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Progression of changes in the sensorial elements of the cochlear and peripheral vestibular systems: the otitis media continuum

Rafael da Costa Monsanto, M.D., Ph.D Student^{1,2}, Patricia Schachern, B.S.¹, Michael M. Paparella, M.D.¹, Sebahattin Cureoglu, M.D.¹, and Norma de Oliveira Penido, M.D., Ph.D²

¹Department of Otolaryngology, University of Minnesota. Address: 2001 6th St. SE (Lions Research Building) – Room 210; Otopathology laboratory. Minneapolis, MN, USA; 55455

²Department of Otorhinolaryngology Head and Neck Surgery, Universidade Federal de São Paulo (UNIFESP), Escola Paulista de Medicina. Address: R. Sena Madureira, 1500 - Vila Clementino, São Paulo - SP, Brazil. Zip code 04021-001

Abstract

Our study aimed to evaluate pathologic changes in the cochlear (inner and outer hair cells and stria vascularis) and vestibular (vestibular hair cells, dark, and transitional cells) sensorial elements in temporal bones from donors who had otitis media. We studied 40 temporal bones from donors who had otitis media. These bones were categorized in serous otitis media (SOM), serous-purulent otitis media (SPOM), mucoid/mucoid-purulent otitis media (MOM/MPOM), and chronic otitis media (COM); control group comprised 10 nondiseased temporal bones. We found significant loss of inner and outer cochlear hair cells in the basal turn of the SPOM, MOM/MPOM and COM groups; significant loss of vestibular hair cells was observed in the MOM/MPOM and COM groups. All otitis media groups had smaller mean area of the stria vascularis in the basal turn of the cochlea when compared to controls. In conclusion, our study demonstrated more severe pathologic changes in the later stages of the continuum of otitis media (MOM/MPOM and COM). Those changes seem to progress from the basal turn of the cochlea (stria vascularis, then inner and outer hair cells) to the middle turn of the cochlea and to the saccule and utricle in the MOM/MPOM and COM stages.

Keywords

Otitis media; cochlear pathology; vestibular pathology; stria vascularis; cochlear hair cells; vestibular hair cells

Corresponding Author: Sebahattin Cureoglu, MD, Associate Professor, Co-Director, Otopathology Laboratory, Department of Otolaryngology, University of Minnesota, 2001 6th St. SE, Minneapolis, MN 55455 - Lions Research Building, Room 210, cureo003@umn.edu.

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1. Introduction

The term “otitis media” refers to a group of inflammatory diseases that affect the middle ear. The inflammatory changes secondary to otitis media progress in degree, over time, as a continuum, as first described by Paparella et al. (Paparella et al., 1990). An estimated 80% of newborns will have at least 1 episode of acute otitis media before the age of 3 (Teele et al., 1989), and 40% will have at least 6 recurrences before the age of 7 (Casselbrant et al., 1995a, 1995b). Worldwide, chronic otitis media affects 10% of the population, with up to 330 million people at risk for complications (Penido et al., 2016).

Hearing loss as a sequela of otitis media is very frequent, with a prevalence of 30.82 per 10,000 cases (Monasta et al., 2012). The early papers published in this regard by Paparella et al. (Paparella et al., 1984, 1972) were followed by several other histopathologic and clinical studies demonstrating sensorineural hearing loss in patients with chronic otitis media (Cureoglu et al., 2004; Kaya et al., 2016; Papp et al., 2003). Analyses of the temporal bones of donors who had chronic otitis media have documented various changes, including the loss of both inner and outer cochlear hair cells (Cureoglu et al., 2004), atrophy of the stria vascularis (Peng and Linthicum, 2016), and a decrease in the number of spiral ganglion cells, especially in the basal turn of the cochlea (Cureoglu et al., 2004; Paparella et al., 1972). Furthermore, clinical studies involving patients who had acute or serous otitis media found a higher incidence of high-frequency hearing loss and tinnitus secondary to the disease, suggesting the possibility of pathologic changes in the inner ear even in the earlier stages of the continuum (Margolis et al., 2000).

Damage to the sensorial epithelium of the vestibule secondary to otitis media has also been hypothesized (Casselbrant et al., 1995a; da Costa Monsanto et al., 2016; Mostafa et al., 2013): evidence shows that 53.5% of patients with chronic otitis media experience dizziness or vertigo during the evolution of the disease (Mostafa et al., 2013).

To our knowledge, no previous study has evaluated the parallel pathologic changes, due to otitis media, in the cochlear and peripheral vestibular systems. Thus, in this study, our objective was to evaluate the possible pathologic changes in those structures. We analyzed human temporal bones from donors whose otitis media had been at different stages of the continuum.

2. Materials and Methods

2.1 Temporal bones

From the human temporal bone collection at the University of Minnesota, we selected temporal bones from donors who had otitis media. We categorized those bones into 4 main types of otitis media, according to the characteristics of the pathologic changes of the middle ear (Fig. 1), as proposed by Paparella et al. (Paparella, 1976): (1) *serous otitis media – SOM* (presence of a pale effusion, constituting a yellow exudate, with low viscosity); (2) *serous-purulent otitis media – SPOM* (serous fluid with inflammatory cells, especially polymorphonuclear leukocytes); (3) *mucoïd/mucoïd-purulent otitis media – MOM/MPOM* (thick, opaque exudate, originating from active secretion of the mucoïd glands of a

metaplastic middle ear mucosa, with or without inflammatory cells); and (4) *chronic otitis media – COM* (presence of intractable changes in the middle ear, such as cholesteatoma, perforation of the eardrum, mature granulation tissue, fibrosis, tympanosclerosis, and cholesterol granuloma).

We excluded temporal bones from donors who had any of the following: tumors affecting the ear; hematologic diseases; irradiation of the head and neck; chemotherapy; a history of aminoglycoside use (either topical or systemic); otologic surgery other than tympanostomy tube insertion; Ménière's disease; clinical otosclerosis; or systemic autoimmune disease. In addition, we excluded temporal bones affected by processing artifacts. Then, we further screened the remaining samples to ensure integrity of the cochlea (organ of Corti, stria vascularis) and of the peripheral vestibular system (crista ampullaris of the lateral and posterior canals, macula of the saccule and utricle).

The selected temporal bones were age- and sex-matched, as closely as possible. Our final 4 otitis media groups included a total of 40 temporal bones (10 SOM, 10 SPOM, 10 MOM/MPOM, and 10 COM). Our control group included 10 temporal bones from donors with no clinical history and no histologic signs of ear diseases; these 10 bones were age- and sex-matched to our otitis media groups.

The temporal bones had previously been harvested during autopsy, fixed in 10% buffered formalin, decalcified with ethylenediaminetetraacetic acid or trichloroacetic acid, dehydrated in graded concentrations of alcohol, and embedded in celloidin. Each bone was serially sectioned in the horizontal plane at a thickness of 20 µm. Every 10th section was stained by hematoxylin81 eosin; those sections were used in our study.

Three of the authors were responsible for scrutinizing the temporal bones. The authors were blinded from the group that each temporal bone belong to and some patient information, including sex, age, medical history. The results found among the authors were compared to ensure interobserver agreement.

The Institutional Review Board of the University of Minnesota (0206M26181) and the Ethics in Research Committee (Comitê de Ética em Pesquisa – CEP) of the Universidade Federal de São Paulo (1.751.916) approved this study.

2.2 Cochlear system

To evaluate the progression of the pathologic changes in the cochlear system, we scrutinized horizontal sections of human temporal bones from the hook of the basal turn to the end of the apical turn, under light microscopy. We assessed for the presence or absence of 2 main types of pathologic changes affecting the cochlea: (1) inflammatory changes (effusion and/or inflammatory cells, granulation tissue, fibrosis) and (2) pathologic changes on the sensory elements of the cochlea (hair cells, stria vascularis).

To evaluate the number of inner and outer hair cells in each cochlear turn, we scrutinized the horizontal sections, under light microscopy (x100). To standardize our assessment for the presence or absence of cochlear hair cells in all turns, we built a cytochleogram for each of the temporal bones. To report the loss of hair cells, we used the following formula: % of

hair cell loss = number of absent hair cells/number of present + absent hair cells in each turn $\times 100$.

We evaluated the stria vascularis in 5 adjacent temporal bone sections: the section at the midmodiolar level (Fig. 2) and 4 adjacent sections (2 above and 2 below the midmodiolar level). Note: These sections were selected because, in this level, the stria vascularis is cut in a perpendicular manner, representing more accurately the area of the stria.

For our study, the measurement of the area of the stria vascularis in the temporal bone sections were performed following the criteria proposed by Pauler et al. (Pauler et al., 1988). To acquire images of the stria vascularis, we used a camera attached to an optical microscope under $\times 20$ magnification, then transferred the images to a personal computer for measurements. Initially, we measured the area of the stria vascularis in each specific turn; next, we separately measured the marginal and intermediate cells. We defined the marginal cells as the cells more intensely stained by hematoxylin-eosin that face the lumen of the scala media of the cochlea and abut the intermediate cells. We defined the intermediate cells as the cells less intensely stained by hematoxylin-eosin, that face the marginal cells and abut the basal cells of the stria vascularis. We excluded areas of edema, blood vessels, and stria concretions from the measurements. The results were expressed as mean area per cochlear turn, in μm^2 .

We evaluated the width of the spiral ligament of the early basal turn of the cochlea in 5 adjacent temporal bone sections: the section at the midmodiolar level (Fig. 2) and 4 adjacent sections (2 above and 2 below the midmodiolar level). The width of the ligament was measured in millimeters, from the basilar crest to the bony wall of the cochlear duct, following the method proposed by Wright and Schuknecht (Wright and Schuknecht, 1972). We evaluated loss of fibrocytes of the ligament in the early cochlear basal turn using a rating scale, defined as follows: 0, within normal limits; 1, loss of one-third of fibrocytes; 2, loss of two-thirds of fibrocytes; and 3, severe or complete loss (Cureoglu et al., 2004).

2.3 Peripheral vestibular system

To evaluate possible pathologic changes in the peripheral vestibular system, we assessed for the presence or absence of pathologic effusion or inflammatory cells in the perilymphatic and endolymphatic fluids; we also calculated the density of vestibular hair cells, dark cells, and transitional cells.

To calculate vestibular hair cell density, we studied horizontal sections of the striolar region of the following vestibular structures: (1) the maculae of the saccule and utricle and (2) the cupulae of the lateral (Fig. 3) and posterior semicircular canals, following Merchant's method (Merchant, 1999). In many temporal bones, the cupulae of the anterior semicircular canal was absent, probably because of removal or processing issues; therefore, we could not evaluate vestibular hair cells in that structure.

We identified type I and type II hair cells by their morphologic appearance (Fig. 4). Type I cells are pyriform, have spherical nuclei, and are surrounded by a nerve chalice. Type II cells, in contrast, have a cylindrical external shape (and cylindrical nuclei as well), and they

are not surrounded by a nerve chalice (da Costa Monsanto et al., 2016). To evaluate both types of hair cells, we used a differential interference contrast microscope (AxioCam, Carl Zeiss Microscopy, Pleasanton, CA, USA) at $\times 1,250$ magnification. To count hair cells, we applied the criteria proposed by Merchant (Merchant, 1999); to correct the raw density, in order to avoid overestimation of data, we used the formula of Abercrombie (Abercrombie, 1946). The final cell density was expressed as the number of cells per surface area of 0.01 mm^2 .

We individualized dark cells by their morphologic appearance (Fig. 5). Dark cells are located in the base of the crista ampullaris, and their nuclei are heavily stained by hematoxylin-eosin; they also have intimate contact with melanin granules (Cureoglu et al., 2003). We counted every dark cell that had an identifiable nucleus and that was within $100 \mu\text{m}$ of the transitional epithelium in the crista ampullaris of the lateral and posterior semicircular canals, according to the method proposed by Cureoglu et al. (Cureoglu et al., 2003) The results were expressed as the number of dark cells per area within $100 \mu\text{m}$ of the transitional epithelium.

The transitional epithelium, located in between the ciliated epithelium and the dark cells in the crista ampullaris, contains a single row of cuboid cells that are lightly stained by hematoxylin-eosin (Fig. 3); the nuclei of these cells are round (da Costa Monsanto et al., 2016) We counted the cells in the transitional epithelium in the crista ampullaris of the lateral and posterior semicircular canals (in the same section that we used to count dark cells). The results were expressed as the number of transitional cells per area in the lateral and posterior semicircular canals.

2.4 Statistical analysis

To calculate and compare our results, we used the nonparametric Mann-Whitney U test. For all of our analyses, we used SPSS 23.0 software for Windows (SPSS Inc., Chicago, IL). Findings were considered statistically significant when the *P* value was less than 0.05.

3. Results

3.1 Donor characteristics

The control group included 5 women and 5 men; their mean age was 57.2 years (standard deviation [SD], 17.98; range, 25–78). The SOM group included 4 women and 6 men; their mean age was 52.5 years (SD, 22.69; range, 20–89). The SPOM group included 2 women and 8 men; their mean age was 57.4 years (SD, 18.55; range, 23–83). The MOM/MPOM group included 3 women and 7 men; their mean age was 52.8 years (SD, 20.13; range, 23–84). The COM group included 5 women and 5 men; their mean age was 63.2 years (SD, 22.04; range, 18–88).

3.2 Middle ear

In the control group, none of the temporal bones had any pathologic changes in the middle ear cleft. But in the SOM, SPOM, and MOM/MPOM groups, the middle ear of all temporal bones had effusions characteristic of their otitis media type. In the COM group, 1 temporal

bone did not have effusion; however, the other 9 had serous, mucoid, purulent, or bloody effusions.

In the 4 otitis media groups, the epithelial lining of the middle ear was hyperplastic or hypervascularized in most or all temporal bones: 7, SOM; 9, SPOM; all 10, MOM/MPOM; and all 10, COM. In the control group, however, we observed no changes in the middle ear mucosa.

In 3 of the 4 otitis media groups, we observed immature granulation tissue in several temporal bones: 2, SPOM; 6, MOM/MPOM; 6, COM. In the COM group, all 10 bones had fibrous tissue; 9 had erosion of the malleus and/or incus; 8 had mature (fibrotic) granulation tissue covering the round window niche, middle ear cleft, and/or mastoid process; 2 had cholesteatoma; and 1 had cholesterol granuloma. We were able to evaluate the tympanic membrane in 9 out of 10 bones in the COM group: all 9 had pathologic changes (3 were perforated and 6 were retracted).

3.3 Cochlear system

We observed a higher percentage of both inner and outer hair cell loss in all 4 otitis media groups, as compared with the control group (Table 1) (Figs. 5, 6). In all 4 otitis media groups, the percentage of outer hair cell loss was generally higher than the percentage of inner hair cell loss.

We also noted a trend toward a higher percentage of both inner and outer hair cell loss in the later stages of the otitis media continuum (i.e., MOM/MPOM and COM). Only in those 2 groups did we observe significant inner and outer hair cell loss in the middle turn, as compared with the control group. But we observed statistically significant inner and outer hair cell loss in the basal turn in the SPOM group, as well as in the MOM/MPOM and COM groups. Only the COM group had statistically significant inner and outer hair cell loss in the apical turn.

The mean area of the stria vascularis in the basal turn was significantly decreased in all 4 otitis media groups, as compared with the control group (Table 2) (Figs. 6, 7). The mean area of the stria vascularis in the middle turn was significantly decreased only in the MOM/MPOM and COM groups, as compared with the control group. Although the mean area of the stria vascularis was smaller in the apical turn in all 4 otitis media groups, as compared with the control group, those differences were not statistically significant. The mean area of the stria vascularis was smaller in the later stages of the otitis media continuum (i.e., MOM/MPOM and COM) than in the earlier stages (i.e., SOM and SPOM).

The mean area of marginal strial cells was significantly decreased in the basal and middle turn only in the COM group. But the mean area of intermediate cells was significantly decreased in the basal and middle turn in both the MOM/MPOM and COM groups, as compared with the control group. In all 4 otitis media groups, atrophy of the area of intermediate cells was more frequent than atrophy of the area of marginal cells. We observed a higher incidence of complete atrophy of the stria vascularis in the middle turn, followed by atrophy of the apical turn (Fig. 2).

The basal turn of the cochlea had serous effusion (serous labyrinthitis) in about half of the temporal bones: 5, SOM; 5, SPOM; 5, MOM/MPOM; and 6, COM. It had purulent effusion (purulent labyrinthitis) in several temporal bones: 2, SPOM; 2, MOM/MPOM; and 1, COM. The presence of effusion in the basal turn of the cochlea was associated with a higher percentage of inner and outer hair cell loss in both the cochlea and the stria vascularis, in all 4 otitis media groups, but the difference was not statistically significant (Table 3).

In the 4 otitis media groups, we found no statistically significant differences in the width or loss of fibrocytes in the early basal turn of the cochlea compared to age- and sex-matched nondiseased temporal bones.

3.4 Peripheral vestibular system

In the control group, none of the temporal bones had any signs of pathologic material or staining in the vestibular compartments. But 5 bones in the SOM group and 4 in the SPOM group had pink-staining material in the vestibule, suggesting serous effusion. In addition, 4 bones in the MOM/MPOM group had pink-staining material in the vestibule, and 1 had purulent effusion in all vestibular compartments. And 6 bones in the COM group had pink-staining material in the endolymphatic or perilymphatic spaces of the vestibule.

We observed a lower density of both type I and type II hair cells in several compartments in 2 of the 4 otitis media groups, as compared with the control group (Table 4) (Fig. 4, 6). In the MOM/MPOM and COM groups, the density of type I and type II hair cells was significantly decreased ($P < 0.05$) in the saccule and utricle. In the COM group, the number of type I hair cells was significantly decreased ($P < 0.05$) in the lateral semicircular canal.

In the 4 otitis media groups, we found no statistically significant differences in the number of vestibular dark cells and transitional cells in the sensory epithelium of the lateral and posterior semicircular canals.

4. Discussion

The sensory epithelium of the cochlea and the vestibule, though morphologically different, has several common functional features (Purves et al., 2001a). Type I vestibular hair cells parallel the function of cochlear inner hair cells, whereas type II vestibular hair cells are similar in function to cochlear outer hair cells (Moravec and Peterson, 2004; Purves et al., 2001b; Ricci et al., 1997). Furthermore, the stria vascularis (marginal and intermediate cells) in the cochlea has an ionic transport mechanism similar to that of dark and transitional cells in the vestibule; both mechanisms contribute to the maintenance of the high K^+ levels in the endolymph and to endolymph production (Ciuman, 2009; Mittal et al., 2016; Nin et al., 2016; Wangemann, 2002, 1995; Zdebik et al., 2009). To our knowledge, ours is the first study of temporal bones to evaluate the parallel pathologic changes, due to otitis media, in the cochlear and peripheral vestibular structures.

We found significant cochlear hair cell loss in the basal turn of temporal bones from donors who had SPOM, MOM/MPOM, and COM—a finding similar to that of previous studies (Cureoglu et al., 2004, 2003; Joglekar et al., 2010; Paparella et al., 1972). However, we also

observed a significant hair cell loss in the middle turn of bones from donors who had MOM/MPOM and in the middle and apical turns of bones from donors who had COM; that finding suggests that disease progression leads to pathologic changes in the upper turns of the cochlea over time, especially in the later stages of the otitis media continuum. Regarding vestibular hair cells, we found a significant decrease in the density of both type I and type II vestibular hair cells in some compartments, most significantly in the saccule and utricle. Those changes were more evident in bones from donors who had MOM/MPOM and COM, as we observed in cochlear hair cells in the middle and apical turns.

Analyzing the patterns of degeneration of both cochlear and vestibular hair cells in parallel, we noted that cochlear hair cells in the basal turn of the cochlea (especially outer hair cells) were affected in the early stages of the otitis media continuum (SPOM). In contrast, cochlear hair cells of the middle and apical turn and vestibular hair cells seemed to be affected only in the later (MOM/MPOM and COM) stages. In the vestibule, we did not find differences in the degeneration of type I and type II vestibular hair cells, as opposed to the cochlea, in which outer hair cells seemed to be more affected by inflammation than inner hair cells. The chronicity of otitis media seemed to increase the chances of cochlear hair cell loss, in both the middle and apical turns of the cochlea, and of vestibular hair cell loss as well.

The mean area of the stria vascularis in the basal turn of the cochlea was significantly decreased in all 4 of our otitis media groups, as compared with the control group. The stria changes were more significant in the basal turn of the cochlea. Yet the incidence of complete atrophy was higher in the intermediate and apical turns (as compared with the basal turn) of bones from donors who had MOM/MPOM and COM ($P > 0.05$). We did not observe complete atrophy of the stria vascularis in our control group or SOM group. Analyzing the intermediate and marginal cells separately, we observed a higher incidence of complete atrophy of intermediate cells than of marginal cells. Marginal cells were present even in some areas that had severe stria atrophy: it was possible to devise a thin layer of marginal cells over basal cells in those areas, but not of intermediate cells, suggesting that intermediate cells were more susceptible to inflammatory changes than marginal cells.

Regarding dark and transitional cells of the peripheral vestibular system, we did not observe statistically significant differences between the number of those cells in the otitis media groups, as compared with the control group. Our results suggest that the stria vascularis was directly affected by the inflammatory changes secondary to otitis media (even in the early stages of the continuum), while vestibular dark and transitional cells were not.

The literature contains very little evidence on pathologic changes in vestibular dark and transitional cells. One study found a significant decrease in the number of dark cells in the lateral and posterior semicircular canals in temporal bones from donors who had COM (da Costa Monsanto et al., 2016), but other authors observed no significant changes in donors who had used ototoxic medications (Cureoglu et al., 2003). It is possible that the more active biologic function of cochlear stria cells—which maintain a high membrane potential (+80 to +100 mV) as compared with vestibular dark and transitional cells (+1 mV)—increases the risk of changes to the stria (Wangemann, 2002; Wilms et al., 2016). Furthermore, during episodes of otitis media, the basal turn of the cochlea suffers direct inflammatory injury

secondary to the passage of toxins and inflammatory products from the middle ear to the cochlea through the round window membrane (Goycoolea et al., 1988; Schachern et al., 1981; Schachern PA et al., 1987).

All of our histopathologic findings of cochlear and vestibular pathology in human temporal bones are supported by clinical studies of patients with otitis media. High-frequency sensorineural hearing loss secondary to COM has long been demonstrated (Costa et al., 2009; Paparella et al., 1984; Papp et al., 2003); more recent studies have shown sensorineural hearing loss, in regular or extended high frequencies, even in the earlier stages of otitis media, such as SOM and SPOM (Löppönen et al., 1992; Margolis et al., 2000; Sharma et al., 2012). In addition, it has been observed that patients who had SOM in childhood had a higher incidence of tinnitus in adulthood, as compared with control patients who did not have otitis media in childhood (Johnston et al., 2004; Mills and Cherry, 1984; van Cauwenberge et al., 1999). Balance disorders leading to altered performance on vestibular function exams have been documented in patients with COM, with rates ranging from 25% to 76%. (Chang et al., 2014; Gianoli and Soileau, 2008; Lee et al., 2009; Wang et al., 2009). Studies also reported that posturography evaluation of children with otitis media (with or without effusion) yielded abnormal results, and those patients were reported as clumsy and fell more often than control patients (Casselbrant et al., 1995a; Casselbrant et al., 1998); moreover, those children had higher chances of developing dizziness in adulthood (Aarhus et al., 2016).

5. Conclusion

In our study, we demonstrated that the later stages of the continuum were associated with more intense pathologic changes in the sensorial elements of the cochlear and peripheral vestibular systems. The changes seemed to begin in the basal turn of the cochlea (the stria vascularis, then the inner and outer hair cells), progressing next to the middle turn of the cochlea and to the saccule and utricle at the MOM/MPOM and COM stages, and finally to the apical turn of the cochlea. The stria vascularis seemed to be the first structure affected by otitis media (especially intermediate cells), followed by the cochlear outer hair cells and then the cochlear inner hair cells. Vestibular hair cells and cochlear hair cells in the middle and apical turns seemed to be affected only in the more advanced stages of the otitis media continuum. We did not observe changes to the vestibular dark and transitional cells.

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Highlights

- We studied cochlear and vestibular pathologic changes due to otitis media
- Cochlear changes preceded vestibular changes in the otitis media groups
- The basal turn of the cochlea was the most affected area of the inner ear
- Cochlear outer hair cells were more affected by otitis media than inner hair cells
- Strial intermediate cells are more affected by otitis media than intermediate cells
- Vestibule and apical turn of the cochlea were affected in later stages of the continuum

Fig. 1.

Epitympanic sections of human temporal bones, showing characteristic effusion and pathologic changes in each group (hematoxylin and eosin, $\times 1$). A = Epitympanum; B = Mastoid antrum. Control: nondiseased temporal bone. SOM: Presence of serous effusion (*) in the mastoid and epitympanic cleft; SPOM: Presence of serous effusion permeated with polymorphonuclear leukocytes (*); COM: Presence of fibrous and granulation tissue in the lateral epitympanum (arrow); mucoid-bloody effusion in the mastoid antrum (*).

Fig. 2.

A representative midmodiolar level human temporal bone section of a nondiseased donor (hematoxylin and eosin, $\times 4$).

* = Middle cochlear scala and the organ of Corti in the basal turn of the cochlea.

Arrows = Stria vascularis

Fig. 3.

A representative horizontal section of a human temporal bone showing the cupulae and crista ampullaris of a lateral semicircular canal (hematoxylin and eosin). A: Cupulae and canal of a lateral semicircular canal, under magnification of 4 $\times$. Squared area includes the area in figure B, under 20 $\times$ magnification. B: distribution of the hair, transitional, and dark cells along the crista ampullaris; (1) vestibular hair cells; (2) vestibular transitional cells; (3) vestibular dark cells.

Fig. 4. Two representative horizontal sections of the maculae of the saccule in human temporal bones, seen under Nomarski microscopy (hematoxylin and eosin; 1250 $\times$): (A) vestibular hair cells types I and II (1, 2) (nondiseased temporal bone); (B) loss of hair cells (*) (chronic otitis media bone).

Fig. 5.

A $\times 40$ view of the organ of Corti of temporal bone sections. (A) Organ of Corti in a nondiseased temporal bone; * = 3 rows of outer hair cells, arrow = inner hair cell. (B) Organ of Corti in a bone from a donor who had chronic otitis media, showing loss of both outer and inner hair cells.

Fig. 6.

Line charts showing tendencies of losses of cochlear and vestibular cells in the control group compared to the otitis media groups.

Fig. 7.

Two representative human temporal bone sections showing the stria vascularis in the middle scala of the basal turn of the cochlea (hematoxylin and eosin, $\times 20$). (A) Nondiseased temporal bone with a normal-sized stria vascularis; (B) Specimen from a donor with chronic otitis media, showing atrophy of the stria vascularis.

Table 1

Inner and outer cochlear hair cell loss (%)—control group vs. 4 otitis media groups

Inner					
	Basal Turn	<i>P</i>	Medial Turn	<i>P</i>	Apical Turn
Control	11%	-	9%	-	20%
SOM	15%	0.131	10%	0.909	21%
SPOM	20%	0.028 *	15%	0.170	21%
MOM/MPOM	28%	0.013 *	19%	0.041 *	26%
COM	32%	0.005 *	26%	0.040 *	48%
Outer					
	Basal Turn	<i>P</i>	Medial Turn	<i>P</i>	Apical Turn
Control	20%	-	17%	-	28%
SOM	27%	0.112	18%	0.364	27%
SPOM	34%	0.049 *	18%	0.545	35%
MOM/MPOM	40%	0.026 *	33%	0.049 *	37%
COM	46%	0.005 *	44%	0.011 *	61%

P = statistical significance of the comparison between the control group and each otitis media group

* = statistically significant association

COM = chronic otitis media; MOM/MPOM = mucoid/mucoid-purulent otitis media; SOM = serous otitis media; SPOM = serous-purulent otitis media

Table 2

Mean area (μm^2) of stria vascularis, and marginal and intermediate cells, in each cochlear turn—control group vs. 4 otitis media groups

Stria Vascularis					
	Basal Turn	<i>P</i>	Middle Turn	<i>P</i>	Apical Turn
Control	2605.276	-	2105.407	-	1090.73
SOM	2097.683	0.041 *	1794.949	0.082	819.83
SPOM	2059.603	0.041 *	1644.866	0.174	796.087
MOM/MPOM	1936.277	0.049 *	1534.501	0.019 *	744.126
COM	1659.981	0.010 *	1156.039	0.001 *	413.245
Marginal Cells					
	Basal Turn	<i>P</i>	Middle Turn	<i>P</i>	Apical Turn
Control	855.9765	-	680.5365	-	479.628
SOM	753.3016	0.199	639.1079	0.597	306.922
SPOM	728.1945	0.096	625.556	0.082	335.076
MOM/MPOM	719.1468	0.226	564.565	0.112	305.184
COM	624.4765	0.013 *	453.9595	0.005 *	170.798
Intermediate Cells					
	Basal Turn	<i>P</i>	Middle Turn	<i>P</i>	Apical Turn
Control	1749.299	-	1424.87	-	611.102
SOM	1344.381	0.059	1155.842	0.070	512.908
SPOM	1331.408	0.059	1019.31	0.112	461.011
MOM/MPOM	1217.13	0.034 *	969.936	0.010 *	438.942
COM	1035.504	0.004 *	702.0795	0.001 *	242.447

P = statistical significance of the comparison between the control group and each otitis media group

* = statistically significant association

COM = chronic otitis media; MOM/MPOM = mucoid/mucoid-purulent otitis media; SOM = serous otitis media; SPOM = serous-purulent otitis media

Table 3

Findings in cochlear and peripheral vestibular systems, by presence or absence of effusion in cochlear basal turn—4 otitis media groups

Cochlear system						
Cochlear hair cell loss (%)	Inner		P	Outer		P
	No Effusion	Effusion		No Effusion	Effusion	
SOM	12%	19%	> 0.05	24%	26%	> 0.05
SPOM	20%	20%	> 0.05	29%	36%	> 0.05
MOM/MPOM	22%	27%	> 0.05	32%	43%	> 0.05
COM	33%	31%	> 0.05	49%	44%	> 0.05
Total	22%	34%		34%	37%	
Stria vascularis (pm ²)	Basal Turn		P			
	No Effusion	Effusion				
SOM	2200.9	1994.465	> 0.05			
SPOM	2014.041	2079.129	> 0.05			
MOM/MPOM	2116.283	1798.813	> 0.05			
COM	1909.338	1573.821	> 0.05			
Total	2060.141	1861.557				
Peripheral vestibular system						
Saccule (cells per 0.01 mm ²)	Type II Hair Cells		P	Type II Hair Cells		P
	No Effusion	Effusion		No Effusion	Effusion	
SOM	31.9	26.9	> 0.05	15.8	15.5	> 0.05
SPOM	29.4	27.1	> 0.05	16.7	14.6	> 0.05
MOM/MPOM	27.0	23.4	> 0.05	14.5	12.4	> 0.05
COM	22.2	25.0	> 0.05	13.6	12.8	> 0.05
Total	27.6	25.6		15.2	13.9	
Utricle (cells per 0.01 mm ²)	Type II Hair Cells		P	Type II Hair Cells		P
	No Effusion	Effusion		No Effusion	Effusion	
SOM	30.7	29.5	> 0.05	16.9	15.3	> 0.05
SPOM	29.7	26.5	> 0.05	16.9	14.0	> 0.05

COM = chronic otitis media; MOM/MPOM = mucoid/mucoid-purulent otitis media; SOM = serous otitis media; SPOM = serous-purulent otitis media

COM = chronic otitis media; MOM/MPOM = mucoid/mucoid-purulent otitis media; SOM = serous otitis media; SPOM = serous-purulent otitis media

Table 4

Mean density (number of cells per surface area of 0.01 mm²) of both types of peripheral vestibular hair cells, in each endolymphatic compartment—control group vs. 4 otitis media groups

Type I						
	Lateral SCC	P	Utricle	P	Sacculle	Posterior SCC
Control	28.83	-	30.45	-	30.61	27.40
SOM	29.16	0.754	30.16	0.695	29.43	27.26
SPOM	28.63	0.961	27.36	0.164	27.13	28.85
MOM/MPOM	25.73	0.090	24.79	0.007 *	24.50	27.69
COM	24.02	0.014 *	24.81	0.003 *	24.32	24.32
Type II						
	Lateral SCC	P	Utricle	P	Sacculle	Posterior SCC
Control	15.64	-	16.4	-	16.85	14.76
SOM	15.48	0.890	16.12	0.641	15.71	15.30
SPOM	14.69	0.162	14.13	0.070	15.33	15.26
MOM/MPOM	14.35	0.150	13.94	0.024 *	13.12	15.17
COM	14.25	0.138	13.81	0.014 *	13.21	15.18

P = statistical significance of the comparison between the control group and each otitis media group

* = statistically significant association

COM = chronic otitis media; MOM/MPOM = mucoid/mucoid-purulent otitis media; SCC = semicircular canal; SOM = serous otitis media; SPOM = serous-purulent otitis media