationship between the duration of illness and complications of meningitis is controversial.[30] Most prospective studies have not reported a significantly higher rate of deafness in children with long histories.[3 5 6 31] However, this negative finding may be due to a lack of statistical power in these studies,[32] and it is interesting to note that some large prospective[33] and retrospective[9 34] studies have reported statistically significant results. In this study, the duration of symptoms was not identified as a definite risk factor for sensorineural hearing loss (see table 3). Nevertheless, hearing loss was nearly three times as common in children who had been ill for over 24 hours. There is therefore some evidence that deafness was uncommon because of early diagnosis and prompt treatment. This hypothesis is supported by our discovery of fleeting hearing loss. As we have already discussed, this phenomenon appears to represent a critical period, around the second day of the illness, during which hearing loss can be reversed.

In summary, we have shown that sensorineural hearing loss develops very early in meningitis. In our study, it was exclusively cochlear in origin. Ten per cent of our patients had a fleeting hearing loss caused by reversible cochlear dysfunction. It is possible that this transient hearing loss would have progressed to permanent deafness if the meningitis had not been treated promptly.

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