Effects of Inner Ear Trauma on the Risk of Pneumococcal Meningitis

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Objective: To examine the risk of pneumococcal meningitis in healthy rats that received a severe surgical trauma to the modiolus and osseous spiral lamina or the standard insertion technique for acute cochlear implantation.

Design: Intervential animal studies.

Subjects: Fifty-four otologically normal adult Hooded-Wistar rats.

Interventions: Fifty-four rats (18 of which received a cochleostomy alone; 18, a cochleostomy and acute cochlear implantation using standard surgical techniques; and 18, a cochleostomy followed by severe inner ear trauma) were infected 4 weeks after surgery with *Streptococcus pneumoniae* via 3 different routes (hematogenous, middle ear, and inner ear) to represent all potential routes of bacterial infection from the upper respiratory tract to the meninges in cochlear implant recipients with meningitis.

Results: Severe trauma to the osseous spiral lamina and modiolus increased the risk of pneumococcal meningitis when the bacteria were given via the middle or inner ear (Fisher exact test, \( P < .05 \)). However, the risk of meningitis did not change when the bacteria were given via the hematogenous route. Acute electrode insertion did not alter the risk of subsequent pneumococcal meningitis for any route of infection.

Conclusions: Severe inner ear surgical trauma to the osseous spiral lamina and modiolus can increase the risk of pneumococcal meningitis. Therefore, every effort should be made to ensure that cochlear implant design and insertion technique cause minimal trauma to the bony structures of the inner ear to reduce the risk of pneumococcal meningitis.

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Since 2002, there has been an increase in the number of reported cases of pneumococcal meningitis in patients with a cochlear implant. Many of the implant recipients had preexisting risk factors for pneumococcal meningitis. Based on available clinical data, it is difficult to determine whether the presence of a cochlear implant increases the risk of meningitis caused by *Streptococcus pneumoniae* in subjects with no preexisting risk factors for the disease. However, animal studies have shown that a minimal threshold of *S pneumoniae* is required to induce meningitis in healthy rats and that this threshold is significantly reduced in the presence of a cochlear implant. Although cochlear implants may increase the risk of pneumococcal meningitis, the incidence of implant-related meningitis is still very low. The benefits of the cochlear implant in subjects with profound deafness far outweigh the risk of infection. Nevertheless, every effort should be made to minimize the infection risk in implant recipients.

The mechanism of cochlear implant–related pneumococcal meningitis is unclear. The surgical technique and insertion trauma to the inner ear structures are proposed to be possible mechanisms. Further study is required to investigate whether trauma to the osseous spiral lamina (OSL) and/or the modiolus, without the presence of an implant, can increase the risk of central nervous system (CNS) infection. Using the threshold principle developed in our previous study, we examined whether the presence of severe inner ear surgical trauma alters the risk of pneumococcal meningitis in rats. Because the bacteria that cause meningitis can reach the CNS from the upper respiratory tract mucosa by different routes (hematogenous or via the inner ear), we examined whether the threshold for infection
studies,5,6 which showed that bacterial inocula of this size did not cause meningitis in rats with a cochlear implant. The effect of surgical intervention on the risk of meningitis was significantly greater than in rats that underwent cochleostomy only (1-tailed Fisher exact test, $P<.05$).

<table>
<thead>
<tr>
<th>Route of Inoculation (CFU of Strep. pneumoniae Administered)</th>
<th>Cochleostomy Only (Group 1)</th>
<th>Electrode Insertion (Group 2)†</th>
<th>Severe Inner Ear Trauma (Group 3)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrapitoneal ($4 \times 10^6$)</td>
<td>0/6</td>
<td>0/6§</td>
<td>0/6§</td>
</tr>
<tr>
<td>Middle ear ($3 \times 10^6$)</td>
<td>0/6</td>
<td>2/6§</td>
<td>5/6</td>
</tr>
<tr>
<td>Inner ear ($1 \times 10^6$)</td>
<td>0/6</td>
<td>0/6§</td>
<td>6/6</td>
</tr>
</tbody>
</table>

Abbreviation: CFU, colony-forming units.

*Data are expressed as the number of rats with meningitis/number inoculated. Rats were monitored for 5 days after inoculation, and meningitis was diagnosed clinically and confirmed by histological examination results.
†The implant was removed immediately after insertion, and the cochleostomy was sealed with fascia.
‡The osseous spiral lamina and modiolus were traumatized by inserting a straight microneedle (catalog No. EN 2171; Kaisers, Perth, Australia) into the scala tympani via cochleostomy.
§The effect of surgical intervention on the risk of meningitis was not significantly greater than in rats that underwent cochleostomy only (1-tailed Fisher exact test, $P>.05$).
||The effect of surgical intervention on the risk of meningitis was significantly greater than in rats that underwent cochleostomy only (1-tailed Fisher exact test, $P<.05$).

was reduced in rats with inner ear surgical trauma for 3 different routes of infection: hematogenous, middle ear, and inner ear.

**METHODS**

**SOURCE OF THE ANIMALS**

All of the experimental animals were bred and housed in the animal house in the Department of Otolaryngology, University of Melbourne. Animals were free of endogenous pathogens, including S pneumoniae. All procedures and animal handling were conducted in accordance with guidelines set by the Animal Research and Ethics Committee of the Royal Victorian Eye and Ear Hospital, East Melbourne, Australia, and the 2004 Australian Code of Practice for the Care and Use of Animals for Scientific Purposes from the Australian National Health and Medical Research Council, Canberra.

In total, 54 otologically normal adult Hooded-Wistar rats (aged 10–16 weeks) weighing 100 to 400 g were randomly divided into 3 groups before receiving surgical intervention to the left ear 4 weeks before inoculation with S pneumoniae. The first group of 18 rats underwent a cochleostomy on the left inner ear (group 1). The second group of 18 rats received a cochlear implant via a cochleostomy of the left inner ear, followed by immediate removal of the implant (group 2). The third group of 18 rats received severe surgical trauma of the modiolus and OSL in the left inner ear (group 3).

The rats from each group (1, 2, and 3) were further subdivided into 3 groups of 6 to study the effect of inner ear trauma on 3 different routes of bacterial infection (middle ear, inner ear, and intrapitoneal [IP]) (Table 1). The dose of S pneumoniae chosen for each route of inoculation was based on our previous studies,5,6 which showed that bacterial inocula of this size did not induce meningitis in healthy rats with a cochleostomy but did cause meningitis in rats with a cochlear implant.

**ANIMAL SURGERY**

**Surgical Anesthesia**

Rats were anesthetized with an IP injection of a mixture of xylazine hydrochloride, 8 mg/kg, and ketamine hydrochloride, 75 mg/kg. A local anesthetic agent (0.1 mL of lidocaine hydrochloride with 0.0182 mg/mL of epinephrine tartrate; Troy Laboratories Pty Ltd, Smithfield, Australia) was injected subcutaneously around the surgical incision. The animals were then placed on a heated pad maintained at 37°C throughout the surgery. The animals were given 0.03 to 0.05 mg/kg of subcutaneous buprenorphine hydrochloride for analgesia immediately after surgery. They underwent continuous assessment for 48 hours for signs of postoperative pain and discomfort, and buprenorphine was given every 8 to 12 hours if there were signs of postoperative pain or discomfort. Animals received 10 mL/kg of subcutaneous isotonic sodium chloride solution for fluid replacement during the postoperative recovery period.

**Scala Tympani Electrode Array Design and Surgical Technique**

The dummy scala tympani electrode used in this study has been described previously. In brief, 4 mm of polyimide tubing (Cole-Parmer Instrument Company, Vernon Hills, Ill) with an outer diameter of 0.10 mm was coated with a layer of silicone (Dow Corning medical grade elastomer Silastic MDX4-4210; Factor II Inc, Lakeside, Ariz) to a diameter of 0.15 mm. The dummy electrodes were cleaned with absolute alcohol in an ultrasonic cleaner, then rinsed with and bathed in MilliQ water (Millipore, Billerica, Mass) for 10 minutes before drying, packaging, and sterilizing using hydrogen peroxide sterilization (STERRAD 100S system; Advanced Sterilization Products, Irvine, Calif).

 Fifty-four adult Hooded-Wistar rats received a cochleostomy to the left inner ear. The bulla and round window niche were exposed, the stapedial artery was cauterized with a bipolar coagulator (MF1; Zencor, Sydney, Australia), and a cochleostomy was performed just below the round window niche and at the location of the previously cauterized stapedial artery. For the control group of 18 rats, the cochleostomy was sealed immediately with fascia. The second group of 18 rats received surgical insertion of the cochlear implant as described in our previous studies.6,7 Bone dust and blood were carefully cleared away from the cochleostomy before placement of the electrode array, which was inserted 2 to 3 mm into the scala tympani. The electrode array was then immediately removed from the inner ear, and the cochleostomy was sealed with temporalis fascia. In the final group of 18 rats, the left inner ear structure was physically traumatized by inserting a straight microneedle (catalog No. EN 2171; Kaisers, Perth, Australia) into the scala tympani via the cochleostomy to fracture the OSL and modiolus. The cochleostomy was sealed with temporalis fas-
cia following the fracture of inner ear bony structures. The degree of trauma to the cochlea was subsequently confirmed by histological examination.

After the surgical procedure, all animals were given 2 subcutaneous doses of prophylactic enrofloxacin, 10 mg/kg, diluted 1:1 with isotonic sodium chloride solution. One dose was given immediately after surgery, and the second dose was given 12 hours later.

**PROCEDURES FOR INFECTION**

Four weeks after surgery, all 54 animals were inoculated with *S pneumoniae* 447A, which carries type 2 capsular antigen and was originally isolated from the cerebrospinal fluid of a child with meningitis. No antibiotics were given after infection.

The meningitis animal model using *S pneumoniae* 447A has been established in our previous work. The preparation of the bacterial inoculum has also been described in detail in our previous studies. Viable counts of the inoculum confirmed that each rat received the number of bacteria indicated in Table 1.

**Middle Ear Inoculation**

Under general anesthesia, the left bulla of 18 rats (6 each from groups 1, 2, and 3) was surgically exposed for direct inoculation of a 10-µL suspension containing 3 × 10^6 colony-forming units (CFUs) of *S pneumoniae* 447A (Table 1).

**Inner Ear Inoculation**

Under general anesthesia, the left bulla of 18 rats (6 each from groups 1, 2, and 3) was surgically exposed and a cochleostomy was performed with a straight Kirschner wire to access the scala tympani. Two microliters of perilymph was removed, and 1 µL of a bacterial suspension containing 1 × 10^4 CFUs of *S pneumoniae* 447A was slowly inoculated into the scala tympani. The cochleostomy was then covered with temporalis fascia and the wound was sutured in 2 layers.

**POSTINFECTION MONITORING**

Following the inoculation, each animal was examined at least twice daily for clinical signs of meningitis for 5 days. The clinical assessment was recorded on a 12-point scored monitoring sheet. Animals were humanely killed if 1 of the following conditions was met: a clinical assessment score of 11 or higher; a weight loss of greater than 25% of the animal’s original body weight; or a clinical assessment score of 5 to 10 with a rectal temperature of greater than 41°C. Animals without clinical evidence of meningitis were humanely killed at the end of the fifth day.

**Microbiological Specimen Collection and Tissue Preparation**

Once early signs of meningitis were evident, rats were deeply anesthetized with isoflurane and oxygen to allow collection of the cerebrospinal fluid, middle ear fluid, and blood for microscopy and culture. The collection methods used have been described previously.

The animals were then given a lethal intramuscular dose of pentobarbital sodium (pentobarbitone sodium [Lethabar]; Virbac Australia Pty Ltd, Peakhurst, Australia), 120 mg/kg of body weight, and were transcardially perfused with 0.9% isotonic sodium chloride solution, then 10% neutral buffered formalin (pH, 7.4) at 4°C. The brain, meninges, and cochlea were harvested and placed in 10% neutral buffered formalin for further processing.

Fifty-four brains with meninges were harvested, stored in 10% neutral buffered formalin for 48 hours, and then embedded in paraffin. The specimens were sectioned at a thickness of 10 µm, stained with hematoxylin-eosin or gram stain, and examined by light microscopy for presence of inflammation and bacteria.

Nine pairs of randomly selected cochleae were harvested from the temporal bones and fixed in 10% neutral buffered formalin. They were decalcified in a solution of 10% EDTA in 0.1M phosphate buffer (pH, 7.4), oriented in the midmodiolar position, and then embedded in Spurr resin. Two sets of twenty-one 2-µm sections were collected at 120-µm intervals throughout the cochlea. One set of 21 sections was stained with hematoxylin-eosin, and the other set, with gram stain.

Cerebrospinal fluid, blood, and middle ear fluid were collected for cultures as an adjunct to the histological analysis of the CNS to determine the presence of the bacteria. The serotype of *S pneumoniae* isolated from the cultures was determined using commercial typing serum samples (Statens Serum Institute, Copenhagen, Denmark) to determine whether the strain causing the disease was the same as that used for the initial inoculum.

**Histological Analysis**

The brain and meninges were examined for the presence of an inflammatory cell response within the subarachnoid space and brain tissue, thickening and hyperplasia of the meningeal cells, and bacteria within the subarachnoid space and brain tissue. The cochleae were examined for the extent of trauma to the OSL and modiolus and for the presence of bacteria and inflammatory cells.

**STATISTICAL ANALYSIS**

The effects of inserting a cochlear implant and surgically induced, severe intracochlear trauma in rats on the risk of developing pneumococcal meningitis for the 3 different routes of bacterial inoculation were evaluated statistically using the Fisher exact test (1-tailed). A *P* < .05 was considered to be significant.

In total, 13 of 54 rats developed meningitis (Table 1). They appeared tired, lethargic, and unresponsive to sound and light and had a hunched body posture, poor grooming, weight loss, and a rectal temperature higher than 38°C. When these signs developed, the histological examination findings of the brain consistently showed evidence...
of meningitis with inflammatory cells and gram-positive diplococci within the subarachnoid space. The correlation between the clinical signs of meningitis and histopathological evidence of meningitis was established in our previous work.\textsuperscript{5-7}

Two of the 18 rats in the cohort that underwent insertion and immediate removal of the scala tympani electrode array (group 2) acquired meningitis 110 to 112 hours after middle ear inoculation. Of the cohort of 18 rats subjected to severe left intracochlear trauma (group 3), 11 (5 inoculated via the middle ear and 6 inoculated directly into the inner ear) developed meningitis 64 to 120 hours after inoculation.

Compared with the control cohort (rats with cochleostomy only), rats subjected to implantation and immediate withdrawal of the scala tympani electrode array from the inner ear exhibited no significant increase in the incidence of meningitis for any of the 3 routes of inoculation (1-tailed Fisher exact test, \(P>0.05\)). However, the attack rate of meningitis was significantly raised in rats with a severe intracochlear trauma when bacteria were given via the middle ear (\(P=0.008\)) or the inner ear (\(P=0.001\)). Severe intracochlear trauma did not increase the risk of pneumococcal meningitis with IP administration of the bacteria (\(P>0.99\)).

**MICROBIOLOGICAL FINDINGS**

Culture results of the cerebrospinal fluid, blood, and middle ear fluid samples are summarized in Table 2. Examination of the pneumococci isolated from these samples showed them to be the same serotype as that used for the initial inoculum.

**COCHLEAR HISTOLOGY**

There was minimal damage to the inner ear structure of the left cochlea of rats for which the intervention was a cochleostomy or a short-term implantation of the electrode array (Figure 1). In 2 cochleae of rats that underwent electrode insertion only, absence of the organ of Corti in the basal turn was observed, but this did not increase the risk of cochlear or CNS infection. By contrast, extensive fractures of the OSL and modiolus were observed in rats subjected to the procedure aiming to traumatize the inner ear architecture (Figure 2).

The pattern and distribution of bacteria and inflammatory cells within the cochlea of rats with clinical and histological evidence of meningitis were consistent with those in our previous studies.\textsuperscript{5,7} In rats with meningitis following middle or inner ear inoculation, the cochlea ipsilateral to the inoculation contained bacteria and inflammatory cells within the scala tympani, scala vestibuli, Rosenthal canal, canaliculi perforantes (the pores within the wall of the OSL, adjacent to the scala tympani), and perineural and perivascular spaces within the modiolus and internal acoustic meatus (IAM) (Figure 3). Far fewer bacteria and inflammatory cells were observed within the ipsilateral scala media. The contralateral cochlea also exhibited bacteria and inflammatory cells within the IAM, modiolus, scala tympani, and scala vestibuli. However, less severe labyrinthitis was observed in these cochleae compared with the ipsilateral side (Figure 3). In the scala tympani of the contralateral ear, bacteria and inflammatory cells were prominent in the basal turn, close to the OSL; there were also more inflammatory cells in the scala tympani than in the scala vestibuli.

In the presence of severe trauma to the OSL and modiolus, numerous bacteria were present within the neural elements at the fracture sites. When the basic architecture of the modiolus and OSL was severely damaged, the perilymphatic spaces of the scala tympani and scala vestibuli were in direct contact with the neural elements within the modiolus and IAM. In these cochleae, there was no intervening fibrosis or osteogenesis between the bony fragments. Gram-positive cocci were observed within the perilymphatic space of the scalae and within the perineural and perivascular spaces of the modiolus and IAM. In a small number of traumatized co-

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**Table 2. Results of Microbiological and Pathological Examination of Rats With Cochlear Implantation and Severe Intracochlear Trauma After Inoculation With Streptococcus pneumoniae via 3 Different Routes**

<table>
<thead>
<tr>
<th>Routes of Inoculation and Procedure</th>
<th>Blood Culture</th>
<th>CSF Culture</th>
<th>Middle Ear Swab Culture</th>
<th>Meningitis Confirmed Histologically</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cochleostomy only (group 1)</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Electrode insertion (group 2)</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Severe inner ear trauma (group 3)</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cochleostomy only (group 1)</td>
<td>2</td>
<td>0</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Electrode insertion (group 2)</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Severe inner ear trauma (group 3)</td>
<td>6</td>
<td>4</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Cochleostomy only (group 1)</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Electrode insertion (group 2)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Severe inner ear trauma (group 3)</td>
<td>5</td>
<td>5</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

**Abbreviation:** CSF: cerebrospinal fluid.

**Note:** Data are expressed as the number of rats (of the 6 inoculated with *S pneumoniae*) with *S pneumoniae* cultured at necropsy. Serotyping of the isolated bacteria showed them to be the same as that used for inoculation.
chleae, extensive fibrosis and osteogenesis were seen within the scala. Despite this, numerous bacteria and inflammatory cells were seen within the fibrous tissue between the new and fractured bones, as well as in the modiolus and IAM (Figure 4 and Figure 5).

In rats without meningitis, the histological appearance of the cochleae was normal in animals undergoing IP inoculation. Small numbers of inflammatory cells and scant serofibrinous exudate were seen in the basal turn of the cochleae of rats inoculated via the middle or inner ear.

Macroscopic examination of the ipsilateral middle ear mucosa of the round window niche revealed evidence of middle ear inflammation in rats inoculated directly into

Figure 1. Low-power hematoxylin-eosin–stained photomicrographs illustrate representative cochlear histological findings in acute implantation (immediate withdrawal of the electrode array after insertion) nonmeningitic animals. Left (A) and right (B) cochleae 120 hours after intraperitoneal (IP) inoculation of 4 × 10^6 colony-forming units (CFUs) of Streptococcus pneumoniae. No inflammatory cells and bacteria were evident within the cochleae. The section of the cochlea at the level of cochleostomy (CO) for acute electrode insertion and fascial plug (FAS) is illustrated in part A. Left (C) and right (D) cochleae 120 hours after middle ear inoculation of 3 × 10^5 CFUs of S pneumoniae. Similarly, no inflammatory cells and bacteria were evident within the cochleae. Left (E) and right (F) cochleae 120 hours after direct inner ear inoculation of 1 × 10^5 CFUs of S pneumoniae into the left cochlea. Inflammatory cell response (IR) was evident in the basal turn of the ipsilateral cochlea. There were no inflammatory cells or bacteria in the more apical region of the cochlea or in the contralateral cochlea. There was no evidence of trauma to the osseous spiral lamina and the modiolus from acute insertion of a scala tympani electrode array. However, an absence of the organ of Corti was observed in the basal turn in the ipsilateral acutely implanted cochleae (A and E). The loss of the organ of Corti did not increase the risk of meningitis in these 2 rats.
the middle ear. The contralateral control bullae showed no evidence of middle ear inflammation. There were also no inflammatory changes in the middle ear mucosa of rats undergoing IP inoculation directly into the inner ear.

**COMMENT**

This study has demonstrated that the presence of severe inner ear trauma increases the risk of pneumococcal meningitis when bacteria were inoculated directly into the middle or inner ear of the ipsilateral side. However, severe inner ear trauma to the OSL and modiolus did not increase the risk of pneumococcal meningitis in cases of IP bacteria inoculation.

We have previously demonstrated that a minimum threshold of bacteria is required to induce meningitis in healthy rats and that this threshold differs according to the route of bacterial inoculation. Furthermore, the presence of a cochlear implant significantly reduces the threshold of bacteria required to induce meningitis for 3 different routes of inoculation routes (IP [hematogenous] or directly into the middle or inner ear). In this study, we showed that severe inner ear trauma as a result of surgery also reduced the threshold of bacteria required to cause meningitis via direct routes of infection, but only for direct routes of infection from the middle or inner ear. The likely explanation is that severe trauma to the OSL and modiolus creates a direct communication route between the inner ear and the subarachnoid space but does not alter the pathway for the bacteria to reach the meninges via the hematogenous route. This and our previous studies have shown that bacteria can reach the CNS via perineural and perivascular spaces within the modiolus and IAM. In normal cochleae, the bacteria were found to traverse the canaliculi perforantes to the Rosenthal canal and proceed from there to the CNS via the perineural and perivascular spaces within the modiolus and IAM. In the present study, there were more bacteria localized in neural structures at the fracture site compared with the cochleae, with minimal or no trauma to the OSL.

On the other hand, inner ear trauma can lead to fibrosis and osteogenesis in the long term, and this may obliterate the direct opening to the CNS created by the initial surgery. Under these circumstances, the threshold of infection may be similar to that in control animals with no inner ear trauma. Although fibrosis and osteogenesis were observed in a number of traumatized cochleae in this study, bacteria and inflammatory cells were found within the fibrous tissue between the bony fragments and in the neural elements within the modiolus and IAM. This is consistent with previous studies of human temporal bone in which inflammatory cells were observed to infiltrate the mature fibrous tract of the fractured temporal bone following meningitis, it is consistent with the observation that patients with fibrous union following a fracture of the base of the skull still have a higher risk of pneumococcal meningitis in the long term.

Previous animal studies have also demonstrated that bacteria and inflammatory cells can infiltrate the well-formed periimplant fibrous seal and fibromuscular wall of the stapedial artery in the event of a severe pneumococcal infection. Even when there is significant fibrous tissue repair within the inner ear, it is still unclear whether the fibrous tissue can resist pneumococcal infection. Be-

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**Figure 2.** Low-power hematoxylin-eosin-stained photomicrographs. A-C, Ipsilateral cochleae of 3 separate rats that received a severe inner ear trauma 120 hours after intraperitoneal inoculation of 4 × 10^6 colony-forming units of *Streptococcus pneumoniae*. These animals did not exhibit any clinical and histological (in the central nervous system) evidence of meningitis. The scalae of the cochleae were devoid of gross infection or inflammation. Extensive fractures (arrowheads) to the osseous spiral lamina (OSL) and modiolus were evident in the photomicrographs. There was no osteogenesis, and very minimal fibrosis was observed within the cochleae as a result of a severe inner ear trauma. C, A section of ipsilateral cochlea taken at the level of basal turn at the level of cochleostomy (CO). The location of the CO to allow surgically inflicted fractures to the OSL and modiolus and the fascial plug (FAS) can be seen.
cause no bacteria were observed within the newly formed bony tissues in this study, ossification (without intervening fibrosis) may resist direct spread of bacteria from the middle ear to the CNS. Complete ossification of the cochlea may follow meningitis, and it is plausible that this may protect against meningitis via the direct otologic route.

In traumatized cochleae in which there was minimal fibrosis and osteogenesis, it is possible that the damage to the inner ear structure was too extensive for complete healing to occur. It is also possible that a period of 4 weeks was insufficient for the rats used for this study to mount sufficient fibrous and bony tissue regrowth to resist the direct spread of infection from the inner ear to the CNS.

This study has demonstrated that insertion implantation of a scala tympani electrode array per se using the standard insertion technique in rats does not alter the threshold for pneumococcal meningitis by any of the 3 different routes of infection examined. Findings from histological examination of cochleae indicated that damage to the membranous labyrinth, OSL, and modiolus in these animals was minimal and insufficient to alter the threshold required for CNS infection. The absence of the organ of Corti in the basal turns was observed in 2 cochleae, and this may have been due to insertion of the electrode array. Nevertheless, loss of the organ of Corti in these animals did not increase their risk of developing meningitis.

Our study also provides novel insights into the possible mechanisms underlying the development of pneumococcal meningitis in patients with different cochlear implant designs. There is a greater incidence of meningitis in patients undergoing implantation with electrode arrays containing a positioner. In a recent clinical study, children receiving an implant with a positioner had 4.5 times the risk of developing meningitis compared with those who received other types of implants. It has been postulated that a 2-part electrode system may increase the likelihood of trauma to the OSL and/or the modiolus, thus allowing bacteria direct access to the subarachnoid space once they have entered the inner ear. Our data support the hypothesis that an extensive fracture to the OSL and modiolus as a result of inner ear sur-

Figure 3. Low-power hematoxylin-eosin-stained photographs illustrate a severely traumatized cochlea (fractures of the osseous spiral lamina [OSL] and modiolus [arrowheads]) (A) and contralateral control cochlea (B) of a rat 72 hours after middle ear inoculation of 3 × 10⁴ colony-forming units of *Streptococcus pneumoniae*. This animal exhibited clinical and histological (in the central nervous system) evidence of meningitis. In this example, there is severe labyrinthitis throughout the ipsilateral cochlea (A), whereas the contralateral cochlea exhibits evidence of infection predominately localized to the scala tympani (arrows) (B). High-power hematoxylin-eosin-stained micrograph of the fractured modiolus (C) and OSL (D) of the ipsilateral cochlea showing extensive inflammatory cells and bacterial infiltration within the fibrous tissue between the bony fragments. BN indicates bone; FIB, fibrous tissue; IC, inflammatory cells; arrowheads, fracture sites; and asterisk, histology process artifact.
Surgery may allow *S. pneumoniae* easier access to the perineural space and the perivascular space within the Rosenthal canal and the modiolus. In a recent study, severe insertion trauma, including fracture of the OSL, was observed when an implant device with a positioner was fully inserted into the cochlea. This injury appeared to occur primarily because the device was too large to permit full insertion into the scala tympani in 70% of the temporal bones examined.

This study compared the effect of severe surgical trauma within the inner ear with that of standard insertion of a single-component electrode array on the risk of pneumococcal meningitis. The effect of a moderate degree of trauma to the inner ear structures on the risk of pneumococcal meningitis was not examined because of the difficulty involved in creating inner ear trauma of varying severity consistently in our animal model. Therefore, a standard insertion technique using a single-component electrode array in human subjects is unlikely to induce a severe intracochlear trauma of the same degree that increased the risk of meningitis in the animal model. Currently, there are no clinical studies, to our knowledge, that examine the risk of meningitis in human subjects as a result of trauma to the OSL or to the other inner ear structures. However, the risk of meningitis was found to be significantly higher in patients who received a cochlear implant with a positioner. Furthermore, a significant trauma to inner ear architecture had also been observed via the inner ear. A severe trauma to the inner ear structures can be induced easily in small animals owing to the small size of the cochlea. However, this degree of trauma is difficult to achieve in human temporal bones during cochlear implantation using a single-component electrode array. If an insertion trauma to the inner ear occurs during human cochlear implantation, the trauma is unlikely to be as severe as the inner ear trauma demonstrated in this animal model.

**Figure 4.** Low-power hematoxylin-eosin–stained photographs illustrate a severely traumatized cochlea (fractures of osseous spiral lamina [OSL] and modiolus) (A) and contralateral control (B) cochlea of a rat 64 hours after inner ear inoculation of 1 × 10³ colony-forming units of *Streptococcus pneumoniae*. This animal exhibited clinical and histological (in the central nervous system) evidence of meningitis. In this example, there is extensive osteogenesis and fibrosis of the traumatized cochlea, especially at the upper cochlear turns. A severe labyrinthitis was also observed throughout the ipsilateral cochlea (A), whereas the contralateral cochlea exhibits a less severe labyrinthitis with the infection predominately localized to the scala tympani (arrows) (B). Higher-power hematoxylin-eosin–stained micrograph of the ossified scala (C and D) of the ipsilateral cochlea illustrates extensive inflammatory cells and bacterial infiltration within the fibrous tissue between the newly formed bony fragments. IC indicates inflammatory cells; OS, osteogenesis of new bone fragments. The approximate location of the higher-power micrographs in parts C and D are illustrated in the squares in part A.
in human temporal bone during implantation of an electrode array coupled with a positioner. Although the exact mechanism is still unclear, the findings from this animal model and previous temporal bone findings and clinical data suggest that a severe inner ear trauma may be one of the contributing factors to postimplantation meningitis.

Apart from the risk of infection, inner ear trauma has further implications for the survival of neural structures within the inner ear. Human temporal bone studies and animal studies have revealed the loss of spiral ganglion cells in regions of intracochlear damage following cochlear implantation. Although there is no clear correlation between speech discrimination performance and spiral ganglion cell counts obtained post mortem, the consequences of the loss of spiral ganglion neurons through cochlear implant trauma warrant further research. Preventing the loss of spiral ganglion cells may be especially important in young children, in whom lifetime use of the cochlear implant is anticipated. Because the indications for cochlear implantation expand to include individuals with some residual hearing, it is also important to reduce inner ear trauma to prevent damage to the residual hair cells. For these reasons, it is important to minimize the extent of insertion trauma within the cochlea to reduce the risk of meningitis and improve survival of hair cells and spiral ganglion neurons.

CONCLUSIONS

Severe trauma to the OSL and modiolus increased the risk of pneumococcal meningitis in healthy rats when *S. pneumoniae* was introduced directly into the middle or inner ear 4 weeks after the trauma. However, the same degree of surgical trauma to the bony structure of the inner ear did not alter the risk of pneumococcal meningitis when the bacteria were given via the hematogenous route. The standard insertion technique of a cochlear implant in healthy rats produced minimal trauma to the membranous OSL and modiolus and did not alter the risk of pneumococcal meningitis.

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