



the REGISTRY

Newsletter of the NIDCD National Temporal Bone, Hearing and Balance Pathology Resource Registry

Inside:

Scientific Article: The Effects of Type 1 Diabetes Mellitus on the Cochlear Structure and Vasculature in Human Temporal Bones 1

In the News: NIDCD has renewed the Registry's contract for five more years 2

Laboratory Spotlight: Temporal Bone Laboratory, University of Minnesota 6

Mini-Travel Fellowship: Two Mini-Travel Fellowships are currently available 8

Research Article 1
News and Announcements 2
TB Lab Spotlight 6

The REGISTRY is published semi-annually by the NIDCD National Temporal Bone, Hearing and Balance Pathology Resource Registry. The Registry was established in 1992 by the National Institute on Deafness and Other Communication Disorders (NIDCD) of the National Institutes of Health to continue and expand upon the former National Temporal Bone Banks (NTBB) Program. The Registry promotes research on hearing and balance disorders and serves as a resource for the public and the scientific community about research on the pathology of the human auditory and vestibular systems.

The Effects of Type 1 Diabetes Mellitus on the Cochlear Structure and Vasculature in Human Temporal Bones

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INTRODUCTION

Diabetes mellitus continues to represent a major medical problem in the world. The relationship between diabetes mellitus and sensorineural hearing loss (SNHL) has been studied for more than one century. Many authors agree that diabetes mellitus can lead to SNHL (1-4). Although histopathological changes such as thickening of the capillary walls in the cochlea (5-9), especially in the stria vascularis have been reported in patients with diabetes. Only a few reports describe damage to the stria vascularis, hair cells and spiral ganglion cells (5,6). It is not always clear whether these changes are primarily due to the disease. Human temporal studies have not revealed a consistent pathologic correlate for diabetes mellitus and previous studies in humans have not sub-classified diabetes mellitus into type 1 and type 2 diabetes. Because most cases of diabetes are type 2, the patients are older resulting in difficulty interpreting if the changes are from diabetes or presbycusis.

To examine the effects of diabetes on the cochlea, we conducted a study in temporal bones from patients with juvenile diabetes to analyze outer hair cells (OHC), inner hair cells (IHC), spiral ganglion cells, and areas of stria vascularis and thickening of the capillary walls of vessels under the basilar membrane. To our knowledge this study is the first to quantitatively document the changes in the cochlea due to type 1 diabetes mellitus in humans.

MATERIALS AND METHODS

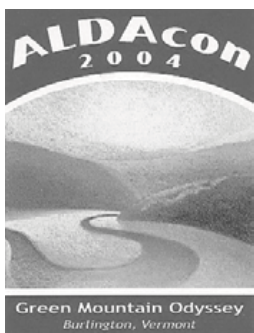
This study included 26 temporal bones from 13 patients with type 1 diabetes (mean age, 37.5 years; age range, 18-68 years) and 30 temporal bones from 17 normal cases (mean age, 38.4 years; age range, 12-67 years). The age of onset ranged from 6 to 34 years with a mean of 15.3 years. The duration of diabetes ranged from 5 to 46 years with a mean of 22.2 years. Excluded were subjects who had a history of acoustic trauma, ototoxic drugs or otologic surgery, and those with any

NEWS AND ANNOUNCEMENTS



In March 2004, the Registry was awarded a contract from the NIDCD. The important work the Registry has been doing will continue into the next five years. The Deafness Research Foundation and the Registry will once again be working together to educate the public about temporal bone donation and research. Thank you all for your continued support of the Registry and it's mission.

Look for the Registry's Exhibit at these upcoming meetings



The Association for Late-Deafened Adults will be holding their international conference at the Wyndham Burlington Hotel in Burlington, Vermont. It will be held from September 1st - 5th, 2004. Please visit their website for more information.
www.alda.org



American Academy of Otolaryngology--Head and Neck Surgery Foundation
2004 Annual Meeting & OTO EXPO
September 19-22
New York, NY
Please visit their website for more information.
www.entnet.org



The Association for Research in Otolaryngology 2005 MidWinter Meeting will be held in Daytona Beach, Florida on February 26th - March 3rd, 2005. More information is available on their website.
www.aro.org

The Registry's DNA Program

Have you signed up to be a part of the Registry's DNA program? All our registered donors are encouraged to join our DNA program. This program greatly enhances your temporal bone donation. It's as easy as brushing your teeth. For further information please contact the Registry at **(800) 822-1327**.



The Deafness Research Foundation has announced a change to their contact numbers. The new numbers are:

202-887-5850 Telephone
202-293-1865 Fax

IN THE NEWS....

Researchers at the Scripps Research Institute in La Jolla, California, The University of California, San Diego and Oregon Hearing Research Center and Vollum Insitute in Portland, Oregon have made a very important discovery about one of the genes involved in hearing.

An article in an upcoming issue of Nature has identified cadherin 23, a protein, as playing a very important role in how we hear. The researchers believe that this gene is responsible for creating tiny links within the cochlea which make hearing possible.

The researchers found that hair cells or stereocilium are bundled together into stereocilia. The tip of each hair cell is bound to the one next to it by a tiny link. The cadherin 23 gene encodes a protein which creates these links. Without these links hearing would be impossible.

Mutations in the cadherin 23 has long been associated with deafness and Usher Syndrome.

Send Us Your News!

Send us your news and announcements regarding hearing and/or balance loss or temporal bone research!
(See page 3 for contact information.)

the REGISTRY

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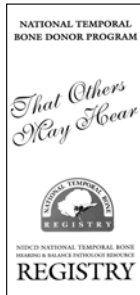
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Brochures about Temporal Bone Research and Donation Order Free-of-Charge for Your Office, Clinic or Organization

The NIDCD National Temporal Bone, Hearing and Balance Pathology Resource Registry, which is dedicated to promoting research on hearing and balance disorders through the study of temporal bones, has published two informational brochures, which you may request for display in your office and/or waiting rooms. Both brochures encourage individuals with hearing or balance disorders to bequeath their temporal bones to scientific research.



That Others May Hear is a short form brochure which describes briefly the functions of the Registry, and answers commonly asked questions regarding the temporal bone donation process. (Dimensions: 9" x 4")

The Gift of Hearing: Learning about Temporal Bone Donation is a 16-page, full-color booklet which describes in more detail and with diagrams, the structures of the ear, types of auditory disorders, the microscopic study of the temporal bone, and the benefits of temporal bone research. It also answers commonly asked questions regarding the temporal bone donation process. (Dimensions: 7" x 10")



If you are willing to display either of these brochures, please complete the form and return it to the Registry, by fax or mail. **The brochures will be sent to you free of charge.**

ORDER FORM

Please send me (circle or fill in quantity):

The Others May Hear: 25 50 100 _____ copies (free of charge)
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Enrollment Packets: 25 50 100 _____ copies (free of charge)

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other otologic diseases, such as otosclerosis and otitis media. All of the temporal bones in this study had been previously removed at autopsy. Temporal bones were serially sectioned in the horizontal plane at a thickness of 20mm. Every 10th section was stained with hematoxylin and eosin (HE) and mounted on glass slides for light microscopic observation.

All statistical analyses were performed using STATVIEW software. Results were presented as mean \pm SD. Statistical evaluation was carried out using non-parametric Mann-Whitney U test. Correlations were calculated with Spearman tests.

RESULTS

Thickness of walls of capillaries-

We found an increased thickness of the capillary walls under the basilar membrane and in the stria vascularis in diabetics. The mean thickness of the capillary walls under the basilar membrane in all turns combined in diabetics ($2.27\mu\text{m} \pm \text{SD } 0.60$) was significantly thicker than that of controls ($1.60\mu\text{m} \pm \text{SD } 0.32$) ($P=0.0001$). There was a correlation between aging and thickness of capillary walls under the basilar membrane. The mean thickness of capillary walls increased with age at a more rapid rate in diabetics than in controls.

Loss of OHC-There was a significantly greater loss of OHC in diabetics ($23.4\% \pm \text{SD } 16.6$) compared with controls ($15.4\% \pm \text{SD } 4.1$) in the lower basal turn ($P<0.01$). There was no significant difference in other turns between groups. In addition, there was a correlation between loss of OHC in the lower basal turn and increased thickness of the capillary walls under the basilar membrane in diabetics.

There was no significant difference between diabetics and controls in the number of IHC.

Atrophy of the stria vascularis-The total area of all five turns of the stria vascularis in diabetics ($19808\mu\text{m}^2 \pm \text{SD } 6910$) was significantly lower than controls ($32113\mu\text{m}^2$

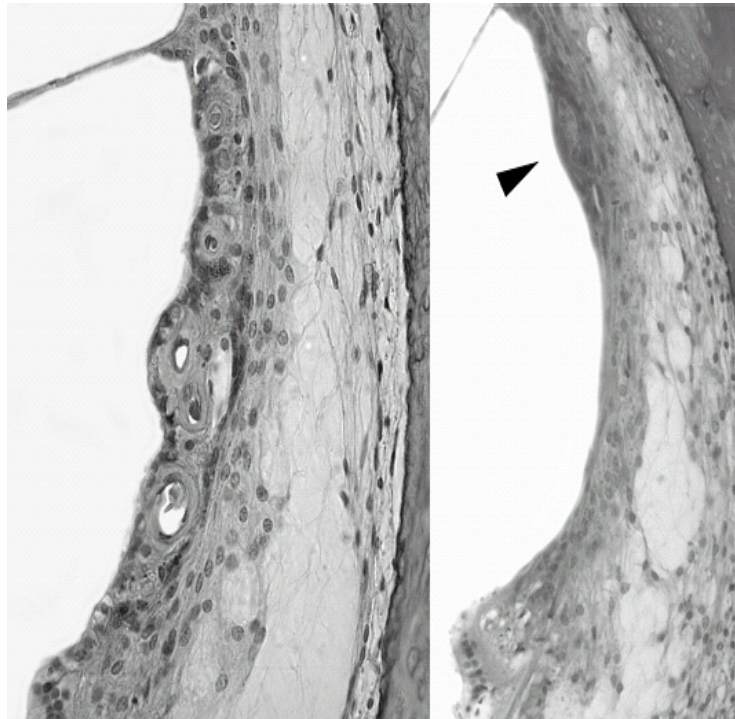


Figure 1-a. There is thickening of the capillary walls in the stria vascularis in lower middle turn of the cochlea from a 39-year old female with a 33-year-history of type 1 diabetes mellitus. HE, X200

Figure 1-b. There is total occlusion of capillary (arrow head) and complete loss of stria vascularis in lower middle turn of the cochlea from a 38-year old female with a 19-year-history of type 1 diabetes mellitus. HE, X200

$\pm \text{SD } 4302$) ($P<0.0001$). There was a correlation between the total area of the stria vascularis and aging in diabetics and in controls. Atrophy of the stria vascularis increased with aging at a more rapid rate in diabetics than in controls. We found not only atrophy of the stria vascularis but also an increased thickness of capillary walls in the stria vascularis (Figure 1-a, b). There was a correlation between thickness of capillary walls under the basilar membrane and total area of the stria vascularis in diabetics.

Spiral ganglion cells-There was no significant difference in the number of spiral ganglion cells in any segment between diabetics and controls.

DISCUSSION

Most audiometric studies of hearing in patients with diabetes showed a gradually progressive, bilateral, high frequency SNHL (1,3,10,11). It is most common among elderly diabetics. They claim there is an association between age and SNHL in diabetics. However, some authors have reported the first effect is an impairment of the low and middle frequencies (1,2,12) and then, as the patient ages, the high frequencies are damaged. Histopathological studies in diabetic humans (5-9) and animal models (8,13,14) showed microangiopathic changes in cochlear vessels. Animal studies have shown a significant loss of outer hair cells (15-20), atrophy of spiral ganglion cells (17,21) and marginal cells (20,22) and edematous changes of the intermediate cells in the stria vascularis (20-22). However, other studies did not confirm these findings in the cochlea of diabetic animal models (23), with exception of thickening of capillary walls (8). In the present study of patients with type 1 diabetes, we showed an increased thickness of capillary walls under the basilar mem-

brane and in the stria vascularis. In addition, there was a correlation between loss of OHC in the lower basal turn and increased thickness of the capillary walls under the basilar membrane and aging.

Although, not reported previously, we found atrophy of the area of the stria vascularis. In addition, there was a correlation between atrophy of the stria vascularis and increased thickness of the capillary walls under the basilar membrane. Capillaries of the stria vascularis and capillaries of the basilar membrane branch from the main cochlear artery. We observed not only an increased thickness of the capillary walls, but also total occlusion of a capillary in the stria vascularis. The increased thickness of the capillary walls may cause atrophy of the stria vascularis. Damage of the stria vascularis causes a flat type of audiometric pattern (24). Even in young patients with diabetics there was an atrophy of the stria vascularis without loss of OHC. This finding suggests that SNHL may be primarily caused by atrophy of the stria vascularis with secondary loss of OHC.

In a study of diabetic humans and animal models, some authors reported loss of spiral ganglion cells (6,17,21), however other studies have not found any decrease in the number of spiral ganglion cells (7,8). In our study, no statistically significant difference was observed in the number of spiral ganglion cells between diabetics and controls. This study suggests that diabetic hearing loss results from microangiopathic involvement of inner ear vessels and subsequently stria vascularis atrophy and hair cell loss.

ACKNOWLEDGEMENTS

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See EFFECTS OF TYPE 1 DIABETES, page 7

LABORATORY SPOTLIGHT

Scientific study of the human temporal bone and related brain tissue is a time-consuming process performed in highly specialized otopathology laboratories by researchers who are dedicated to enhancing our understanding of the pathology underlying disorders of hearing and balance. "Laboratory Spotlight" is a continuing series of articles offering a glimpse inside the laboratories in the United States and abroad conducting temporal bone research.

TEMPORAL BONE LABORATORY OF THE UNIVERSITY OF MINNESOTA

Michael Paparella, M.D., Director

The University of Minnesota Otopathology Laboratory has been under the direction of Dr. Michael Paparella for 37 years. The laboratory has collected 1,911 human temporal bones representing most diseases and conditions of the ear. It also houses temporal bones from a variety of animal species including rat, mouse, guinea pig, chinchilla, dolphin, owl, sheep, and dog. The laboratory has trained more than 120 research fellows from 26 countries. Over 200 studies of human temporal bones and more than 50 experimental animal studies on a variety of subjects have been published.

Carolyn Sutherland is the technician who acquires, processes, cuts and stains the specimens. The laboratory is also staffed with a full time Otolaryngologist, Sebahattin Cureoglu, M.D., Vladimir Tsuprun, Ph.D., and a Sr. Scientist, Pat Schachern. We currently are fortunate to have four visiting research fellows from Japan and one fellow from Turkey. A Fulbright scholar from Brazil was recently trained in our laboratory in the art of temporal bone processing and has returned home to establish the first temporal bone laboratory in South America. A variety of techniques are utilized

in our laboratory including those of light microscopy, electron microscopy, histochemistry, immunohistochemistry, immunogold and *in situ* hybridization.

In addition to clinical studies, current projects in the laboratory include: the relationship between congenital heart disease and ear anomalies, the relationship between Type I diabetes and ear pathology, studies involving the MIF knockout mouse in otitis media, Mucopolysaccharidosis I, III, and VII, remodeling of the extracellular matrix in otitis media, remodeling of the extracellular matrix in otosclerosis, structure of stereocilia

side links and morphology of auditory hair bundle related to noise exposure, a longitudinal study of Scheibes dysplasia in Dalmatian dogs, age related changes of the organ of Corti, cochlear pathology induced by gentamycin, and gentamycin induced vestibular pathology.

The laboratory is supported by the International Hearing Foundation, the 5 M Lions International, NIH NIDCD P30 DC 4660, and the American Hearing Foundation.

University of Minnesota Otopathology Laboratory Staff

Left to right: Shin Kariya MD, Hisaki Fukushima MD, Kazuyasu Baba MD, Vladimir Tsuprun PhD, Carolyn Sutherland and Pat Schachern. Not pictured: Sebahattin Cureoglu and Takeshi Kusunoki.



The Otopathology lab of the University of Minnesota is located in the Phillips Wangenstein Building at the Minneapolis, MN campus.



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REGISTRY NEWSLETTER AVAILABLE ON-LINE



The National Temporal Bone Registry's biannual newsletter, *The Registry*, is now available for viewing on the Registry's Website. Subscribers can be notified via email about current issues and will be directed right to the newsletter by a link to the site.

The archives of *The Registry* have recently been updated to include all the back issues. We now have a complete listing of all the past issues of *The Registry* available for download.

Please visit the Registry's website.

www.tbregistry.org

HOT OFF THE PRESSES

Dora Weber, one of the Registry's registered temporal bone donors, has written a follow-up to her popular book "*Journey out of Silence*". The book deals with the challenges she faced to hear again by opting to have a cochlear implant. Below is a brief synopsis of her new book.

Dora Weber who shared her long and arduous journey out of silence in her book "*Journey Out of Silence*" now shares her story which chronicles her passage into the hearing world in her new book, "*IDanced-A Cochlear Implant Odyssey*". She shares the challenges that she faced to retain her hearing when problems arose and the inspiration that she received to help her to meet these challenges. She shares her experiences with sequential cochlear implants, an unexpected surgery and the triumphal surprise ending that awaited her.

"*IDanced-A Cochlear Implant Odyssey*" will be released in early summer by Beaver's Pond Press, Inc., 7104 Ohms Lane, Edina, Minnesota. If you are interested in obtaining a copy of Dora's book please contact Dora Weber at 580-80th Ave NE, Spring Lake Park, MN 55432.

Questions and Answers

(The Registry recently received these questions from people interested in becoming donors.)

Q. Are there any costs associated with the temporal bone removal my family needs to pay? Port Huron, Michigan

A. No. The medical professionals who remove the temporal bones donate their time or are paid by the laboratory receiving the temporal bones.

Q. I am considering donation but my funeral director believes my family will not be able to view the body after the removal. Is this true? Williamsburg, VA

A. No. Removal of the temporal bones (and brain stem) does not change the appearance of the head, face or outer ear. So it does not affect funeral or burial arrangements, including an open casket.



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Thank you!

Otopathology Mini-Travel Fellowship Program

The NIDCD National Temporal Bone Registry is pleased to announce the availability of two mini-travel fellowships. The fellowships provides travel funds for research technicians and young investigators to visit a temporal bone laboratory for a brief educational visit, lasting approximately one week. *The emphasis is on the training of research assistants, technicians and junior faculty.* The fellowships are available to:

- 1) U.S. hospital departments who aspire to start a new temporal bone laboratory
- 2) Inactive U.S. temporal bone laboratories that wish to reactivate their collections or
- 3) Active U.S. temporal bone laboratories that wish to learn new research techniques

Two fellowship awards will be made each year (\$1,000 per fellowship). The funds may be used to defray travel and lodging expenses. Applications will be decided on merit. Those awarded the fellowship will be required to submit a brief report, which may be published in the Registry's newsletter.

Interested applicants should submit the following:

- 1) A 1-2 page outline of the education or training aspect of the proposed fellowship
- 2) Applicant's curriculum vitae
- 3) Letter of support from applicant's temporal bone laboratory director or department chairman
- 4) Letter from the host temporal bone laboratory, indicating willingness to receive the traveling fellow

Applications should be sent to:

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