Genetic Associations in Age-Related Hearing Thresholds

George A. Gates, MD; Nat N. Couropmitree, MPH; Richard H. Myers, PhD

Objective: To determine the inheritance of age-related hearing loss.

Design: Cohort study comparing aggregation of hearing levels in genetically unrelated people (spouse pairs) and in genetically related people (sibling pairs, parent-child pairs).


Subjects: Members of the Framingham cohorts with hearing tests and with a relative in the Framingham hearing study.

Main Outcome Measures: Audiometric pure-tone thresholds at 250 to 8000 Hz were obtained and pure-tone average (PTA) hearing thresholds were calculated for the middle (0.5-2 kHz), high (4-8 kHz), and low (0.25-1 kHz) frequencies for each ear. The shape of the audiogram was categorized as either normal, abrupt high-frequency loss (sensory phenotype) or flat loss (strial phenotype). Correlations were made using the Familial Correlations program of the Statistical Analysis for Genetic Epidemiology software system. The level of significance was $P = .01$.

Results: Hearing threshold levels did not aggregate in spouses. Significant aggregation was noted in siblings and parent-child pairings for PTA at low, middle, and high frequencies. Sisters but not brothers had significant aggregation of each PTA measure. Mother-daughter and mother-son pairs but not father-son pairs had significant aggregation of hearing levels. For the sensory phenotype, there was significant aggregation in all related pairs except for father-child pairs. For the strial phenotype, there was significant aggregation of hearing levels in the related female pairs but not in the related male pairs.

Conclusions: A clear familial aggregation occurs for age-related hearing levels, sensory presbycusis phenotypes, and strial presbycusis phenotypes. The aggregations are stronger in women than in men. The heritability estimate was greater for the strial phenotypes than for the sensory phenotypes. The data support a genetic effect on the inheritance of presbycusis in women and a mixed, genetically acquired cause in men.


Many people with age-related hearing loss (presbycusis) have a family history of age-related hearing loss in their parents, siblings, or other close relatives. However, the nature and extent of the familial hearing impairment are often difficult to document, and this information is seldom obtained. Many authors have held that presbycusis has a genetic basis, but evidence for this theory is scant and largely anecdotal. Nonetheless, there is a widespread presumption based on clinical observation that presbycusis is an inherited disorder and that genetic factors may influence both the rate and severity of the hearing loss. The genetic factors that underlie this observation are unknown. The number of recognized genetic hearing disorders is increasing annually because of a strong emphasis upon genetics in auditory research. Thus, it is appropriate to begin to address the genetic aspects of age-related hearing loss.

The term presbycusis literally means old hearing (ie, the hearing of elderly people). Although some have used presbycusis specifically to indicate the aging process as it occurs in the auditory system, we follow the more recent convention that presbycusis is a global term describing the accumulated effects of aging, trauma, disease, and any other factors that affect the auditory system over time. Given the absence of any independent marker of aging in the auditory system, this nosologic approach appears reasonable.
METHODS

Audiometric examination was done for 2293 members of the original FHS cohort at Examination 15 and for 1414 members of the offspring group at Examination 6 using conventional clinical pure-tone threshold estimation techniques. Written informed consent for the hearing studies was obtained using forms and procedures approved by the institutional review board of the University of Washington, Seattle. The original cohort data have been previously reported. Pure-tone hearing thresholds averaged across the frequencies of 500, 1000, and 2000 Hz were calculated separately for each ear. Pure-tone averages (PTAs) were also calculated for the better ear and worse ear. The better ear was the ear with the lower PTA. If the PTAs were equal, the right ear was designated as the better ear. The PTAs of the spouse and sibling groups combined were compared with PTAs of the remainder of the cohort to assess group comparability. The high-frequency PTA was calculated as the average threshold across the 4-, 6-, and 8-kHz thresholds. The low-frequency PTA was calculated as the average across the 0.25-, 0.5-, and 1.0-kHz thresholds.

Subjects with a family member in the hearing data sets were selected for familial analysis. Those with unilateral or asymmetric loss (>15-dB difference in PTA) and those with a known cause, such as trauma, Ménière disease, or surgery, were excluded from these analyses. A history of noise exposure was not an exclusion criterion. Correction for conductive loss was not attempted because bone-conduction thresholds were only available for 1 and 4 kHz. Therefore, those with a bone-air gap of greater than 15 dB at 1 kHz were excluded. There were 1079 members of the cohort and 1232 members of the offspring group remaining for this analysis.

For each of the PTAs (low, middle, and high), multiple linear regression analyses were done to adjust for the effects of age and sex on hearing sensitivity. The regression analyses were run separately for the men and women in the original and offspring cohorts. The standardized residuals generated from the regression analyses have means of 0 and SDs of 1 and were used as the phenotypic variables for all analyses.

The first analysis was done for the entire group. Secondary analyses were done within subgroups of subjects with normal hearing in both ears and either a sensory phenotype or a strial phenotype of presbycusis in both ears. Categorization of the phenotype was based on Schuknecht’s descriptions of the clinical features of the 2 most common subtypes of presbycusis, sensory and strial (or metabolic). The sensory presbycusis phenotype indicates elevated high-frequency thresholds with normal or nearly normal low-tone thresholds and proportionate speech intelligibility tests. The strial presbycusis phenotype indicates abnormal pure-tone thresholds across the frequency spectrum, producing a relatively flat audiometric threshold profile. The prevalence of Schuknecht’s other 2 phenotypes, neural and cochlear conductive, was too low to be considered in this report. These phenotypes are arbitrary categorizations of the pure-tone threshold pattern and are not based on cochlear histopathologic examination.

We computed familial correlations using the FCOR (Familial Correlations) program of the Statistical Analysis in Genetic Epidemiology software package. To be included in the analysis, subjects needed to have measurements in both ears and families needed to have at least 2 members with hearing tests. Ninety-nine percent confidence intervals were constructed using the Fisher z transformation to test for statistical significance. We used 99% confidence intervals instead of 95% confidence intervals to adjust for multiple comparisons. Heritability was estimated by the formula:

\[ h^2 = \frac{r_{\text{parent-offspring}}(1 + r_{\text{spouse}})}{1 + r_{\text{spouse}} + 2r_{\text{spouse}}(1 - r_{\text{parent-offspring}})} \]

Correlations were done first for the entire group and then for the 2 subgroups with the sensory presbycusis phenotype and strial presbycusis phenotype. Normal-hearing subjects were included in all comparisons as a genetic control group.

Many studies have documented the progressive worsening of auditory function with age. However, the rate of change is not linear and is highly variable, and the variance in hearing level is only weakly associated with age. These observations suggest that age-related changes do not occur uniformly and that more than one pathologic process may be acting upon the auditory system. Thus, documenting the role of genetic factors in the etiology of presbycusis has been difficult.

Detailed, controlled examination of a large, population-based cohort is a useful method to approach this difficulty. We have studied the hearing of the members of the Framingham Heart Study (FHS) cohort and herein report our preliminary observations about the role of inheritance in regulating hearing levels with age and in the 2 most common forms of presbycusis, sensory and strial.

The FHS began in 1948 with more than 6000 individuals recruited from a two-thirds-sample, stratified by family size, of the families of the city of Framingham in eastern Massachusetts. Five thousand two hundred nine people between the ages of 30 and 60 years who were found to be free of cardiovascular disease made up the heart study cohort and have had biennial health examinations since. Audiometry was done during biennial examinations and hearing loss in older people. The Framingham Offspring Study began in 1972 to evaluate the role of genetic factors in cardiovascular and other diseases. Offspring have been examined at regular intervals; hearing testing began in 1993. The family groups within the cohort are complex and include spouse pairs, sibling pairs, and a few parent-child pairs.

This report uses the age-adjusted hearing thresholds from family group members tested at biennial Examination 15 of the FHS cohort (1977-1979) and Examination 6 of the offspring group (1996-present) to compare the auditory status in genetically unrelated people (spouse pairs) and genetically related people (sibling pairs, parent-child pairs). Our first working
hypothesis was that the correlation of hearing thresholds in related pairs would be greater than in unrelated pairs if genetic factors contributed to hearing status. Our second hypothesis was that in cases of asymmetric hearing loss, genetic factors would be implicated if familial aggregation of hearing threshold levels occurred in the better-hearing ear.

RESULTS

HEARING LEVEL

The age and PTAs of the 2311 subjects are shown in Table 1. The data are displayed by family group status (ie, husbands, wives, brothers, and sisters). Of this group, 1394 were in the original cohort and 917 were in the offspring group. The women had better (lower) PTAs than the men, and the left ear was slightly better than the right in both sexes. Many people belonged to more than one family group (eg, a subject could be a wife, a sister, and a mother). Thus, the number of pair groups exceeds the number of people. For family subgroups (ie, sibling pairs) with more than one pair, each person’s data are given equal weight as a sibship with only one pair.

The age-adjusted PTA of the spouses and siblings was compared by analysis of variance with the age-adjusted PTA of the rest of the cohort, who had hearing tests at biennial Examination 15 but were not included in the familial analyses (data not shown). There was no difference in hearing status based on the family status (ie, having a spouse or sibling in the study). Thus, we conclude that there was no selection bias based on family membership.

FAMILIAL ANALYSIS OF HEARING LEVEL

Age-adjusted correlations of PTA within family pair groups are shown in Table 2. These show all possible pairwise combinations within each category (spouses, siblings); the number of pairs exceeds the number of people.

These correlations show a substantial familial aggregation of hearing threshold levels. The correlations were greatest for mother-daughter pairs, for sister pairs, and for the high-frequency thresholds.

PRESBYCUSIS ANALYSES

Sensory Presbycusis Phenotype

Familial correlations were performed for subjects with normal hearing or sensory presbycusis phenotype in both ears (Table 3).

These correlations show a strong familial aggregation of age-adjusted hearing sensitivity in people with a normal or sensory hearing loss pattern. The associations were greatest for the mother-daughter, sister-sister, and brother-brother pairs. Correlations for the father-child pairs were not significant. The strong correlations for sibling pairs and the absence of significant correlations for father-child pairs suggest the effect of extrinsic factors on fathers’ hearing loss patterns.

The pattern of aggregation for the low-frequency thresholds was similar to that for middle-frequency PTA in Table 3. This is probably the result of the frequency overlap of the 2 averages.

### Table 1. Pure-Tone Average (PTA) and Age by Family Group Status

<table>
<thead>
<tr>
<th>Family Group</th>
<th>No. of Subjects</th>
<th>Age, y*</th>
<th>PTA† Better Ears</th>
<th>PTA† Worse Ears</th>
</tr>
</thead>
<tbody>
<tr>
<td>Husbands</td>
<td>486</td>
<td>70.9 ± 6.8</td>
<td>20.5 ± 13.8</td>
<td>28.9 ± 18.5</td>
</tr>
<tr>
<td>Wives</td>
<td>593</td>
<td>69.5 ± 6.7</td>
<td>17.5 ± 12.7</td>
<td>24.6 ± 17.4</td>
</tr>
<tr>
<td>Brothers</td>
<td>546</td>
<td>59.7 ± 10.0</td>
<td>14.5 ± 11.7</td>
<td>19.8 ± 15.7</td>
</tr>
<tr>
<td>Sisters</td>
<td>686</td>
<td>60.1 ± 10.6</td>
<td>13.0 ± 11.7</td>
<td>17.1 ± 14.4</td>
</tr>
</tbody>
</table>

*Values are mean ± SD.
†In dB HL re ANSI (1969).

### Table 2. Correlations of Age-Adjusted Pure-Tone Average (PTA) Hearing Thresholds by Family Group

<table>
<thead>
<tr>
<th>Family Group</th>
<th>No. of Pairs</th>
<th>Correlation Coefficient (r)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Middle-Frequency PTA†</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Better Ear</td>
</tr>
<tr>
<td>Spouse-spouse</td>
<td>488</td>
<td>0.11</td>
</tr>
<tr>
<td>Parent-child</td>
<td>1316</td>
<td>0.10</td>
</tr>
<tr>
<td>Mother-daughter</td>
<td>404</td>
<td>0.15</td>
</tr>
<tr>
<td>Mother-son</td>
<td>326</td>
<td>0.18</td>
</tr>
<tr>
<td>Father-daughter</td>
<td>315</td>
<td>0.09</td>
</tr>
<tr>
<td>Father-son</td>
<td>271</td>
<td>−0.03</td>
</tr>
<tr>
<td>Sibling-sibling</td>
<td>852</td>
<td>0.18</td>
</tr>
<tr>
<td>Sister-sister</td>
<td>277</td>
<td>0.21</td>
</tr>
<tr>
<td>Sister-brother</td>
<td>414</td>
<td>0.18</td>
</tr>
<tr>
<td>Brother-brother</td>
<td>161</td>
<td>0.15</td>
</tr>
<tr>
<td>Heritability (h²)†‡</td>
<td>. . .</td>
<td>0.27</td>
</tr>
</tbody>
</table>

*significant correlations (P < .01) are in boldface.
†Averaged across frequencies of 0.5, 1.0, and 2.0 kHz.
‡Averaged across frequencies of 4.0, 6.0, and 8.0 kHz.
§Averaged across frequencies of 0.25, 0.5, and 1.0 kHz.
The pattern of aggregation for the high-frequency thresholds in subjects was similar to that for middle-frequency PTA, except that fewer pairs aggregated, and none of the brother-sister or brother-brother pairs showed a significant association. This suggests the effect of extraneous factors on men’s high-frequency hearing.

**Strial Presbycusis Phenotype**

Subjects with a flat audiometric pattern of loss in both ears and subjects with normal hearing in both ears were included in this analysis (Table 4).

The aggregations of PTA in subjects with the strial presbycusis phenotype in Table 4 show a strong familial association in the sister-sister and mother-daughter pairs. The small number of father-son or brother-brother pairs prevents a significance estimate. Although the sister-brother aggregations are significant, the coefficients are very low.

**Genetic Component**

The heritability estimates suggest that 35% to 55% of the variance of the sensory presbycusis phenotype and 25% to 42% of the variance of the strial presbycusis phenotype is attributable to the effects of genes. The genetic component appears to be stronger for the low-frequency PTA ($h^2=0.50-0.53$) than for the sensory presbycusis phenotype. If women are less likely to be exposed to noise or other environmental sources of age-associated hearing loss, they may provide a less biased estimate of the genetic component for presbycusis generally and for the strial phenotype in particular.

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**Table 3. Correlations of Age-Adjusted Pure-Tone Average (PTA) Hearing Thresholds in Ears With Sensory Presbycusis Phenotype or Normal Hearing**

<table>
<thead>
<tr>
<th>Family Group</th>
<th>No. of Pairs</th>
<th>Better Ear</th>
<th>Worse Ear</th>
<th>Better Ear</th>
<th>Worse Ear</th>
<th>Better Ear</th>
<th>Worse Ear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parent-child</td>
<td>588</td>
<td>0.26</td>
<td>0.26</td>
<td>0.20</td>
<td>0.21</td>
<td>0.22</td>
<td>0.22</td>
</tr>
<tr>
<td>Mother-daughter</td>
<td>177</td>
<td>0.47</td>
<td>0.47</td>
<td>0.22</td>
<td>0.19</td>
<td>0.38</td>
<td>0.35</td>
</tr>
<tr>
<td>Mother-son</td>
<td>154</td>
<td>0.35</td>
<td>0.29</td>
<td>0.19</td>
<td>0.23</td>
<td>0.34</td>
<td>0.22</td>
</tr>
<tr>
<td>Father-daughter</td>
<td>141</td>
<td>0.10</td>
<td>0.15</td>
<td>0.07</td>
<td>0.13</td>
<td>0.15</td>
<td>0.22</td>
</tr>
<tr>
<td>Father-son</td>
<td>116</td>
<td>0.06</td>
<td>0.14</td>
<td>0.11</td>
<td>0.11</td>
<td>-0.02</td>
<td>0.14</td>
</tr>
<tr>
<td>Sibling-sibling</td>
<td>472</td>
<td>0.39</td>
<td>0.37</td>
<td>0.17</td>
<td>0.20</td>
<td>0.35</td>
<td>0.39</td>
</tr>
<tr>
<td>Sister-sister</td>
<td>161</td>
<td>0.46</td>
<td>0.46</td>
<td>0.32</td>
<td>0.31</td>
<td>0.42</td>
<td>0.42</td>
</tr>
<tr>
<td>Sister-brother</td>
<td>229</td>
<td>0.37</td>
<td>0.35</td>
<td>0.13</td>
<td>0.17</td>
<td>0.35</td>
<td>0.41</td>
</tr>
<tr>
<td>Brother-brother</td>
<td>82</td>
<td>0.42</td>
<td>0.37</td>
<td>0.10</td>
<td>0.16</td>
<td>0.32</td>
<td>0.34</td>
</tr>
</tbody>
</table>

**Table 4. Correlations of Age-Adjusted Pure-Tone Average (PTA) Hearing Thresholds in Ears With Clinical Strial Presbycusis or Normal Hearing**

<table>
<thead>
<tr>
<th>Family Group</th>
<th>No. of Pairs</th>
<th>Better Ear</th>
<th>Worse Ear</th>
<th>Better Ear</th>
<th>Worse Ear</th>
<th>Better Ear</th>
<th>Worse Ear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spouse-spouse</td>
<td>9</td>
<td>-0.87</td>
<td>-0.63</td>
<td>-0.76</td>
<td>-0.83</td>
<td>-0.85</td>
<td>-0.75</td>
</tr>
<tr>
<td>Parent-child</td>
<td>109</td>
<td>0.25</td>
<td>0.25</td>
<td>0.01</td>
<td>0.06</td>
<td>0.21</td>
<td>0.25</td>
</tr>
<tr>
<td>Mother-daughter</td>
<td>71</td>
<td>0.34</td>
<td>0.36</td>
<td>-0.08</td>
<td>-0.08</td>
<td>0.22</td>
<td>0.24</td>
</tr>
<tr>
<td>Mother-son</td>
<td>23</td>
<td>-0.05</td>
<td>-0.05</td>
<td>0.13</td>
<td>0.18</td>
<td>0.08</td>
<td>0.12</td>
</tr>
<tr>
<td>Father-daughter</td>
<td>12</td>
<td>0.02</td>
<td>0.01</td>
<td>0.09</td>
<td>0.35</td>
<td>0.03</td>
<td>0.28</td>
</tr>
<tr>
<td>Father-son</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sibling-sibling</td>
<td>133</td>
<td>0.32</td>
<td>0.38</td>
<td>0.25</td>
<td>0.27</td>
<td>0.35</td>
<td>0.36</td>
</tr>
<tr>
<td>Sister-sister</td>
<td>65</td>
<td>0.43</td>
<td>0.53</td>
<td>0.38</td>
<td>0.40</td>
<td>0.50</td>
<td>0.50</td>
</tr>
<tr>
<td>Sibling-brother</td>
<td>56</td>
<td>0.12</td>
<td>0.12</td>
<td>0.13</td>
<td>0.12</td>
<td>0.07</td>
<td>0.06</td>
</tr>
<tr>
<td>Brother-brother</td>
<td>12</td>
<td>0.63</td>
<td>0.63</td>
<td>0.68</td>
<td>0.43</td>
<td>0.47</td>
<td>0.47</td>
</tr>
<tr>
<td>Heritability ($h^2$)</td>
<td>. . .</td>
<td>0.26</td>
<td>0.42</td>
<td>0.25</td>
<td>0.28</td>
<td>0.28</td>
<td>0.35</td>
</tr>
</tbody>
</table>

* Significant correlations (P<.01) are in boldface.
† Averaged across frequencies of 0.5, 1.0, and 2.0 kHz.
‡ Averaged across frequencies of 4.0, 6.0, and 8.0 kHz.
§ Averaged across frequencies of 0.25, 0.5, and 1.0 kHz.
|| Insufficient number of cases.

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Establishing a genetic etiology for a multifactorial disease such as presbycusis is a complex process. To provide objective data to support the anecdotal evidence of familial patterns, we performed exploratory analyses using the FHS databases. Because the family relationships have been established, we were able to use existing hearing data from biennial Examination 15 of the original FHS cohort and Examination 6 of the offspring cohort to assess the extent to which hearing thresholds and type of hearing loss aggregate within families. We separately examined the aggregation of auditory threshold sensitivity for all subjects using 3 separate PTAs and 2 specific clinical phenotypes of presbycusis, sensory and strial.

HEARING THRESHOLDS

Hearing thresholds indicate the sensitivity of the auditory system to acoustic stimuli. The hearing threshold levels in genetically related people in this study aggregated within families in all parts—low, middle, and high frequencies—of the clinical auditory spectrum. This demonstrates that hearing sensitivity in this large group of biologically related people is more similar than in unrelated people in the same general environment. These findings suggest a genetic basis for this association because the environmental factors that might influence hearing are presumed to be fairly constant within family groups. One exception to this generalization is occupational and recreational noise exposure, which tends to differ between men and women. Men generally have greater exposure to gun shooting and other noisy recreational and occupational activities. We presume, but cannot verify, that the lack of association between fathers and children is largely due to the effects of noise exposure in the fathers.

The phenotypes described herein are compatible with and based on the definitions of presbycusis subtypes described by Schuknecht. While it is likely that subjects with those histologic patterns are included in our phenotypes, we do not presume that these phenotypes exclude other types of cochlear pathology. Given that a phenotype is a clinical description of certain attributes of the subjects in question, this clinical approach to the study of the genetics of presbycusis is both appropriate and necessary.

SENSORY PRESBYCUSIS PHENOTYPE

The associations for the sensory presbycusis phenotype (Table 2) support a hereditary basis for hearing threshold level. The association was significant in the parent-offspring and sibling groups for the low-, middle-, and high-frequency thresholds and in the sister-sister, brother-brother, and sister-brother pairs for the middle-frequency thresholds. However, there were frequency-dependent variations in aggregation in the low and high frequencies; most notably, there was a lack of association in the brother-brother and father-son pairs for both the high- and low-frequency PTAs. The low-frequency PTA showed the strongest correlations, particularly in the sister-sister and mother-daughter pairs.

STRIAL PRESBYCUSIS PHENOTYPE

The hearing level in people with hearing loss that clinically suggests strial presbycusis supports a genetic etiology in the female subjects. Low-frequency hearing loss is typical of strial presbycusis and is known to be more common in women than in men. The aggregation patterns in women were similar for low-frequency PTA in the whole data set and in the subgroup with the strial presbycusis phenotype, which demonstrates congruent familial patterns for low-frequency hearing sensitivity.

SYMMETRY

Genetic causes of hearing loss should affect both ears equally, and extrinsic causes superimposed on genetic causes should be more evident in the worse ear. Langenbeck’s law indicates that genetic hearing loss must be symmetric. However, symmetric thresholds occurred in fewer than half of our older subjects. Whether this is due to the variable effects of extrinsic agents, asymmetric expression of heritable factors, test-retest reliability, or other factors is not clear. Given the high rate of occupational noise exposure of the cohort in general, it may be that the asymmetries indicate the effect of noise exposure or other toxic agents. Given that presbycusis is considered to be a multifactorial disorder, genetic factors and environmental factors are likely to interact in individual cases.

The issue of genetic susceptibility to extrinsic factors cannot be addressed by this exploratory analysis. However, a recent example that underlies this possibility is the observation of genetic susceptibility to aminoglycoside antibiotics caused by a mutation of ribosomal DNA. The work of Erway et al demonstrates differential susceptibility to noise among genetically different strains of mice. Thus, we need to continue to explore the interactions of extrinsic and intrinsic factors in trying to understand the variability of presbycusis.

CONCLUSIONS

The heritability estimates found here are likely to represent a multifactorial etiology of combined genetic and environmental effects. Some people may be genetically more susceptible to hearing loss following noise exposure, while others may be genetically resistant to noise. These analyses cannot differentiate the contributions of genes alone from those that may involve gene-environment interactions. Nevertheless, these heritability estimates are fairly strong and are stronger than or comparable to those seen for blood pressure or cholesterol levels. The finding of a substantial genetic basis for presbycusis may further justify the use of statistical genetic analyses to identify the patterns of familial transmission of presbycusis and molecular genetic linkage studies to locate the genes responsible for this trait.

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REFERENCES


16. References
Hot-Water Irrigation in the Treatment of Posterior Epistaxis

I read with interest the article by Stangerup et al and was particularly astonished by the section entitled “Pain During and After Treatment.” The authors mention that phenylephrine hydrochloride and tetracaine were used for anesthesia for the tamponade group, while lidocaine gel alone was used for the hot-water irrigation group.

Experimental design should call for the same anesthesia between groups. Perhaps phenylephrine or tetracaine irritated or altered the nasal mucosa of some patients and accounted for some of the differences seen. Clearly, phenylephrine, a potent vasoconstrictor, could have some effect on bleeding in and of itself. Furthermore, this medication could have caused enough vasoconstriction to be responsible in part for the additional damage observed on rhinoscopy in the tamponade group.

Michael D. Seidman, MD
Detroit, Mich


In reply

In our department, it is a routine procedure to tamponade the bleeding nasal cavity for 5 to 10 minutes with a cotton or gauze mesh embedded with a solution of phenylephrine hydrochloride and tetracaine. This is done to obtain some degree of hemostasis and local anesthesia before inspection of the nasal cavity at the initial contact with the otolaryngologist on call. This measure provides an opportunity to detect the source of the nosebleed for possible cauterization in case of anterior bleeding or, if the source of bleeding cannot be visualized, to facilitate the final tamponade with as little pain as possible.

As mentioned in our article, the hypothesis of the hemostatic effect of hot-water irrigation, based on an animal experimental study, is (1) edema and narrowing of the intranasal lumen, creating internal and external compression of the leaking vessel, and (2) vasodilatation of the mucosal vessels, decreasing the blood flow and subsequently the intraluminal pressure. It is obvious that using phenylephrine before hot-water irrigation could counteract this desired effect and muddle the results of treatment. The small amount of lidocaine gel (1 mL) applied on the tip of the catheter during the hot-water irrigation was chosen in order to facilitate insertion of the hot-water irrigation catheter through the nasal cavity, not to anesthetize the nasal cavity.

Seidman’s comment that using phenylephrine could be responsible for the damage of the nasal mucosa observed on rhinoscopy in the tamponade group is not in agreement with our experience. We routinely use cotton embedded with a solution of phenylephrine hydrochloride and tetracaine for 5 to 10 minutes in order to obtain some degree of shrinking and local anesthetization of the nasal mucosa before introducing a fiberscope to inspect the nasal cavity, rhinopharynx, and larynx. We have never seen any damage of the nasal mucosa after these procedures.

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Correction

Error in Financial Support Acknowledgment. In the original article titled “Genetic Associations in Age-Related Hearing Thresholds,” published in the June issue of the ARCHIVES (1999;125:654-659), the acknowledgment of financial support was omitted. The acknowledgment is printed here: “This study was supported by grant RO1 DC01525 from the National Institute of Deafness and Other Communication Disorders, Bethesda, Md; and by funding from the Virginia Merrill Bloedel Hearing Research Center, Seattle, Wash.”