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Paparella's Otolaryngology

Head & Neck Surgery



Volume **1**

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Foreword
Richard A Chole



Paparella's Otolaryngology Head and Neck Surgery

VOLUME 1

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VOLUME 1

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Chapter

2

Otopathology

Joseph Nadol

HISTORY OF OTOPATHOLOGY

Although the development of the light microscope can be dated at least to 1590, microscopic examination of biologic material was initiated by Robert Hook in 1665 with the identification of the cell and by Leeuwenhoek who, in 1700 described the cellular nucleus. It was, however, several decades before microscopic anatomy and pathology were applied to medical subjects. Marcello Malpighi (1628–1694), an Italian anatomist, is considered to be the Father of Histology and Rudolf Virchow (1821–1902), a German pathologist, who demonstrated that injuries of various causes also alter the cellular structure, is also considered by many to be the pioneer of cellular pathology. It was much later that microscopic anatomy and pathology was applied to the ear. In his book “Diseases of the Ear” (1860), Joseph Toynbee stated: “To quote from Mr Wilde’s introduction to his valuable treatise on aural surgery, medical men are too ready to affirm that they know nothing about the diseases of the organ of hearing and many looking upon the difficulties that surround the investigation as insurmountable have tacitly abandoned their pursuit. Yet if we carefully survey the history of the rise and progress of aural surgery as a distinct branch of scientific surgery, one main cause of the disrepute into which it has fallen may be traced to the neglect of the pathology of the organ of hearing” and Toynbee himself in his book of 1860 depended heavily on macroscopic dissections rather than microscopic pathology. He was one of the first people to describe the pathologic change in otosclerosis as “ankylosis of the stapes to the fenestra ovalis” as observed in 136 dissections. Camera lucida renderings of the normal labyrinth were available as early as 1800 as accomplished by Antonio Scarpa, in 1851 by Alfonso Corti and in 1884 by Gustav Retzius. However, it was five decades more before histologic

descriptions of presbycusis were documented by Crowe and his colleagues at Johns Hopkins in 1934. In Adam Politzer’s book, “Diseases of the Ear” published in 1902, the word “presbycusis” is not in the index, and Politzer introduced his section on “The diseases of the labyrinth, of the auditory nerve and of its central course” by the statement “our knowledge regarding the pathology of the sound-perceiving apparatus is still very imperfect in spite of the numerous scientific investigations that have been undertaken in the past few years in order to ascertain the anatomical and clinical conditions in diseases of the auditory nerve apparatus. This is most easily explained by the fact that we are seldom in a position to make a thorough anatomic examination of the ears of those individuals who, from careful clinical investigations undertaken during life, are known to have been afflicted with a disease condition of the auditory nerve apparatus”. The modern era of otopathology waited for two further developments—first the invention of the audiometer by David Edward Hughes in 1879 and by Schwartze in 1919 and commercialized by Bell Laboratories in 1920 and second the development of photography. The daguerreotype was developed by Louis Daguerre of Paris in 1839. However, it was not until 1884 that dry gel on paper was introduced as a film by George Eastman of Westchester, New York, and the simplest of cameras were not available until the first decades of the 20th century. Until that time the camera lucida was still the standard tool of microscopist for documentation. Thus, the combination of the microscope, audiometer, recognition of cellular anatomy and pathology and the development of photography allowed the birth of contemporary temporal bone otopathology in Europe and in the United States as described by Schuknecht.¹ The modern history of temporal bone collections has been beautifully updated by Saumil Merchant.² Because of a

recent contraction of the number of laboratories processing human temporal bones, concern has been raised as to whether or not the profession is losing critical mass in the area of otopathology.^{3,4}

■ CONTEMPORARY ROLE OF HUMAN OTOPATHOLOGY

Histologic study of the human temporal bone remains critical for the following applications: (1) establishment of the pathologic basis of human disease, (2) verification of the applicability and equivalency of animal models of disease, (3) verification of equivalency of animal models of normal human anatomy, (4) evaluation of medical and surgical treatments for otologic disorders, and (5) the opportunity to apply modern neuropathologic and clinicopathologic techniques to human disease.

Acquisition of Temporal Bones

Documentation of Clinical Symptoms and Pathology

A national registry program has been established in the United States in 1992 called the “National Temporal Bone Hearing and Balance Pathology Research Registry” (www.tbregistry.org), which is sponsored by the National Institutes on Deafness and Other Communication Disorders of the National Institutes of Health (NIH). This took the place of an earlier program entitled “National Temporal Bone Bank Program”, which began in the United States in 1960. The registry has several functions, including enrolling temporal bone donors during life, maintenance of a national network to coordinate collection of temporal bones after death, maintenance of a computerized database of temporal bone findings and collections in the United States, conservation of existing collections that may be at risk of loss, dissemination of information concerning the importance of temporal bone donation and research, and finally the sponsorship of professional educational activities in otopathology.⁵

Removal of the Temporal Bone

Information on the various techniques of removal of the temporal bone can be found in the Registry Website: www.tbregistry.org or in the publication by Nadol.⁶ The most common technique to remove the temporal bone is by the intracranial method using a temporal bone plug cutter or an oscillating autopsy saw. When the intracranial method is not possible, an extracranial method may be used.⁷

Histologic and Other Preparation Techniques

Tissue fixation begins immediately after the removal of the temporal bones by immersion of the specimens in 10% neutral buffered formalin. Decalcification is done using a chelating agent such as ethylene diamine tetra-acetate (EDTA) or less frequently acid decalcification in 5% trichloroacetic acid. A chelating agent is preferred because of less histologic artefact and better preservation of subcellular organelles. Further details concerning dehydration, embedment, hardening, blocking, sectioning and staining are reviewed by Merchant.² Other techniques may be applied to the human temporal bone such as transmission electron microscopy (TEM) in specimens with a short postmortem time. Other methods include the microslicing technique of the undecalcified specimen (3-mm sections).^{8,9} In addition, modern molecular biologic techniques are feasible for postmortem human specimens, including DNA retrieval,^{10,11} retrieval and amplification of RNA from archival human temporal bone specimens.^{12,13}

Immunostaining

Immunostaining of archival temporal bones embedded in celloidin or paraffin allows the application of immunohistochemical techniques.^{14,15}

Mass Spectrometry

Protocols to retrieve proteins from the cochlea using liquid chromatography and mass spectrometry have been described by Palmer-Toy et al.¹⁶⁻¹⁸

Reconstruction of Serial Sections: Two-dimensional Reconstruction

Two-dimensional (2D) reconstruction of serial sections may be accomplished using either a manual methodology^{19,20} or computer-assisted techniques (Matlab). The 2D rendition of the cochlea is usually combined with a quantitative cytochleogram demonstrating the presentation of inner and outer hair cells, cochlear neurons, stria vascularis and other cytologic elements of the cochlea as desired.

Three-dimensional Reconstruction of the Temporal Bone

Three-dimensional (3D) reconstruction of the temporal bone may be used to augment the 2D technique that suffers from inherent error in failing to consider the height of the cochlear duct or may be used in the creation of 3D

anatomic models (see Otopathology Research Collaboration Network: <http://otopathologynetwork.org>).

Quantitative Vestibular Otopathology

Techniques to quantify loss of hair cells and neurons may be applied to the vestibular system using Nomarski differential interference contrast microscopy.^{21,22}

Examples of the Contemporary Role of Human Otopathology

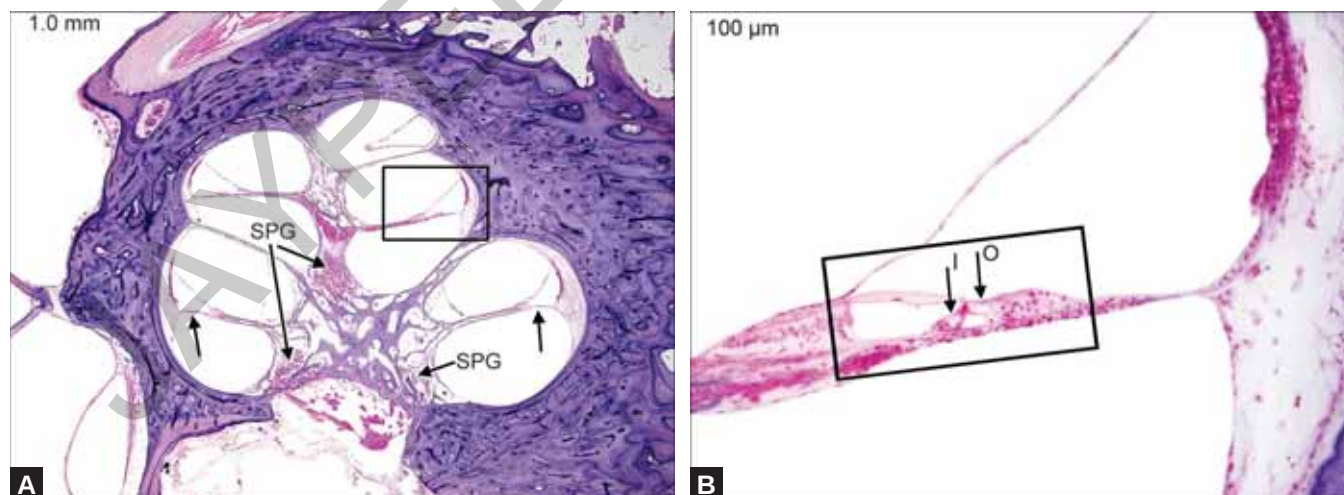
Establishment of the Pathologic Basis of the Diseases

Genetically determined sensorineural hearing loss: Of the approximately 600 genetically determined syndromic and nonsyndromic disorders of hearing, adequate human otopathology is available in <100. Rapid accrual of new gene localizations makes temporal bone comparative pathology all the more pressing. In addition, for some disorders such as Usher's syndrome, there are several subtypes, perhaps as many as 11, which deserve pathologic comparison. In addition, as in the case of DFNA9 unique histopathologic changes in the inner ear have led to identification of probable proteomic alterations that may be characterized to better understand the pathogenesis of hearing loss due to genetic disorders. Finally, for several of the most common

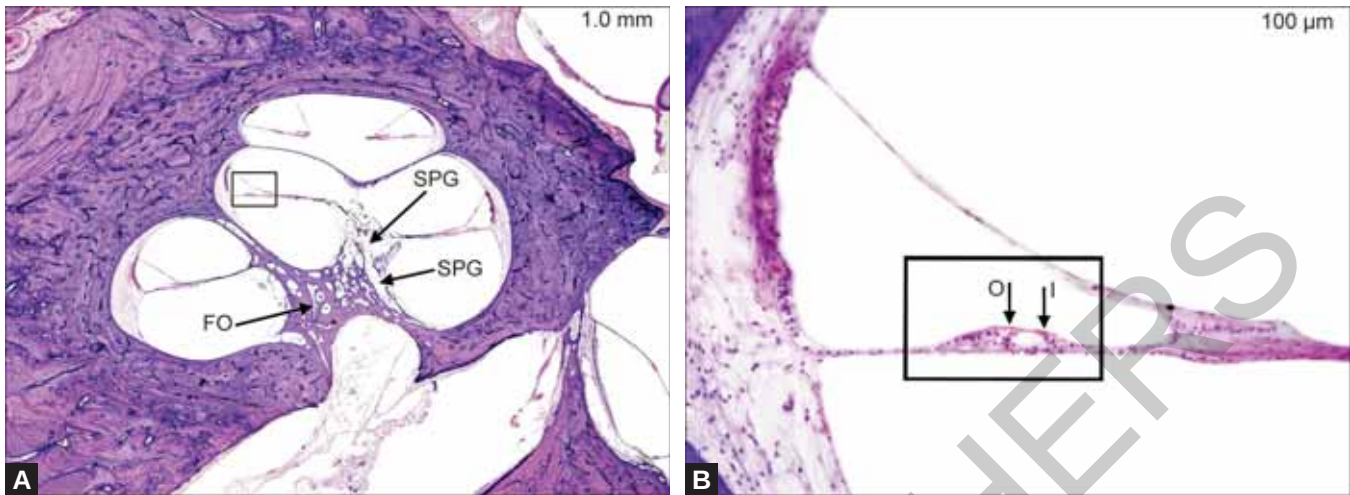
genetically determined causes of sensorineural hearing loss, such as Connexin 26, there is no reported otopathology available from individuals who, in life, were diagnosed with those disorders.

Idiopathic sudden sensorineural hearing loss: Idiopathic sudden sensorineural hearing loss is a relatively common disorder with variable presentation. Thus, the hearing loss may be partial or complete and may or may not include vestibular symptoms. Similarly, the otopathologic findings may vary considerably (Figs. 2.1 and 2.2).

Acoustic neuroma: Although hearing loss is the most common presenting symptoms of acoustic neuroma, the pathophysiology of sensorineural loss is unknown. The presence of an acoustic neuroma displacing the auditory nerve intuitively suggests that the cause of hearing loss is due to nerve compression. However, Ylikoski et al.²³ and Mahmud et al.²⁴ found no significant correlation between the nerve fiber population of the auditory nerve and clinical hearing levels. Similarly, there is a poor correlation between tumor size and clinical hearing in cases of acoustic neuroma.²⁵⁻²⁷ This and the other evidence suggest that simple tumor compression of the auditory nerve is insufficient to explain the degree of hearing loss. Indeed, there is considerable evidence for abnormalities within the inner ear itself.²⁷⁻³⁰ An example of pathologic change in the cochlea presumably secondary to the presence of an acoustic neuroma is shown in Figures 2.3A to E.



Figs. 2.1A and B: (A) Sudden idiopathic sensorineural hearing loss—hair cell loss. This 48-year-old woman suffered a sudden loss of hearing in the left ear at age 43 in association with mild imbalance. Audiometry demonstrated a profound sensorineural hearing loss in the left ear. The histopathologic correlate of the hearing loss in the left ear was severe atrophy of the organ of Corti particularly in the basal 24 mm of the cochlea (arrows) with a few scattered hair cells remaining in the apical cochlea. There was secondary degeneration of many cochlear neurons within the spiral ganglion (SPG) especially in the basal 24 mm of the cochlea. There was no significant pathology seen in the vestibular labyrinth; (B) The boxed area as seen in Figure 2.1(A) is shown at higher magnification. In this section, there was loss of both inner (I) and outer (O) hair cells.



Figs. 2.2A and B: A Sudden idiopathic sensorineural hearing loss—neuronal loss. This 41-year-old woman suffered a sudden hearing loss in the right ear at age 18. It is not known whether or not she suffered vestibular symptoms. Audiometry demonstrated profound sensorineural loss in the right ear. In this case, the histopathologic correlate of the sudden idiopathic sensorineural loss was the total loss of spiral ganglion cells (SPG), with fibro-osseous obliteration (FO) of Rosenthal's canal. There was severe atrophy of the vestibular nerves, although the five neuroepithelial vestibular end organs were normal; (B) The boxed area as seen in (A) is shown at a higher magnification. Inner (I) and outer (O) hair cells were present. In contrast to the case illustrated in Figure 2.1, this case suggests cochleovestibular neuritis with degeneration as the cause of the sudden hearing loss.

The mechanism by which an acoustic neuroma may induce cochlear degeneration is unclear, although preliminary genetic analysis suggests differences in gene products of acoustic neuromas may vary and may be responsible for hearing loss in this disorder.^{31,32}

Hearing loss due to superficial siderosis of the CNS: Hearing loss is the most common presenting symptom of superficial siderosis of the central nervous system. Other symptoms include cerebellar ataxia, pyramidal signs, dementia, bladder disturbances, anosmia and anisocoria and sensory signs.³³

Superficial siderosis of the central nervous system is due to subarachnoid hemorrhage resulting in deposition of hemosiderin in the meninges and around the brainstem, spinal cord, cerebellum and cranial nerves.³⁴ Despite the fact that the most common presenting symptom of superficial siderosis of the CNS is sensorineural hearing loss, until recently there has been no published example of otopathology in this disorder³⁵ (Figs. 2.4A to E).

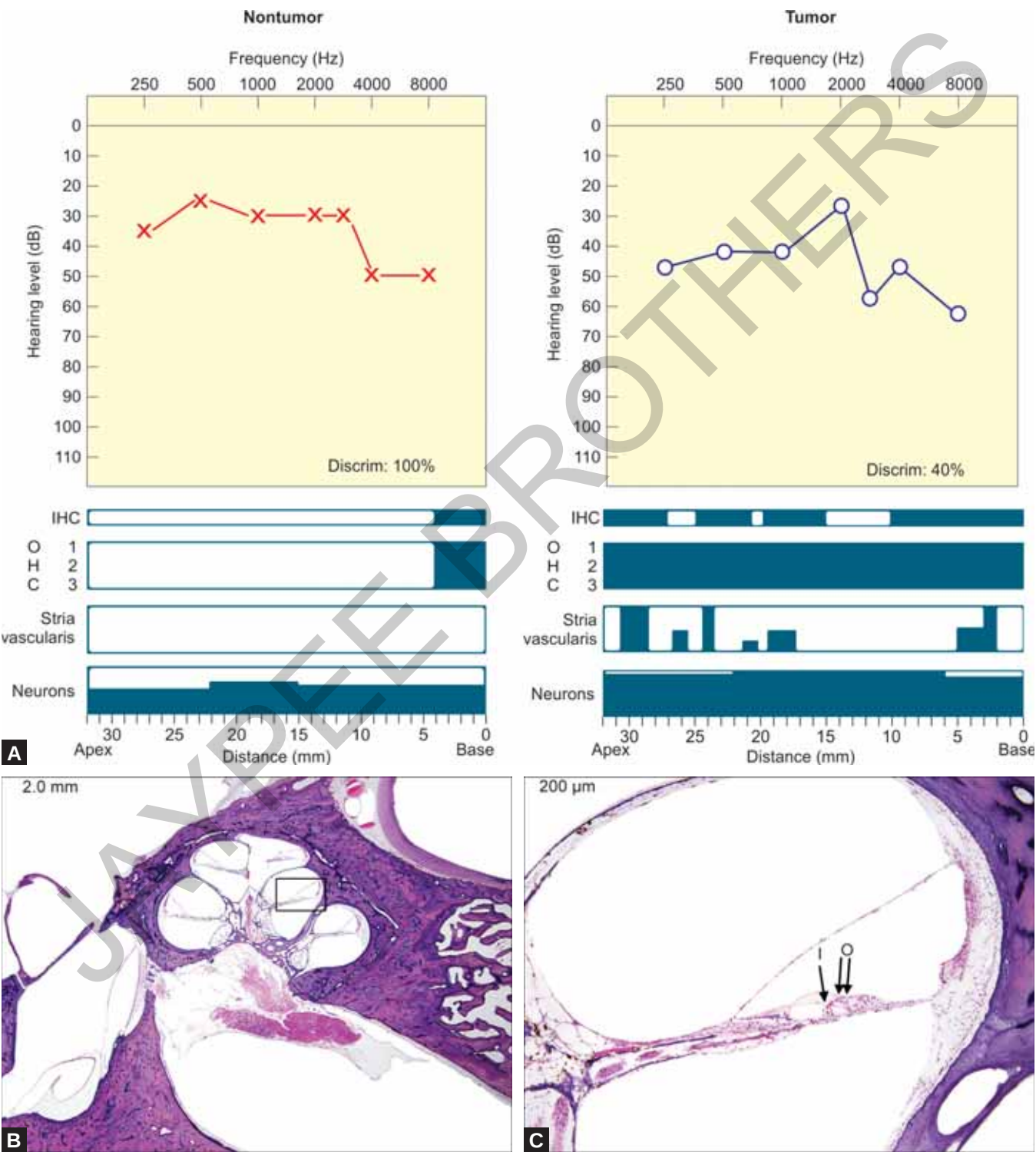
The pathophysiologic mechanism causing neural degeneration in superficial siderosis is not fully understood but may be secondary to hemosiderin deposition within the CNS and also iron-catalyzed lipid peroxidation.³⁴ The presence of iron staining within the cochlear nucleus suggests the possibility of retrograde degeneration of the spiral ganglion cells secondary to damage to auditory axons in the pontine cistern.^{36,37} This case is an excellent

example of a disease for which otopathology has only recently been demonstrated.

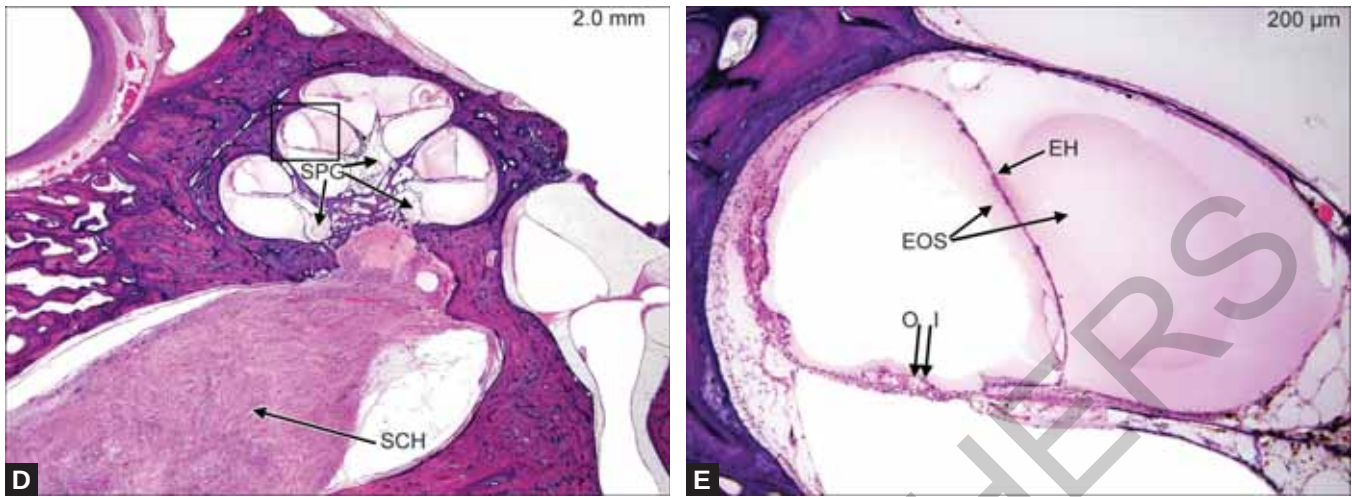
Susac's syndrome: Susac's syndrome is a presumed immune-mediated disorder affecting arterioles characterized by encephalopathy, hearing loss and retinal defects.³⁸ Microinfarcts of the corpus callosum on magnetic resonance imaging (MRI) scan are considered pathognomonic for Susac's syndrome. In the eye, branch retinal artery occlusion is seen best using fluorescein angiography. The first reported otopathologic documentation of the inner ear involvement in Susac syndrome has been recently published by Francis et al.³⁹ In this case, a 51-year-old woman had a progressive encephalopathy, low-frequency sensorineural loss and characteristic MRI findings in the corpus callosum and on fluorescein angiography of the eyes. Otopathologic findings included widespread atrophy of the contents of the cochlear duct in the apical half of the cochlea, including hair cells, stria vascularis and spiral ligament. On light microscopy, there was evidence of occlusion of capillary vessels within the stria vascularis. The cause of Susac's syndrome is not fully understood, although an immune-mediated disorder of endothelial cells has been suggested resulting in ischemic injuries to the affected tissue. The inner ear findings were consistent with patchy infarction of the cochlear duct and support a similar mechanism of damage in the inner ear as is seen in the retina.

Bell's palsy: A leading hypothesis of the pathogenesis of Bell's palsy is as a cranial neuropathy secondary to viral infection, perhaps Herpes Simplex virus,^{40,41} Varicella

Zoster,¹⁰ the mumps virus⁴² and others. The histopathology of patients who in life suffered from Bell's palsy shows nonspecific changes consistent with degenerated motor



Figs. 2.3A to C



Figs. 2.3D and E

Figs. 2.3A to E: Unilateral acoustic neuroma. This 75-year-old man had a bilateral sensorineural loss, worse on the right with significant discrepancy in word discrimination (40%, right ear, 100% left ear). Auditory brainstem responses revealed poor wave morphology on the right side and prolonged latency of waves I–III, diagnostic of a retrocochlear lesion. A mass suggestive of a right acoustic neuroma was found radiographically. No medical or surgical intervention was done. The audiogram and cytochleogram is shown for the tumor and nontumor sides. (A) As can be seen in the cytochleogram, there was almost complete loss of outer hair cells, severe loss of inner hair cells and loss of cochlear neurons on the tumor side, in marked contrast to the nontumor side; (B) A midmodiolar section of the nontumor (left) side demonstrated some loss of spiral ganglion cells particularly in the basal turn; (C) The boxed area shown in Figure 2.3B is shown at higher magnification. Both inner (I) and outer (O) hair cells were seen; (D) A midmodiolar section of the tumor side (right). Degeneration of the spiral ganglion (SPG) and the presence of a schwannoma (SCH) were seen. The boxed area of the organ of Corti is shown at higher magnification in Figure 2.3E; (E) There was significant additional pathology on the tumor side within the cochlea, including endolymphatic hydrops (EH), loss of both inner (I) and outer (O) hair cells and an eosinophilic deposit (EOS) in both the endolymphatic and perilymphatic spaces.

fibers, lymphocytic infiltration and Schwann cell proliferation. The most specific otopathologic findings to explain the pathogenesis of Bell's palsy have been generated by polymerase chain reaction amplification of DNA obtained from archival celloidin-embedded sections of human temporal bones.¹⁰ This technique was applied to sections from a patient who in life had suffered from Bell's palsy.⁴¹ In this case, Herpes simplex virus type I (HSV-1) was identified in the geniculate ganglion. Whether or not this was causative and what other mechanisms may play a role in the pathogenesis of this cranial neuropathy have yet to be identified.⁴³

Verification of the Applicability and Equivalency of Animal Models of the Diseases

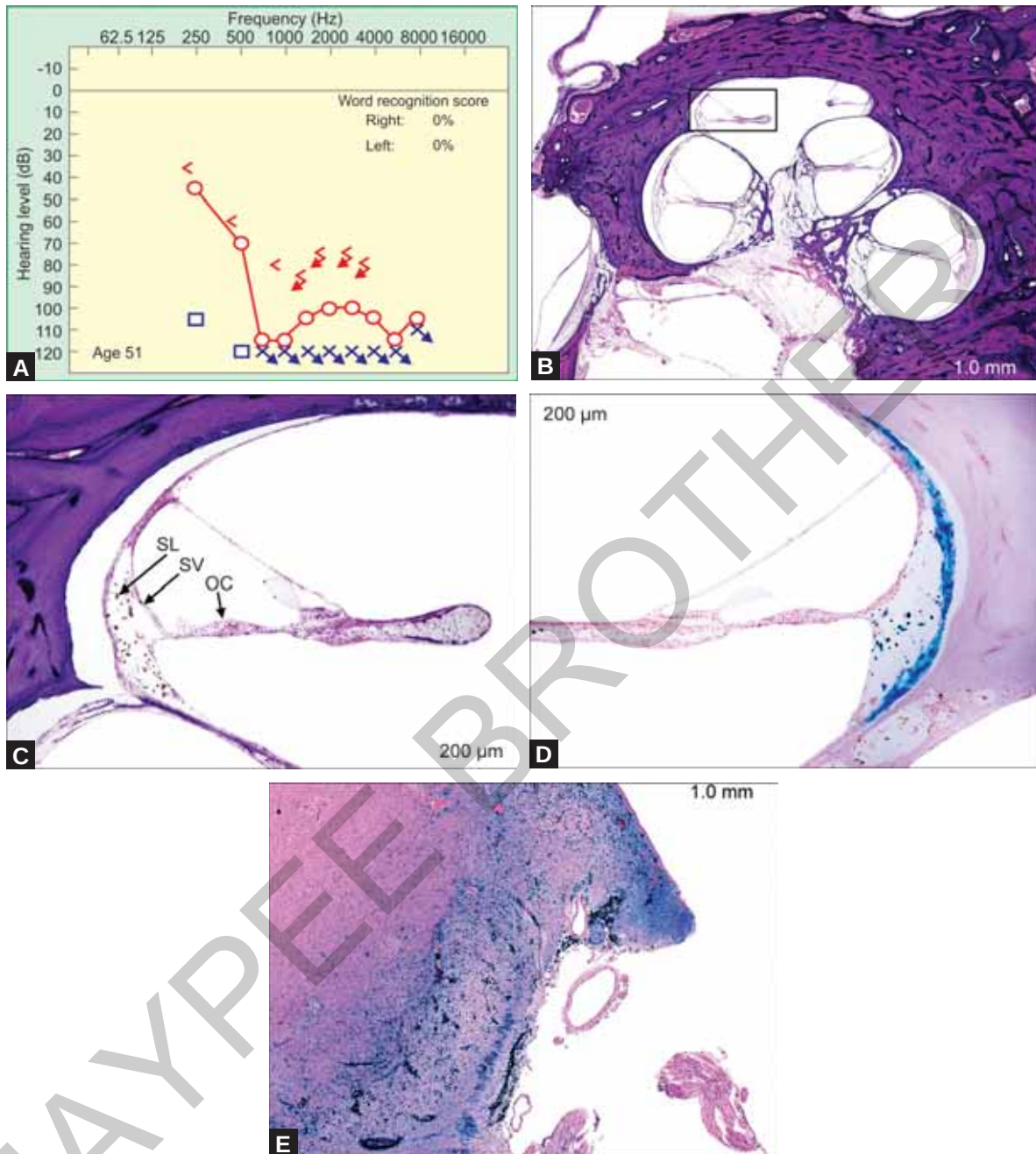
Norrie's disease: Norrie's disease is an x-lined recessive disorder causing progressive ocular changes and mental retardation beginning as early as 3 years of age and progressive hearing loss.⁴⁴ The first description of the otopathology of Norrie's disease was published in 1990.⁴⁵ The principle histopathologic findings were marked atrophy of the stria vascularis, severe degeneration of inner and outer hair cells and cochlear neurons and connective tissue proliferation within the spiral ganglia, spiral lamina

and walls of the membranous vestibular labyrinth (Figs. 2.5A to C). Fibrous tissue deposition was particularly prominent around some blood vessels seen in the osseous spiral lamina. The histopathologic findings in a knockout mouse model with the Norrie disease protein (NDP) gene defect⁴⁶ demonstrated identical findings in the striavascularis, organ of Corti and spiral ganglion. Fluorescent dye showed abnormality of the vasculature within the stria vascularis, and on this basis the principle function of the gene product norrin has been hypothesized to regulate interaction of the cochlea with its vasculature,⁴⁶ possibly via the Wnt signaling pathway.⁴⁷

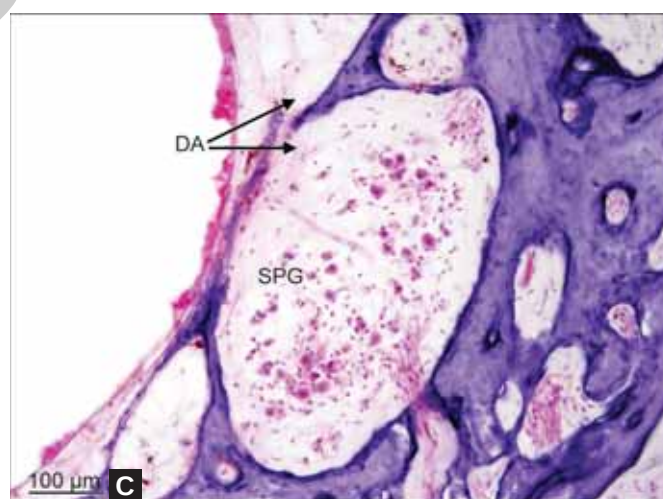
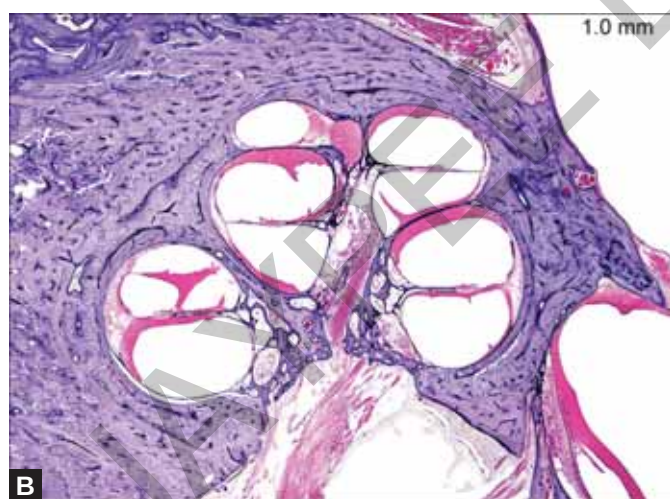
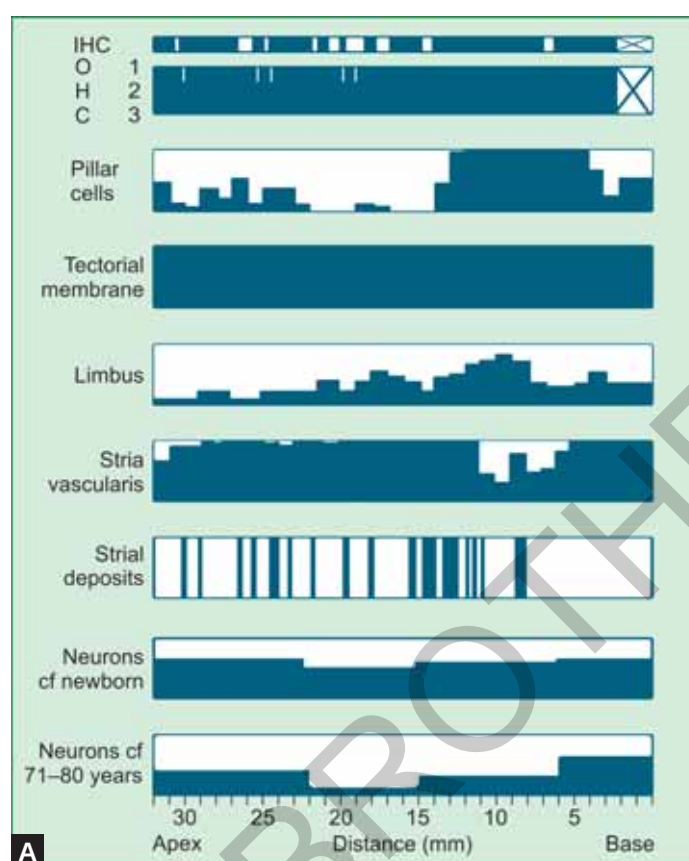
Thus, the histopathology of the inner ear of Norrie's disease in the human and in the NDP knockout mouse model is essentially identical in their inner ear.

DFNA9: DFNA9 is an autosomal dominant nonsyndromic sensorineural loss and vestibulopathy caused by mutations in the *COCH* gene located at 14q12-q13. The otopathology of this disorder is unique in the human. It has been described by Khetarpal⁴⁸ and Robertson.⁴⁹

The principal histopathologic correlate of sensorineural loss seems to be loss of dendritic fibers of the spiral ganglion cells. There was likewise severe degeneration of the dendritic processes of Scarpa's ganglion cells. The *COCH*



Figs. 2.4A to E: Superficial siderosis of the central nervous system. This 57-year-old patient first noted a hearing loss in both ears starting in his late 30s. He was known to the neurology service with a diagnosis of idiopathic intrathecal bleeding. His neurologic symptoms included spastic paresis, neurogenic bladder and progressive lower body sensory loss. A diagnosis of superficial siderosis was made on the basis of a magnetic resonance imaging scan and the finding of xanthochromic spinal fluid obtained on lumbar puncture. Angiography of the brain and spinal cord failed to reveal the source of bleeding. (A) An audiogram at the age of 51, 6 years prior to death, demonstrated a severe to profound sensorineural hearing loss on the right and a profound sensorineural hearing loss on the left, both with word recognition scores of 0%; (B) Midmodiolar section of the left temporal bone. Marked loss of spiral ganglion cells was seen. Boxed area is shown in Figure 2.4C; (C) There was severe bilateral degeneration of the organ of Corti (OC), stria vascularis (SV), spiral ligament (SL) and spiral ganglion cells; (D) The Gomori iron stain (in blue) demonstrated deposition of iron within the SL and SV of the OC in this left ear; (E) The Gomori iron stain also shows a deposition of iron in the subpial region of the cochlear nucleus. The principal histopathologic correlate of the hearing loss appeared to be severe degeneration of spiral ganglion cells of both ears in the presence of some remaining hair cells in the middle and apical turns, most consistent with primary cochlear neuronal degeneration.



Figs. 2.5A to C: Norrie's disease. This 77-year-old man was a known member of a pedigree with Norrie's disease. The patient was determined to be blind shortly after birth and was developmentally delayed. Hearing loss was first noted at the age of 3 years and was progressive. At the age of 75, 2 years prior to death, audiometric testing revealed bilateral profound sensorineural loss. There was no history of vestibular disorders. (A) Histogram of abnormalities in the organ of Corti, spiral ganglion and stria vascularis in the right ear as demonstrated by serial section reconstruction (blue areas reveal loss of structures). Areas shown with boxes indicate areas in which accurate determination could not be made; (B) In a midmodiolar section of the right cochlea, there was endolymphatic hydrops and eosinophilic proteinaceous material in all turns. There was severe degeneration of the organ of Corti particularly in the basal turn and marked degeneration of the spiral ganglion in all turns; (C) Higher magnification of the basal turn of the spiral ganglion demonstrates severe degeneration of the spiral ganglion (SPG) cells especially their dendritic arborization (DA).

gene encodes the gene product cochlin^{49,50} and its localization corresponds to the areas of eosinophilic deposits described in Figures 2.6A to C.

A targeted missense mutation in the form of a knock-in of DFNA9 has been studied in the mouse model of DFNA9. Despite documented hearing loss and vestibular dysfunction in this mouse model, the eosinophilic deposits so characteristic of DFNA9 in the human were not seen.^{49,50} Thus, the *COCH* G88E/G88E knock-in mouse model is not an exact model for human DFNA9 at least as evaluated histopathologically.

Verification of Equivalency of Animal Models of Normal Anatomy Reciprocal Synapses

In the study of anatomy, pathology, physiology and pathophysiology of the inner ear, animal models are commonly used with the assumption that anatomy and physiology of the animal and man are similar if not identical. However, similar to the comparison between molecular genetic models of ear disease the similarity of animal and human anatomy of the inner ear needs to be verified. As an example, a dual innervation of outer hair cells of the organ of Corti including both afferent and efferent fibers has been recognized for many years.⁵¹

In 1981, a variation on the dual innervation of outer hair cells in the human organ of Corti was described.⁵² Specifically, a reciprocal synaptic relationship was first observed in the cochlea in the human. Some of the nonvesiculated nerve terminals on outer hair cells demonstrated two distinct types of synaptic specialization: first, the typical afferent synapse with pre- and postsynaptic membrane thickening and presynaptic body on the hair cell side of the synapse, and second, between the same apparent afferent ending and the hair cell a collection of vesicles on the nerve terminal side and subsynaptic cisterna within the apposed hair cell cytoplasm, very suggestive of a small efferent terminal (Figs. 2.7A and B).

It was subsequently shown⁵³ that >50% of outer hair cells possess such reciprocal synapses, and the incidence of the synapses increased from the first to the third row of outer hair cells. The identification of this variant of synaptic morphology at the base of outer hair cells in the human suggested a need for a closer look at the synaptic morphology in animal models. Reciprocal synapses were soon identified at the base of outer hair cells in the organ of Corti of the chimpanzee⁵⁴ and the incidence and density

pattern of such synapses in the three rows of outer hair cells was found to be quite similar to the human.⁵⁵ A very similar synaptic relationship was identified between type 2 neurons at the base of outer hair cells in the cat.⁵⁶ In the cat model, the identification of the neuron involved in reciprocal synapses as type 2 neurons was convincingly demonstrated in specimens in which the olivocochlear (efferent) bundle had been previously sectioned.

In retrospect, reciprocal synapses between type 2 terminals and outer hair cells were reported previously in the chinchilla⁵⁷ and also in the cat.⁵⁸ However, in both reports the finding was not interpreted as normal anatomy but rather pathology secondary to deafferentation in the cochlea. It was thus not until after this synaptic relationship was identified in the human that the presence of reciprocal synapses between outer hair cells and type 2 neurons in the animal model was accepted as normal anatomy.

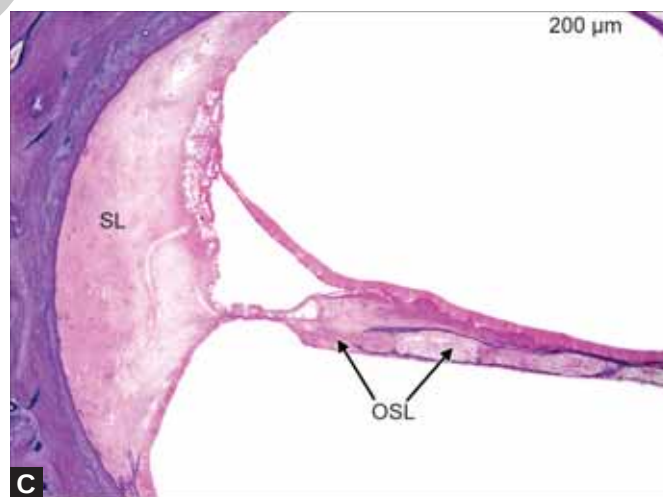
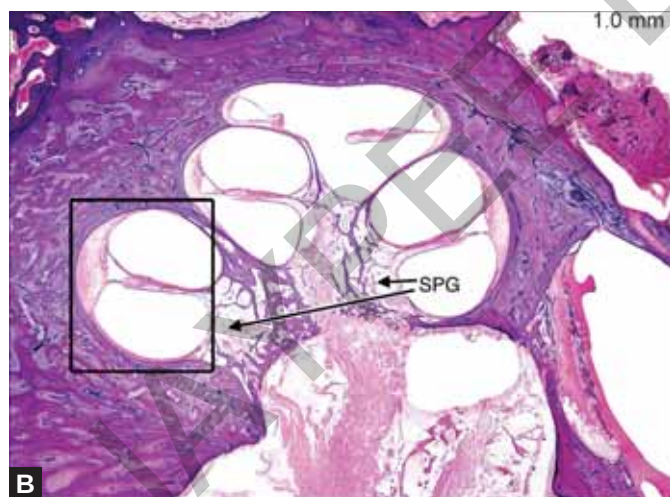
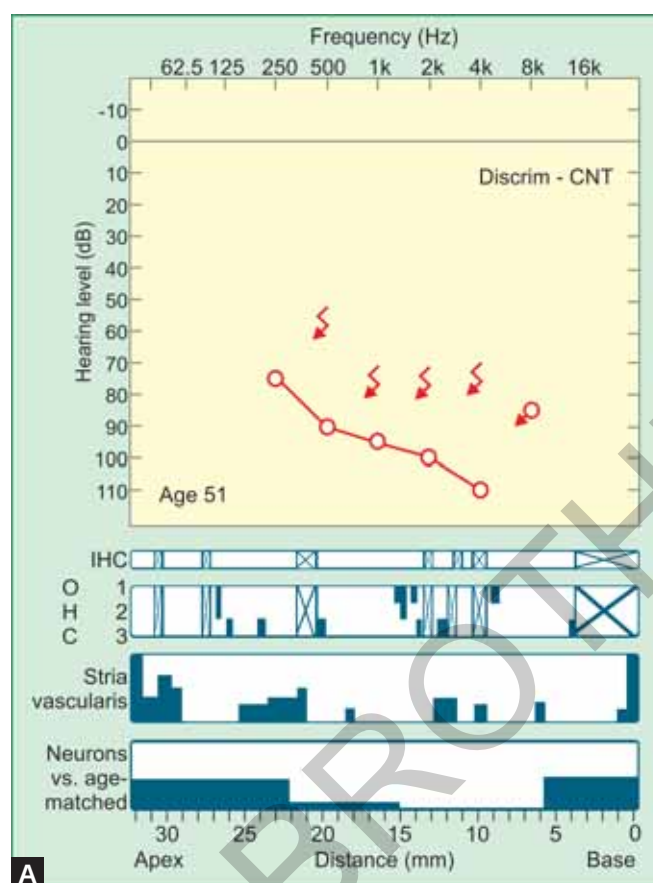
Evaluation of Medical and Surgical Treatments for Otologic Disorders

Residual and Recurrent Conductive Hearing Loss Following Stapedectomy

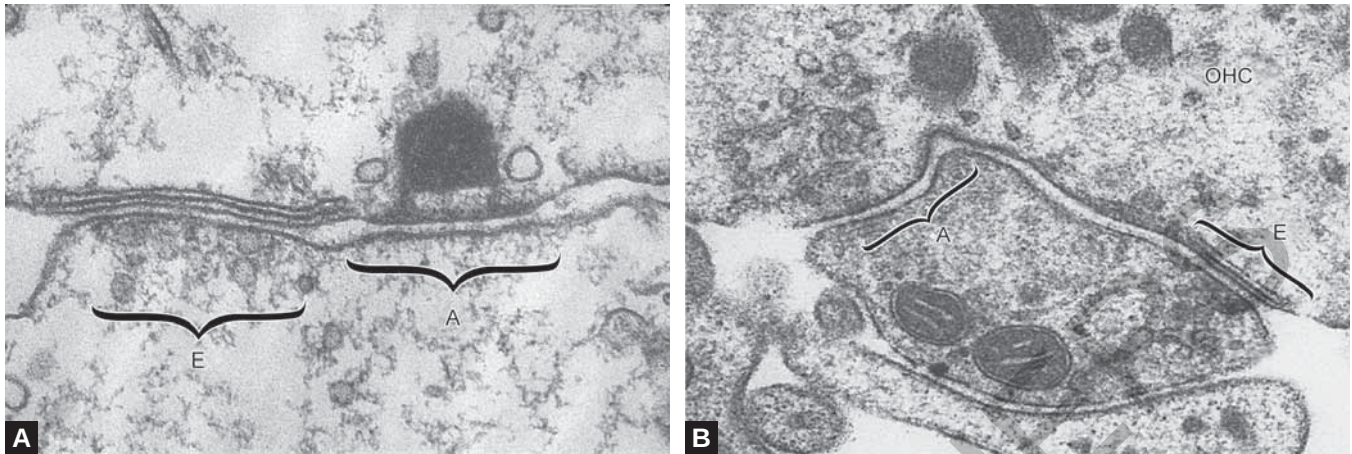
Closure of the air bone gap to within 10 dB is attainable in 90% of stapedectomies.⁵⁹ Recurrent conductive hearing loss is known to occur after stapedectomy.⁶⁰ Although clinical observations made at revision surgery for failed stapedectomy caused by both residual and recurrent conductive hearing loss provide insight into causation,⁶¹⁻⁶³ otopathologic examination of specimens from patients who in life had either recurrent or residual conductive loss after stapedectomy provides more detail. Figures 2.8 and 2.9 provide illustrative cases as to the otopathologic correlates of residual and recurrent conductive hearing loss following stapedectomy.

Residual Conductive Loss after Stapedectomy

Malleus fixation: Harris⁶⁴ found that fixation of the malleus may cause an air bone gap of up to 28 dB. In a human temporal bone study, Oktay et al.⁶⁵ found that the incidence of malleus fixation was 8%. The obvious clinical lesson is that during an exploratory tympanotomy for conductive hearing loss, a systematic search for a cause, including palpation of the malleus for ankylosis, should be done (Fig. 2.8A).



Figs. 2.6A to C: DFNA9. This 59-year-old woman had a history of progressive hearing loss since the age of 21 years. She was identified as part of a pedigree with DFNA9. (A) *Audiocytocochleogram*: There was severe to profound sensorineural loss with no measurable speech discrimination in both ears (right shown here). Despite postmortem autolysis, hair cells could be seen throughout the cochlea; (B) Midmodiolar section of the right ear. Spiral ganglion cells showed moderate degeneration. Boxed area of the basal turn shown in higher power in Figure 2.6C; (C) The spiral ligament (SL) and osseous spiral lamina (OSL) were severely degenerated and replaced by an amorphous deposition of eosinophilic material. There was a similar pattern of degeneration in the vestibular system with atrophy of the dendritic processes of the vestibular nerves.



Figs. 2.7A and B: (A) Reciprocal synapse. At the base of an outer hair cell in the human organ of Corti were synaptic specializations consistent with both afferent (A) and efferent (E) synaptic relationships between nerve ending on an outer hair cell; (B) Reciprocal synapse at the base of an outer hair cell in the cat. Afferent (A) and efferent (E) specializations are found between the same neuron terminal and a single outer hair cell (OHC).

Obliteration of the round window: In addition to stapes fixation due to otosclerosis, obliteration of the round window may occur. This is a common site of predilection of otosclerosis (Fig. 2.8B). The clinical lesson illustrated by this case is that during exploratory tympanotomy for possible stapedectomy, a systemic review of other sites that could cause conductive hearing loss such as round window obliteration should be undertaken.

Prosthesis lying on residual fixed footplate: If in the course of a stapedectomy if the fenestration of the footplate is insufficient or in some cases the prosthesis too short, the prosthesis may be found to lie on the residual fixed portion of the footplate causing a residual conductive hearing loss even if the fenestrated portion of the footplate is adjacent (Fig. 2.8C).

Residual conductive hearing loss due to malpositioned prosthesis: Even in a total or subtotal stapedectomy if the prosthesis is positioned at a margin of the oval window niche, a residual conductive hearing loss may occur (Fig. 2.8D).

Recurrent Conductive Hearing Loss after Stapedectomy

Resorptive osteitis of the incus: Over time, resorptive osteitis may result in discontinuity of the incus and a resultant recurrent conductive hearing loss (Fig. 2.9A). Resorptive osteitis of the incus at the site of attachment of the stapes prosthesis to the incus is a common finding,⁶⁶ seemingly

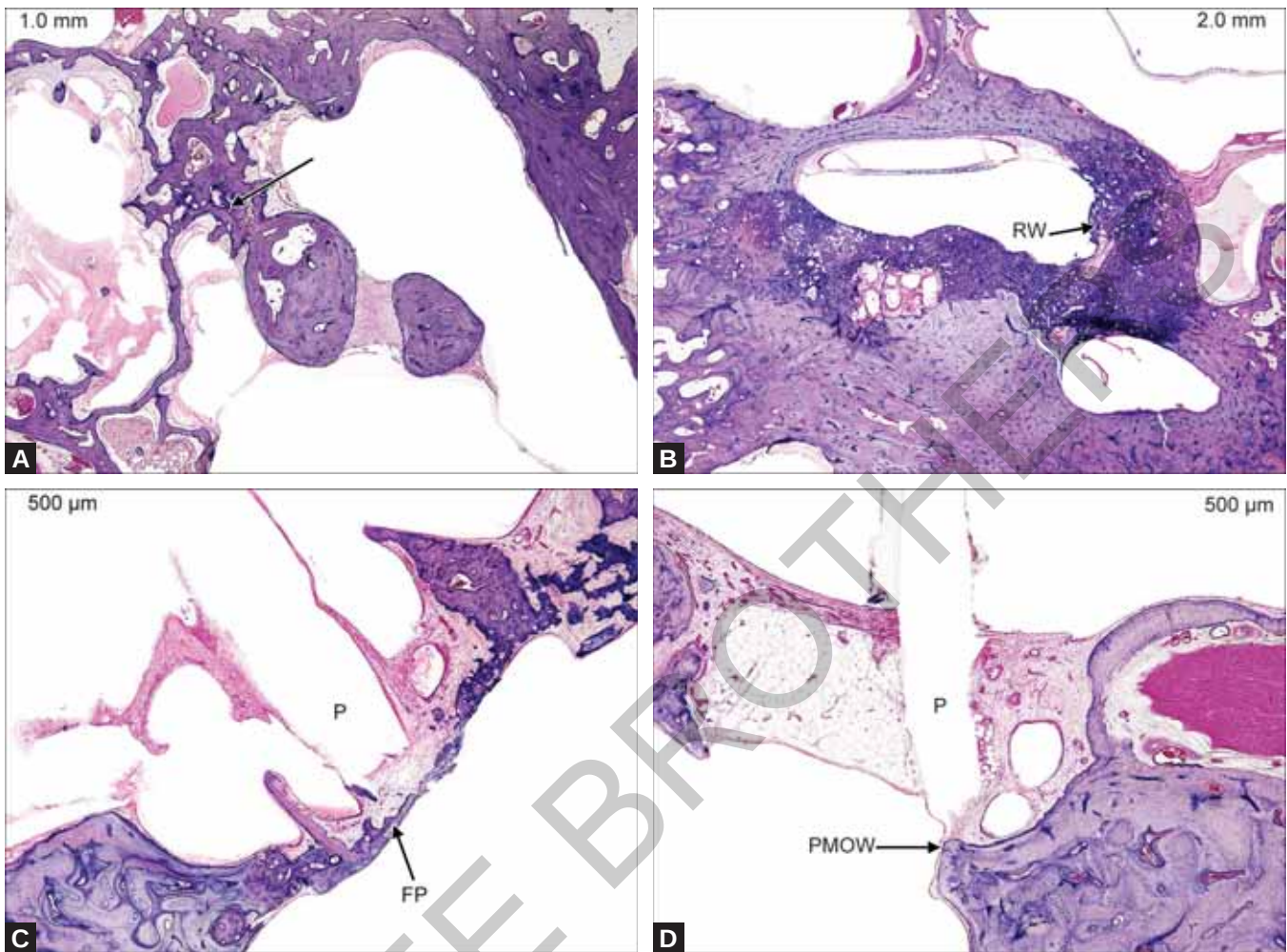
regardless of the specific type of prosthesis used. The pathogenesis of resorptive osteitis of the incus is unknown and in fact may occur without previous stapedectomy.^{67,68}

Recurrent conductive hearing loss following a drill out for oblitative otosclerosis of the oval window: Although refixation of the prosthesis in the oval window is unusual following stapedectomy, it may occur and may be more common after extensive drill out procedures for oblitative otosclerosis. Fixation of the stapes prosthesis may be caused by reparative new bone formation rather than otosclerosis (Fig. 2.9B).

Cochlear Implantation

Cochlear implantation may result in immediate trauma due to dissection of the lateral cochlear wall, rupture of the basilar membrane, dislocation of the basilar membrane (Fig. 2.10A) and fracture dislocation of the osseous spiral lamina. Delayed effects of cochlear implantation include formation of a fibrous sheath surrounding the electrode and neo-osteogenesis at the cochleostomy site and also in the ascending and descending limbs of the basal turn (Figs. 2.10A and B).⁶⁹

Although biocompatible, a cochlear implant is often not bioinert and lymphocytic infiltration around the electrode may be seen (Fig. 2.10C). Occasionally, the cellular immune response may be so exuberant as to result in total destruction of the organ of Corti and marked degeneration of the remaining spiral ganglion cells in Rosenthal's canal (Figs. 2.10D and E).



Figs. 2.8A to D: (A) Residual conductive hearing loss, malleus fixation. This 96-year-old woman had a progressive bilateral hearing loss for the past 30 years of her life. In the epitympanum on the right ear, the head of the malleus was ankylosed to the anterior epitympanic wall by bone (arrow); (B) Residual conductive hearing loss, round window obliteration. This 92-year-old woman underwent a right stapedectomy at the age 70 using a fat wire prosthesis without significant improvement in hearing. Otopathology of the oval window showed stapes prostheses in good position with a healthy fat graft and the presence of otosclerosis, anteriorly and posteriorly. However, the round window (RW) was totally obliterated by otosclerotic bone; (C) Residual conductive hearing loss. This 70-year-old woman with a clinical diagnosis of otosclerosis underwent a stapedectomy on the left ear using Teflon wire prosthesis at the age 66. A postoperative audiogram demonstrated improvement but not closure of the air bone gap. Otopathologic examination demonstrated the outline of a Teflon prosthesis (P), which did not penetrate into the vestibule but rather lay against some residual fixed footplate (FP) fragments in the oval window niche. There was a small central surgical defect in the footplate that was enough to allow improvement in the air-bone gap but the position of the piston against the residual fixed footplate segment presumably prevented closure of the gap; (D) Residual conductive hearing loss. This 57-year-old woman underwent insertion of fat wire prosthesis for otosclerosis in the right ear. Histopathology demonstrated the silhouette of the prosthesis (P) directed toward the posterior margin of the oval window (PMOW).

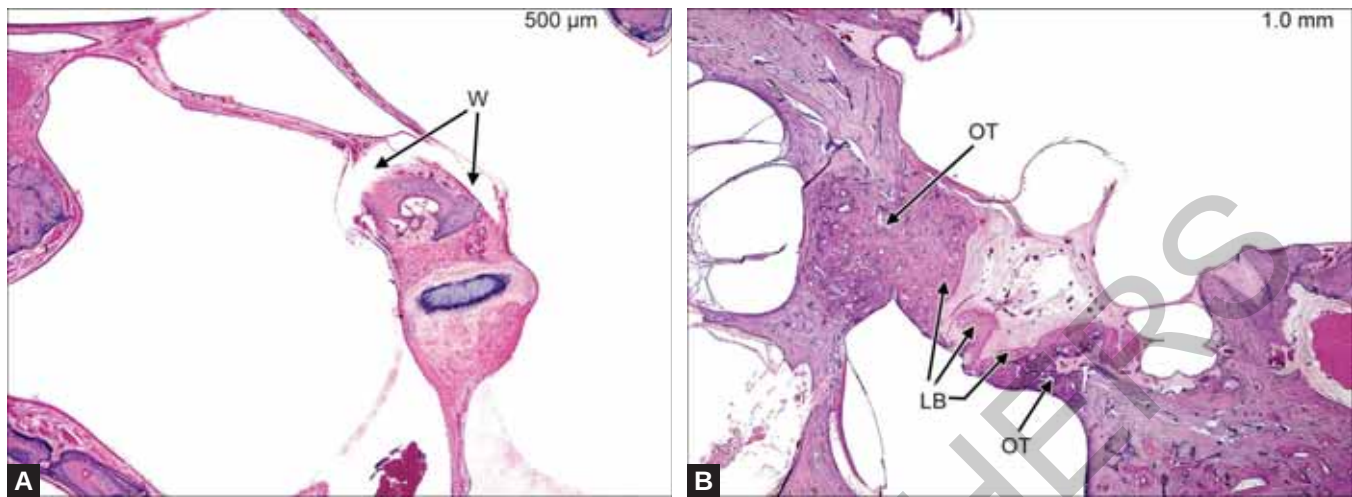
Application of Modern Neuropathologic and Clinicopathologic Techniques to the Human Diseases

Several techniques may be applied to postmortem human temporal bones in conjunction with light microscopy. Examples include correlation of human otopathology with

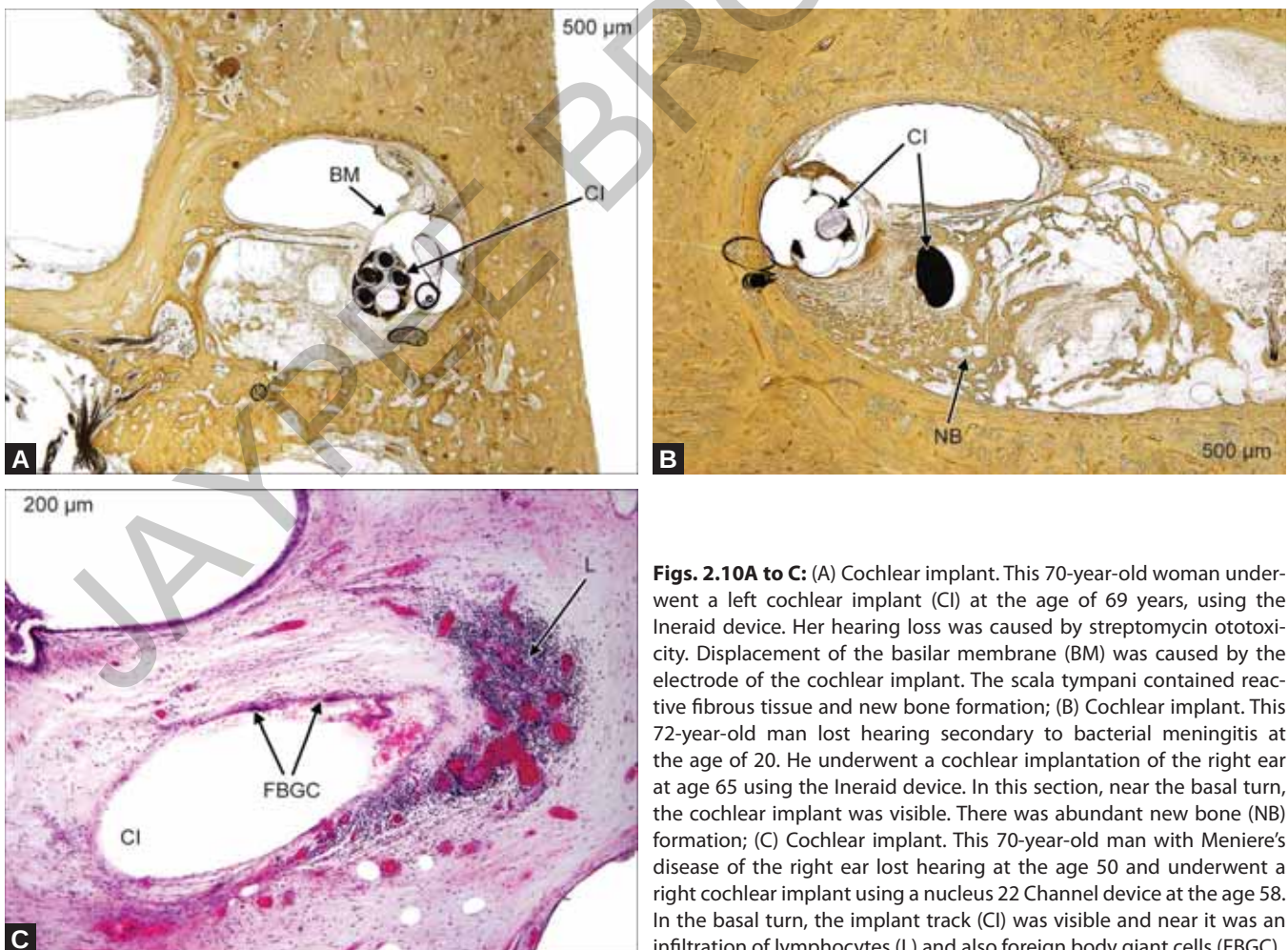
modern imaging techniques, including computed tomography (CT) scan,⁷⁰ transmission electron microscopy, study of nucleic acids,⁷¹ immunostaining⁷² and proteomics.^{16,73,74}

SUMMARY

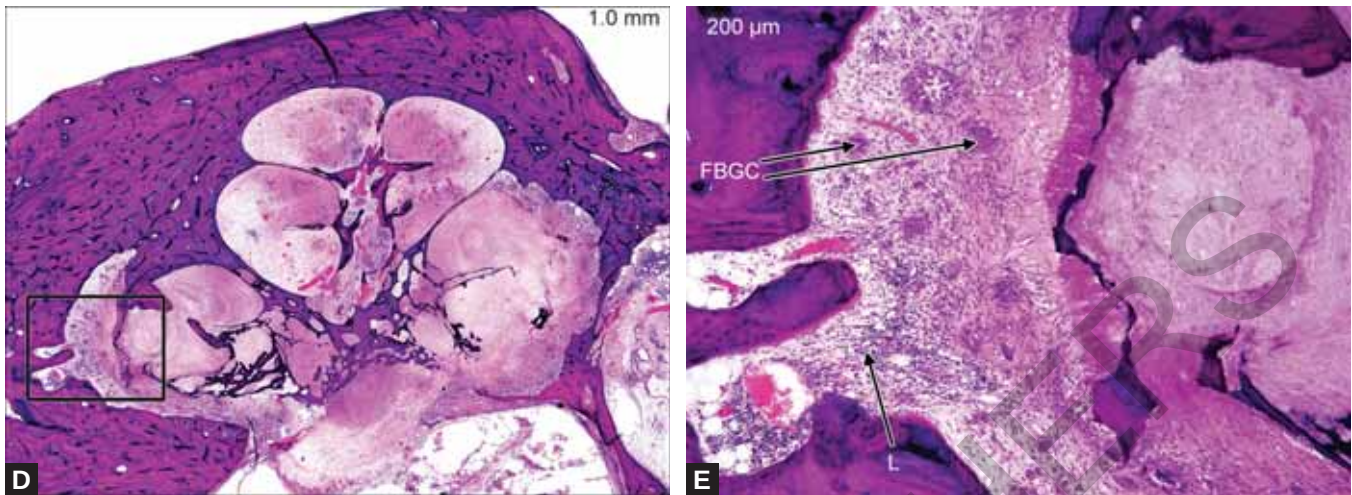
Conventional otopathologic techniques still provide considerable new information concerning the pathologic



Figs. 2.9A and B: (A) Recurrent conductive hearing loss, resorptive osteitis. This 62-year-old man with otosclerosis underwent a left stapedectomy with insertion of a Teflon wire prosthesis at age 57. Although hearing improvement was sustained, a moderate degree of resorptive osteitis of the incus was identified otopathologically at the site of the wire attachment (W) to the incus; (B) Recurrent conductive hearing loss. This 65-year-old man underwent a right stapedectomy at the age of 64. Oblitative otosclerosis was identified at the oval window and was drilled away with subsequent placement of fat wire prosthesis. Histologic section of the oval window demonstrated oblitative otosclerosis (OT) and postoperative deposition of new lamellar bone (LB) (nonotosclerotic) at the site of the previous drill out procedure 1 year later. At 7-month postoperatively, his air bone gap recurred presumably due to narrowing of the oval window fenestration secondary to new bone formation.



Figs. 2.10A to C: (A) Cochlear implant. This 70-year-old woman underwent a left cochlear implant (CI) at the age of 69 years, using the Ineraid device. Her hearing loss was caused by streptomycin ototoxicity. Displacement of the basilar membrane (BM) was caused by the electrode of the cochlear implant. The scala tympani contained reactive fibrous tissue and new bone formation; (B) Cochlear implant. This 72-year-old man lost hearing secondary to bacterial meningitis at the age of 20. He underwent a cochlear implantation of the right ear at age 65 using the Ineraid device. In this section, near the basal turn, the cochlear implant was visible. There was abundant new bone (NB) formation; (C) Cochlear implant. This 70-year-old man with Meniere's disease of the right ear lost hearing at the age 50 and underwent a right cochlear implant using a nucleus 22 Channel device at the age 58. In the basal turn, the implant track (CI) was visible and near it was an infiltration of lymphocytes (L) and also foreign body giant cells (FBGC).



Figs. 2.10D and E: (D) Cochlear implant. This 71-year-old man had a presumably genetically determined bilateral progressive hearing loss starting at age 16. At the age 58, he underwent a right cochlear implant using a nucleus device. At 8 months postoperatively, his central institute of the deaf (CID) sentence score was 78% but by 12 months it had dropped to 18%, and he developed some facial nerve stimulation with the cochlear implant. Integrity testing of the device was normal. At the age 59, he underwent a contralateral left cochlear implant with full insertion. By 5 months, he had sound awareness only with a new onset of facial nerve stimulation. At the age 60, he underwent explantation and then reimplantation of the left ear with full insertion but no improvement in word recognition. Integrity testing was normal. At the age 66, a computed tomography scan was done that showed no significant abnormality. In this midmodiolar section of the right temporal bone, the scala vestibuli, scala tympani and scala media were replaced by granulation tissue, which included multiple sites of lymphocytic infiltration and many foreign body giant cells. There was complete loss of the organ of Corti and marked degeneration of remaining spiral ganglion cells in Rosenthal's canal. The boxed area is shown at higher magnification in Figure 2.10E; (E) Higher power magnification of granulation tissue in the basal turn of the right ear with infiltration of lymphocytes (L) and multiple foreign body giant cells (FBGC).

basis of the diseases, verification of the applicability and equivalency of animal models of the diseases for human disorders, verification of equivalency of animal models for normal anatomy and the evaluation of medical and surgical interventions as treatment for otologic disorders. The information provided by standard serial section light microscopy may be amplified significantly by the use of immunostaining, proteomic techniques and transmission electron microscopy.

REFERENCES

- Schuknecht HF. Temporal bone collections in Europe and the United States: observations on a productive laboratory, pathologic findings of clinical relevance and recommendations. *Ann Otol Rhinol Laryngol.* 1987;96(Suppl 130): 1-19.
- Merchant SN. History of temporal bone collections. In: Merchant SN, Nadol JB Jr, (Eds). *Schuknecht's Pathology of the Ear*, 3rd edition. Shelton, CT: People's Medical Publishing House-USA; 2010. pp. 4-8.
- Chole RA, McKenna MJ. A silent and imminent threat. *Newsletter of NIDCD National Temporal Bone, Hearing, and Balance Resource Registry*, Winter. 2012;20:1-2.
- Chole RA, McKenna MJ. A silent and imminent threat. *Bull Amer Acad Otolaryng.* 2013.
- Merchant SN, Schuknecht HF, Rauch SD, McKenna MJ, Adams JC, Wudarsky R, et al. The national temporal bone, hearing, and balance pathology resource registry. *Arch Otolaryngol, Head Neck Surg.* 1993;119:846-53.
- Nadol JB Jr. Techniques for human temporal bone removal: information for the scientific community. *Otolaryngol-Head Neck Surg.* 1996;115:298-305.
- Nadol JB Jr. Extracranial technique for temporal bone removal. *Ann Otol Rhinol Laryngol.* 1980;89:251-2.
- Michaels L, Wells M, Frohlich HA. A new technique for the study of temporal bone pathology. *Clin Otolaryngol.* 1983; 8:77-85.
- Michaels SL, Gould SJ, Wells M. Microslicing method in the study of temporal bone changes in the perinatal period: an interim report. *Acta Otolaryngologica (Stockh).* 1985;423(suppl):9-14.
- Wackym PA, Simpson TA, Gantz BJ, Smith RJ. Polymerase chain reaction amplification of DNA for archival celloidin embedded human temporal bone sections. *Laryngoscope.* 1993;103:583-8.
- McKenna MJ, Kristiansen A, Haines J. Isolation and identification of nucleic acid sequences from celloidin and paraffin embedded human temporal bone sections. In: Mogi G, Veldman JE, Kawauchi H (Eds). *Immunobiology in Otorhinolaryngology*. Amsterdam, The Netherlands: Kugler Publications; 1994. pp. 283-8.

12. Ohtani F, Furuta Y, Iino Y, Inuyama Y, Fukuda S. Amplification of RNA from archival human temporal bone sections. *Laryngoscope*. 1999;109:617-20.
13. Kimura Y, Kubo S, Koda H, Noguchi Y, Sawabe M, Maruyama N, et al. Quantitative analysis of mRNA in human temporal bones. *Acta Otolaryngol*. 2007;127:1024-30.
14. Adams JC. Clinical implications of inflammatory cytokines in the cochlea. A technical note. *Otol Neurotol*. 2002;23:316-22.
15. Doherty JK, Linthicum FH, Jr. Spiral ligament and stria vascularis changes in cochlear otosclerosis: effect on hearing level. *Otol Neurotol*. 2004;25:457-64.
16. Palmer-Toy DE, Krastins B, Sarracino DA, Nadol JB, Jr., Merchant SN. Efficient method for the proteomic analysis of fixed and embedded tissues. *J Proteome Res*. 2005;4:2404-11.
17. Robertson NG, Cremers CW, Huygen PL, Ikezono T, Krastins B, Kremer H, et al. Cochlin immunostaining of inner ear pathologic deposits and proteomic analysis in DFNA9 deafness and vestibular dysfunction. *Hum Molec Genet*. 2006;15:1071-85.
18. Merchant SN, Krastins B, Palmer-Toy DE, O'Malley J, Adams JC, Nadol JB Jr, et al. Application of proteomics to human temporal bone research. *ARO Abstracts*. 2007;777.
19. Guild SR. A graphic reconstruction method for the study of the organ of Corti. *Anat Rec*. 1921;22:141-57.
20. Schuknecht HF. Cochlear reconstruction and quantification. In: *Pathology of the Ear*, 2nd edition. New York: Lea and Febiger; 1993. pp. 21-9.
21. Merchant SN. A method for quantitative assessment of vestibular otopathology. *Laryngoscope*. 1999;109:1560-9.
22. Merchant SN, Velazquez-Villasenor L, Tsuji K, Glynn RJ, Wall C, III, Rauch SD. Temporal bone studies of the human peripheral vestibular system. Normative vestibular hair cell data. *Ann Otol Rhinol Laryngol*. 2000; 109 (Suppl 181):3-13.
23. Ylikoski J, Collan Y, Palva T, Jauhiainen T. Cochlear nerve in neurilemmomas. *Audiology and histopathology. Arch Otolaryngol*. 1978;104:679-84.
24. Mahmud MR, Khan AM, Nadol JB Jr. Histopathology of the inner ear in unoperated acoustic neuroma. *Ann Otol Rhinol Laryngol*. 2003;112:979-86.
25. Arriaga MA, Long S, Nelson R. Clinical correlates of acoustic neuroma volume. *Am J Otol*. 1993;14:465-8.
26. Nadol JB Jr, Diamond PF, Thornton AR. Correlation of hearing loss and radiologic dimensions of vestibular schwannomas (acoustic neuromas). *Am J Otol*. 1996;17:312-6.
27. Roosli C, Linthicum FH, Cureoglu S, Merchant SN. Dysfunction of the cochlea contributing to hearing loss in acoustic neuromas. An underappreciated entity. *Otol Neurotol*. 2012;33:473-80.
28. Eckermeier L, Pirsig W, Mueller D. Histopathology of 30 non-operated acoustic schwannomas. *Arch Otorhinolaryngol*. 1979;222:1-9.
29. Silverstein H. Inner ear fluid proteins in acoustic neuroma Meniere's disease and otosclerosis. *Ann Otol Rhinol Laryngol*. 1971;30:27-35.
30. Palva T, Raunio V. Cerebellar spinal fluid and acoustic neuroma specific proteins in perilymph. *Acta Otolaryngologica (Stock)*. 1982;93:201-3.
31. Welling DB, Lasak JM, Akhmametyeva E, Ghaheri B, Chang LS. c-DNA microarray analysis of vestibular schwannomas. *Otol Neurotol*. 2002;23:736-48.
32. Stankovic KM, Mrugala MM, Martuza R, Silva M, Betensky RA, Nadol JB Jr, et al. Genetic determinants of hearing loss associated with vestibular schwannomas. *Otol Neurotol*. 2009;30:661-7.
33. Fearnley JM, Stevens JM, Rudge P. Superficial siderosis of the central nervous system. *Brain*. 1985;118:1051-66.
34. Koeppe AH, Michael SC, Danhong LZC, et al. The pathology of superficial siderosis of the central nervous system. *Acta Neuropathol*. 2008;116:371-82.
35. Nadol JB Jr, Adams JC, O'Malley JT. Temporal bone histopathology in a case of sensorineural hearing loss caused by superficial siderosis of the central nervous system and treated by cochlear implantation. *Otol Neurotol*. 2011;32:748-55.
36. Spoendlin H. Retrograde degeneration of the cochlear nerve. *Acta Otolaryngol*. 1975;79:266-75.
37. Sekiya T, Yagihashi A, Shimamura N, et al. Apoptosis of auditory neurons following central process injury. *Exper Neurol*. 2003;184:648-58.
38. Susac JO, Egan RA, Rennebohm RM, Lubow M. Susac syndrome: 1975-2005 microangiography/autoimmune endo-theliopathy. *J Neurologic Sci*. 2007;257:270-2.
39. Francis HW, Makary C, Halpin C, Crane BT, Merchant SN. Temporal bone findings in a case of Susac syndrome. *Otol & Neurotol*. 2011;32:1198-204.
40. Adour KK, Bell DN, Hilsinger RL Jr. Herpes simplex virus in idiopathic facial paralysis (Bell's Palsy). *JAMA*. 1975; 233:527-30.
41. Burgess RC, Michaels L, Bale JF Jr, Smith RJ. Polymerase chain reaction amplification of Herpes Simplex virus DNA from the geniculate ganglion of a patient with Bell's palsy. *Ann Otol Rhinol Laryngol*. 1994;103:775-9.
42. Djupesland G, Degré M, Stien R, Skrede S. Acute peripheral facial palsy. Part of a cranial polyneuropathy? *Arch Otolaryngol*. 1977;103:641-4.
43. Murakami S, Mizobuchi M, Nakashiro Y, Doi T, Hato N, Yanagihara N. Bell palsy and Herpes Simplex virus: identification of viral DNA in endothelial fluid and muscle. *Ann Int Med*. 1996;124:27-30.
44. Warburg M. Norrie's disease: a congenital progressive oculo-acoustico-cerebral degeneration. *Acta Ophthalmol (Copenhagen)*. 1966;89(suppl):1-47.
45. Nadol JB Jr, Eavey RD, Liberfarb RM, Merchant SN, Williams R, Cliemehager D, et al. Histopathology of the ears, eyes and brain in Norrie's disease (oculo-acoustico-cerebral degeneration). *Am J Otolaryngol*. 1990;11:112-24.
46. Rehm HL, Zhang DS, Brown MC, Burgess B, Halpin C, Berger W, et al. Vascular defects and sensorineural deafness in a mouse model of Norrie disease. *J Neurosci*. 2002; 22:4286-92.

47. Deng C, Reddy P, Cheng Y, Luo CW, Hsiao CL, Hsueh AJ. Multi-functional norrin is a ligand for the LGR 4 receptor. *J Cell Sci.* 2013;126:2060-8.
48. Khetarpal U, Schuknecht HF, Gacek RR, Holmes LB. Autosomal dominant sensorineural hearing loss: pedigrees, audiologic findings and temporal bone findings in two kindreds. *Arch Otolaryngol Head Neck Surg.* 1991;117:1032-42.
49. Robertson NG, Lu L, Heller S, Merchant SN, Eavey RD, McKenna M, et al. Mutations in a normal cochlear gene cause DFNA9, a human nonsyndromic deafness with a vestibular dysfunction. *Nature Genet.* 1998;20:299-303.
50. Robertson NG, Jones SM, Sivakumaran TA, Giersch ABS, Jurado SA, Call LM, et al. A targeted *COCH* missense mutation: a knock-in mouse model for DFNA9 late-onset hearing loss and vestibular dysfunction. *Hum Mol Genet.* 2008; 17:3426-34.
51. Engstrom H. On the double innervation of the sensory epithelia of the inner ear. *Acta Otolaryngol (Stockh).* 1958; 49:109-18.
52. Nadol JB Jr. Reciprocal synapses of the base of outer hair cells in the organ of Corti of man. *Ann Otol Rhinol Laryngol.* 1981;90:12-7.
53. Nadol JB Jr. Incidence of reciprocal synapses on outer hair cells of the human organ of Corti. *Ann Otol Rhinol Laryngol.* 1984;93:247-50.
54. Nadol JB Jr, Burgess BJ. Morphology of synapses at the base of hair cells in the organ of Corti of the chimpanzee. *Ann Otol Rhinol Laryngol.* 1990;99:215-20.
55. Francis HW, Nadol JB Jr. Patterns of innervation of outer hair cells in a chimpanzee: I. Afferent and reciprocal synapses. *Hear Res.* 1993;64:184-90.
56. Thiers FA, Nadol JB Jr, Liberman MC. Reciprocal synapses between outer hair cells and their afferent terminals: evidence for local neural network in mammalian cochlea. *JARO.* 2008;9:477-89.
57. Iurato S, Smith CA, Eldrege DH, Henderson D, Carr C, Ueno Y, et al. Distribution of the crossed olivocochlear bundle in the chinchilla's cochlea. *J Comp Neurol.* 1978;182:57-76.
58. Pujol R, Carlier E. Cochlear synaptogenesis after sectioning of the efferent bundle. *Brain Res.* 1982;255:151-4.
59. Shea JJ Jr. Forty years of stapes surgery. *Am J Otol.* 1998; 19:52-5.
60. Langmann AW, Jackler RK, Sooy FA. Stapedectomy: long-term hearing results. *Laryngoscope.* 1991;101:810-4.
61. Han WW, Incesulu A, McKenna MJ, Rauch SD, Nadol JB Jr, Glynn RJ. Revision stapedectomy: intraoperative findings, results and review of the literature. *Laryngoscope.* 1997;107:1185-92.
62. Feldman BA, Schuknecht HF. Experience with revision stapedectomy procedures. *Laryngoscope.* 1970;80:1281-91.
63. Derlacki EL. Revision stapes surgery: problems with some solution. *Laryngoscope.* 1985;95:1047-53.
64. Harris JP, Metha RP, Nadol JB Jr. Malleus fixation: clinical and histopathologic findings. *Ann Otol Rhinol Laryngol.* 2002;111:246-54.
65. Oktay MF, Cureoglu S, Schachern PA, Gulbahce E, Paparella MM, Hayasi H. Histologic changes in the anterior malleolar ligament and the head of the malleus in otosclerosis. *Otolaryngol Head Neck Surg.* 2006;134:232-5.
66. Schuknecht HF, Jones DD. Stapedectomy: postmortem findings. *Ann Otol Rhinol Laryngol.* 1997;88(55):1-43.
67. Lannigan FJ, O'Higgins P, Oxnard CE, McPhie P. Age-related bone resorption in the normal incus: a case of maladaptive remodeling? *J Anat.* 1995;186:651-5.
68. Imauchi Y, Carino S, Yamasoba T. Acquired atrophy of the long process of the incus. *Otol Head Neck Surg.* 2005; 132:156-8.
69. Nadol JB Jr, Shiao JY, Burgess BJ, Ketten DR, Eddington DK, Gantz BJ, et al. Histopathology of cochlear implants in humans. *Ann Otol Rhinol Laryngol.* 2001;110:883-91.
70. Quesnel AM, Moonis G, Appel J, O'Malley JT, McKenna MJ, Curtin HD, et al. Correlation of computed tomography with histopathology and otosclerosis. *Otol Neurotol.* 2013;34:22-8.
71. McKenna MJ, Kristiansen AG, Haines J. Polymerase chain reaction amplification of the measles virus sequenced from human temporal bone sections with active otosclerosis. *Am J Otol.* 1996;17:827-30.
72. O'Malley JT, Merchant SN, Burgess BJ, Jones DD, Adams JC. Effects of fixative and embedding medium on morphology in immunostaining of the cochlea. *Audiol Neurotol.* 2009;14:78-87.
73. Markaryan A, Nelson EG, Helseth LD, Hinojosa R. Proteomic analysis of formalin fixed celloidin-embedded whole cochlear and laser microdissected spiral ganglion tissues. *Acta Otolaryngol.* 2010;130:984-9.
74. Aarnisalo AA, Green KM, O'Malley J, Makary C, Adams J, Merchant SN, et al. A method for MSE differential proteomic analysis of archival formalin fixed celloidin embedded human inner ear tissue. *Hear Res.* 2010;270: 15-20.

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