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A Comparative Analysis of the Genetic Epidemiology of Deafness in the United States in Two Sets of Pedigrees Collected More than a Century Apart

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In 1898, E.A. Fay published an analysis of nearly 5000 marriages among deaf individuals in America collected during the 19th century. Each pedigree included three-generation data on marriage partners that included at least one deaf proband, who were ascertained by complete selection. We recently proposed that the intense phenotypic assortative mating among the deaf might have greatly accelerated the normally slow response to relaxed genetic selection against deafness that began in many Western countries with the introduction of sign language and the establishment of residential schools. Simulation studies suggest that this mechanism might have doubled the frequency of the commonest forms of recessive deafness (DFNB1) in this country during the past 200 years. To test this prediction, we collected pedigree data on 311 contemporary marriages among deaf individuals that were comparable to those collected by Fay. Segregation analysis of the resulting data revealed that the estimated proportion of noncomplementary matings that can produce only deaf children has increased by a factor of more than five in the past 100 years. Additional analysis within our sample of contemporary pedigrees showed that there was a statistically significant linear increase in the prevalence of pathologic *GJB2* mutations when the data on 441 probands were partitioned into three 20-year birth cohorts (1920 through 1980). These data are consistent with the increase in the frequency of DFNB1 predicted by our previous simulation studies and provide convincing evidence for the important influence that assortative mating can have on the frequency of common genes for deafness.

Introduction

The importance of heredity as a cause of hearing loss has been recognized at least since the beginning of the 19th Century. For example, in 1857, the Irish otologist William Wilde concluded from an analysis of questions about deaf individuals in census data that parental consanguinity and the existence of deafness in one or both parents were important indicators of a hereditary etiology in some cases.[1] In 1883, Alexander Graham Bell published a report titled *Memoir upon the Formation of a Deaf Variety of the Human Race*, which included a retrospective analysis of records from schools for the deaf in the United States.[2] Bell expressed his concern about "the formation of a deaf variety of the human race in America," based on analyses of the frequency of deaf relatives of deaf students and the hearing status of the offspring of marriages among those who were congenitally deaf compared to those who were adventitiously deaf. Bell argued that the use of sign language, the trend toward education in residential schools, and the creation of societies and conventions for deaf people restricted mating choices and fostered intermarriage, leading to a steady increase in the frequency of congenital deafness. Geneticists have generally discounted Bell's concerns once the extreme heterogeneity of genes for deafness was recognized; however, as described below, recent evidence suggests that, in combination with relaxed selection, assortative mating among the deaf population might in fact have preferentially amplified the commonest forms of recessive deafness.[3]

In 1898, Edward Allen Fay, a professor at what is now Gallaudet University, a liberal-arts educational institution for deaf and hard-of-hearing students that was established in 1864, published his monumental treatise *Marriages among the Deaf in America*, documenting the family-history data from 4471 marriages of deaf individuals that occurred between 1801 and 1894.[4,5] Fay distributed questionnaires to schools for the deaf, to deaf people themselves, and to the friends and relatives of deaf people.[6] Other data were collected from the United States Census, school records, and periodicals for deaf people. Although it was collected before the rediscovery of Mendel's work, Fay's remarkable data set consists of three-generation pedigrees including the offspring, siblings, and parents of deaf probands. The proband matings were repeatedly reanalyzed during the subsequent century[7] and remain unique because the families were ascertained by complete selection through the deaf parents. Even though he lacked knowledge of Mendelian genetics, Fay, like Bell, recognized the heterogeneous nature of deafness, including the important difference between congenital and acquired deafness, as well as the significance of consanguinity or a positive family history as hallmarks of hereditary deafness.

In 1975, Rose partitioned the Fay data to conduct separate segregation analyses[8] of: (1) the nuclear families of the deaf probands and their children, designated the

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"proband matings" under a model of complete selection and (2) nuclear families consisting of the probands and their siblings and parents, who were designated "proband sibships," which were analyzed under a model of truncate selection through an affected child. Each of the two sets of nuclear families was further subdivided by parental-mating type. Overall, Rose found that sporadic deafness accounted for 49% of all cases of deafness in the Fay data. Among the genetic cases, 12%–14% were attributable to autosomal-dominant forms of deafness with incomplete penetrance and 86%–88% to recessive deafness that appeared to be caused by genes at 10 independent loci, under the simplifying assumption that all ten forms were equally frequent. The Fay data included 1299 proband matings in which both partners were deaf (deaf × deaf; hereafter, D × D) and 423 in which one partner was hearing (deaf × hearing). Analysis of the D × D matings showed that 79% were "complementary" matings (i.e., only hearing offspring), 4.2% were "noncomplementary" matings (only capable of producing deaf offspring), and the remaining 16.8% were "segregating" matings, in which the parents were capable of producing both deaf and hearing offspring.

Contemporary Studies of the Etiology of Congenital and Early-Onset Deafness

Contemporary studies of the causes of congenital and early-onset deafness have incorporated the tools of genetic epidemiology, including linkage analysis and molecular testing, to identify a growing number of potential genetic and environmental causes. The overall prevalence and causes of deafness can vary widely at different times and among populations, as documented by Morton,[9] who estimated that autosomal-recessive, dominant, and X-linked genes were responsible for 77%, 22%, and 1% of the genetic cases, respectively. Analysis of data from a national sample of deaf U.S. school children showed that deafness in 37% of the probands was sporadic (nongenetic), whereas deafness in 63% (including a large proportion of the simplex cases) was attributable to genetic causes (75% of these autosomal- recessive inheritance and 25% autosomal-dominant inheritance).[10] Although data are lacking on the frequency of the major genetic and environmental causes of deafness in the same population of newborn infants, with the combination of data from a variety of sources it has recently been estimated that in the United States, clinically significant hearing loss is present in at least 1.9 per 1000 infants at birth.[11]

Because of the large number of recognized genes for deafness, the discovery that mutations at a single locus, DFNB1 (MIM 220290), account for 30%–40% of nonsyndromic deafness in many populations came as a great surprise.[12,13] DFNB1 includes the *GJB2* (MIM 121011) and *GJB6* (MIM 604418) genes, coding for the Connexin 26 (Cx26) and Connexin 30 (Cx30) subunits of homologous gap-junction proteins. These subunits are expressed in the inner ear, where they form heteromeric gap-junction channels between adjacent cells that permit the exchange of small molecules and may facilitate the recycling of potassium ions from the hair cells, after acoustic stimulation, back into the cochlear endolymph. More than 154 *GJB2* mutations have been identified in the coding exon of *GJB2*, but a single chain-termination mutation, 35 del G, accounts for up to 70% of pathologic alleles in many populations. Although DFNB1 is common in Western Europe and the Middle East,[14,15] much lower frequencies have been observed in Asia.[16–18] The 35 del G mutation exhibits linkage disequilibrium, and haplotype analysis suggests that it arose from a single individual in the Middle East approximately 10,000 years ago.[19,20] Genetic deafness is usually transmitted as a monogenic trait; however, interesting examples of digenic transmission have also been identified.[21–24] del Castillo[25] described a 309 kb deletion, spanning the *GJB6* locus, that causes deafness when present in *trans* with a single pathologic *GJB2* mutation, and two additional deletions with similar effects have subsequently been described.[26,27] These two genes map within 35 kb of each other near the centromeric end of chromosome 13q, and although it is still not clear whether deafness results from an influence of the deletion on the expression of the adjacent normal *GJB2* gene or from a digenic interaction, the observation that deafness in digenic compound heterozygotes is more severe than that seen in *GJB2* 35 del G homozygotes, as well as the fact that deafness is seen with three different deletions, supports the latter interpretation.[28]

In 2000, we proposed that the high frequency of DFNB1 deafness reflects the joint effect of intense assortative mating and the relaxed genetic selection against deafness, which occurred after the introduction of sign language 400 years ago in many Western countries and the subsequent establishment of residential schools for the deaf.[29] Using computer simulation, we showed that this mechanism could have doubled the frequency of DFNB1 deafness in the United States during the past 200 years.[3]

Importance of the Mating Structure of the Population

Along with consanguinity, assortative mating is an important characteristic of a population that can have a profound influence on the incidence of deafness. When a new recessive mutation first arises, there is a substantial risk that it will be lost by stochastic processes. Consanguinity helps ensure that at least some recessive mutations are expressed phenotypically where they can be exposed to positive or negative selection. Only after genes for deafness are expressed can assortative mating accelerate their increase in response to relaxed selection. Consanguinity, of course, affects all recessive genes indiscriminately, but the effect of assortative mating among the deaf is limited to genes for deafness, in which it preferentially increases the frequency of the commonest form of recessive deafness in a population.[3] Acting together, these genetic mechanisms can thus promote the survival, expression, and spread of genes for deafness. The acquisition of either a traditional or an indigenous sign language, especially when used by both deaf and hearing family members, is perhaps the

most important factor that can improve the "genetic fitness" of the deaf population. Although their fitness was generally quite low in Europe prior to the time that sign language and schools for the deaf were introduced, it is now becoming apparent from a growing number of examples that a similar amplification of the frequency of specific genes for deafness can result from the development of indigenous sign languages that are used within extended families to allow deaf and hearing family members to communicate with one another.[30–33] As a result of the integration of the deaf population into the community, the fitness of deaf individuals can be unimpaired in this setting, and when D × D marriages occur, virtually all are noncomplementary, as expected, because there is usually only one form of genetic deafness in the community. Although gene drift and endogamy undoubtedly play essential roles in the survival and initial phenotypic expression of genes in such populations, it is hard to escape the conclusion that relaxed selection and assortative mating must also contribute to the remarkable increases that can be seen in both gene and phenotype frequencies and to the strong evidence for a founder effect.

In the present study, the results of a segregation analysis on living deaf probands who are alumni of Gallaudet University are described and compared to an identical analysis of Fay's deaf probands who lived 100–200 years ago. Replication of Rose's 1975 analyses of the Fay data allows us to detect changes in relevant genetic parameters that have occurred during the past century.

Subjects and Methods

Subject Ascertainment

Subjects were ascertained from the living alumni of Gallaudet University after IRB approval for the study was obtained. A brief family-history survey was initially mailed to 6906 alumni along with a cover letter inviting participation in the project from the Director of the Office of Alumni Relations. Of these, affirmative responses were obtained from 1697 deaf probands. After informed consent was granted, a more detailed interview was then conducted by the project staff for the collection of information on associated clinical findings; the hearing status of parents, siblings, children, other relatives, and spouses; and the ethnicity, age, birth year, marital status, and fertility of all deaf individuals in the pedigree as well as their hearing siblings. Whenever possible, the family histories were traced back to before 1900 to allow us to attempt to link the pedigrees to the extensive genealogic data, collected by E.A. Fay, on 5000 marriages among the deaf during the 19th century.[4]

Detailed pedigree information was obtained from 662 probands. Deaf probands who had no children (296) or who had children with a hearing partner (55) were not included in the segregation analysis. The remaining 311 probands with deaf partners were subjected to segregation analysis assuming complete selection through the deaf parents. The pedigrees of eight of these 311 probands could be linked to the genealogic data collected by Fay over a century before. Interestingly, five of these eight probands were homozygous and one was heterozygous for *GJB2* mutations. Additionally, another of these probands was heterozygous for the *GJB6* deletion.

Segregation Analysis

Segregation analysis of proband matings permits the estimation of several important genetic parameters, including the segregation ratio (p), the proportion of sporadic cases (x), the proportion of complementary matings that produce all nondeaf children (h), the proportion of noncomplementary matings that can only produce affected children (y), and the proportion of segregating matings that are capable of producing both deaf and hearing children ($1-h-y$).[34] The analysis was performed with the computer program SEGRAN[8] after it was recompiled for Microsoft Windows.

SEGRAN is well suited to the analysis of nuclear families segregating for a genetically heterogeneous monogenic trait, such as deafness. Of particular relevance to deafness, it is the only comparable program that is suitable for the analysis of marriages between affected individuals. The probands were grouped according to their specific mating type.

For D × D matings, ascertained by complete selection through affected parents regardless of the offspring phenotypes, under complete ascertainment, the distribution of r affected children in sibships of size s is given by $P(r = 0) = h + (1 - h - y)(1 - p)^s$ for sibships with no deaf offspring, $P(r = s) = y + (1 - h - y)p^s$ for sibships with all deaf offspring, and $P(0 < r < s) = (1 - h - y)\binom{s}{r}p^r(1 - p)^{s-r}$ for sibships with deaf and hearing offspring.

The variable y represents the proportion of noncomplementary matings (NCM), in which the parents are genetically incapable of having hearing offspring. For a trait like deafness, the vast majority of NCMs will reflect families in which both parents are homozygous for the same form of recessive deafness, but homozygosity for a dominant gene for deafness, two noncomplementary recessive genes for digenic deafness, or a fully penetrant gene for mitochondrial deafness are other possible causes for deafness in such families. The frequency of NCMs (y) is the key parameter that we wish to estimate and should be at least $y \geq 0.35 \times 0.35 = 0.1225$ if the current frequency of *GJB2* deafness among the deaf population is 35%. If we also consider only D × D matings in which both parents have recessive deafness, shown by their family histories, then y should meet or exceed 0.25, on the basis of the estimate that *GJB2* now accounts for approximately 50% of all recessive deafness. In her analysis of the Fay data, Rose[7] estimated that $y = 0.042 \pm 0.007$ for all 1299 D × D matings and that $y = 0.081 \pm 0.042$ for a subset of 65 recessive by recessive matings.

It is, of course, possible that y will not reach the value we have predicted. If so, we would have to find an explanation for why the reported frequency of deafness resulting from *GJB2* mutations cannot be used for predicting the frequency of matings between partners with *GJB2* deafness.

Results

The results of a segregation analysis of the pedigree data for the Gallaudet Alumni (311 D × D matings) are shown in Table 1 in comparison to the previous analysis of the Fay data performed in 1975.[7] In the latter, only 4.2% of marriages among the deaf were noncomplementary, and the observed segregation ratio of 32% was thought to be consistent with dominant forms of profound deafness, such as Waardenburg syndrome, which show a substantially reduced penetrance for bilateral deafness. In contrast, analysis of the contemporary Gallaudet alumni data shows a 5-fold increase in the proportion of NCMs (y), as well as

Table 1. A Comparison of Segregation Analyses of the Offspring of Deaf by Deaf Matings Ascertained by Complete Selection through the Parent(s): Two Data Sets Collected a Century Apart

Source of Data (Year)	Number of Matings	Percentage of Matings			Segregation Ratio
		Complementary ± SE	Noncomplementary ± SE	Segregating	
E.A. Fay (1899)	1299	78.9 ± 1.8	4.2 ± 0.7	16.9	32 ± 3
Gallaudet Alumni (2007)	311	42 ± 3	23 ± 3	35	43 ± 7

an increase in the segregation ratio (r) in the segregating sibships, which strongly suggests a recent admixture of fully penetrant phenotypes. Given that marriages between individuals with DFNB1 deafness are by far the commonest cause of noncomplementary matings, the increased proportion of segregating matings ($1 - h - s$) and the increase in the segregation ratio almost certainly reflect the inclusion of many families showing pseudodominant transmission of fully penetrant *GJB2* or *GJB6* mutations in this group.

To provide further support for our conclusion that the observed increase in NCMs reflects a large increase in the frequency of DFNB1 deafness during the past two centuries, we sought to determine whether we could detect the increase within the age range encompassed by the alumni data. To this end, we determined the frequency of pathologic *GJB2* and *GJB6* mutations in 441 Gallaudet student and alumni probands on whom DFNB1 typing was available as part of our alumni-study protocol, partitioned into three 20-year birth cohorts (1920 through 1980). Samples from all probands were screened for mutations in exons 1 and 2 of the *GJB2* gene via cycle sequencing. All were also tested for the Δ(GJB6-D13S1830) deletion of *GJB6* with the use of the method described by del Castillo et al.[25] As shown in Table 2, there was a statistically significant linear increase in the frequency of *GJB2* and *GJB6* mutations, even across this brief interval of time. Individuals who were homozygous or heterozygous for either *GJB2* or *GJB6* mutations were included in this analysis. No significant differences in the distributions of mutant alleles were noted across the birth cohorts of 1921–1940, 1941–1960, or 1961–1980; for example, the 35 del G mutation accounted for 69%, 73%, and 73% of all mutations in the respective birth cohorts. In a separate analysis, we compared the frequencies of *GJB2* and *GJB6* mutations over the same three intervals in 199 probands with at least one deaf parent. Although statistical significance was not achieved, a similar increase in the frequency of *GJB2* and *GJB6* mutations was observed, as shown in Table 3.

Discussion

The observed increase in the proportion of noncomplementary matings in contemporary pedigrees is what would be expected if mutations involving a single locus for deafness had become more frequent in the population. Specifically, these data from Gallaudet alumni are consistent with the dramatic increase in the frequency of DFNB1 deafness predicted by our simulation studies[3] and provide convincing evidence for the important influence that assortative mating can have on the frequency of genes for deafness. In addition to that of noncomplementary matings, the proportion of segregating matings also increased, as did the segregation ratio, more nearly approaching the 50% figure that one would expect for a fully penetrant dominant trait. Another important effect of assortative mating is the bringing together of rare, nonallelic genes for the same phenotype, creating a nonrandom distribution of genes that has been termed "gametic-phase disequilibrium."[35] Pedigree analysis suggests that many of the additional segregating matings reflect pseudodominant transmission in families in which one parent with deafness resulting from *GJB2* and/or *GJB6* mutations marries a partner who is deaf for some other reason but is also a heterozygous carrier of a single *GJB2* or *GJB6* mutation. A pedigree illustrating this concept is shown in Figure 1A. In this family, the deaf proband, his parents, and his sibling were screened for mutations in the *GJB2* and *GJB6* genes by the methodology described above. As shown, the proband's father, individual II1, was heterozygous for *GJB2* mutations and the proband's mother, II2, was homozygous. This pedigree structure suggests that, in addition to being *GJB2* heterozygotes, individuals II1 and III2 had deafness that must have been the consequence of a mutation or mutations involving another gene. The co-occurrence of nonallelic genes in the father and sister of the proband is an example of gametic-phase disequilibrium, which is one of the major genetic consequences of intense assortative mating among deaf individuals. Figure 1B demonstrates the concept of linguistic homogamy, another phenomenon which tends to bring together recessive genes for deafness and can result in pseudodominant transmission, also shown here. In this family, the proband, who is homozygous for *GJB2* mutations, has a deaf father (IV6) and a hearing mother (IV7).

Table 2. Secular Trend in the Frequency of Pathologic *GJB2* and *GJB6* Mutations among the Deaf: 1920–1980

Statistic	Birth Cohorts			Total
	1920–1940	1941–1960	1961–1980	
Number of Subjects	87	170	184	441
Number of Genes	174	340	368	882
Number of Mutations	49	122	143	314
Frequency of Mutations (%)	28	36	39	36

Linear-trend analysis: Z score 2.33, $p < 0.01$ (one-sided).

Table 3. Secular Trend in the Frequency of Pathologic *GJB2* and *GJB6* Mutations among the Deaf: Deaf Probands with One or Two Deaf Parents

	Birth Cohorts			
Statistic	**1920–1940**	**1941–1960**	**1961–1980**	**Total**
Number of Subjects	31	76	92	199
Number of Genes	62	152	184	398
Number of Mutations	31	80	101	212
Frequency of Mutations (%)	50	53	55	53

Linear-trend analysis: Z score 0.69, not significant.

The hearing mother of the proband had deaf parents and learned American Sign Language as her first language. The hearing children of deaf parents are the largest group of hearing individuals who are "native signers" and make up a disproportionate percentage of the spouses of the 10%–15% of deaf individuals who select hearing partners. It is for this reason that we believe that the mating structure of the deaf population is actually based on linguistic homogamy rather than on assortative mating for deafness per se. The occurrence of *GJB2* mutations in this family shows "pseudodominant" transmission, because the deafness would, superficially, appear to have been transmitted from one affected parent. These issues have important practical implications and should be considered whenever genetic counseling is provided to deaf and hearing partners, even when the deaf member of the pair is known to have a recessive form of deafness.

A number of other possible explanations for the observed rise in noncomplementary matings need to be considered. We selected Gallaudet University alumni for our study in an attempt to make our sample comparable to the Fay study, which also included the collection of data from this source. Even so, it is likely that Fay's sample was more comprehensive than the current study of Gallaudet alumni. It is likely that Fay's subjects were more representative of the entire deaf population at that time, given that he attempted to collect pedigree information for as many sources and deaf couples as possible. In addition to interviewing deaf individuals and their relatives, he collected data from the United States Census, school records, and periodicals for deaf people. This is in contrast to the current study, which involved ascertainment from only one source, with pedigree information collected through interviews of the deaf subjects. It also seems possible that the Gallaudet alumni population might include more individuals with deaf parents, because higher levels of academic achievement are known to be associated with the deaf offspring of deaf parents.[36–38] Expansion of our study to include individuals who have not attended college would be helpful in assessing the generality of our results.

Other factors, such as racial and ethnic differences, differences in age at onset, and the decrease in environmental factors as a cause for deafness in the past 100–200 years, might have also influenced our results, but they are difficult to compare with the Fay data set, which does not include information on race and ethnicity or explicit age at onset. Given the structure of the US population in the 1800s, it seems likely that the vast majority of Fay's subjects were white and of Northern European ancestry. In our sample of Gallaudet alumni, 95% reported that they were non-Hispanic white. We also collected information on our subjects' countries of origin. Fifty-three percent of the white subjects were of mixed European background, and 28% were of Northern European background. It is possible that the effects of immigration during the late 1800s and early 1900s of individuals from countries, such as Italy and Spain, with high frequencies of DFNB1 mutations might have also influenced our results. Differences in the reported age at onset for the two samples are also interesting and might have influenced our results, although age-at-onset data, even on current Gallaudet alumni, are crude at best because few of our subjects were young enough to have been identified as deaf through audiologic newborn-hearing-screening programs. Fay divided his subjects by age at onset on the basis of three categories, which he referred to as "congenital," "adventitious," and "unknown." His requirements for assigning the status of "adventitious" were not clear, but he reported that 31% of his subjects had congenital deafness and that the deafness was adventitious in 54% and unknown in 14%. Among our alumni subjects, 69% reported that their hearing loss was congenital, an additional 15% reported that their hearing loss occurred before the age of two, and 13% reported onset of hearing loss during childhood, and for 3% the information was not available. Because DFNB1 deafness is known to have a penetrance of 95% or more at birth, the apparent differences in the age at onset in the two population samples might well be consistent with an increase in the proportion of DFNB1 deafness in the contemporary population. Finally, the observed increase in noncomplementary matings might also reflect a decrease in the incidence of deafness caused by environmental factors over the last 100–200 years, or during the past 60 years that were covered by our cohort study. However, the presence of an affected parent is usually considered to be a reasonably accurate indication that the deafness in a proband is genetic in origin, and we observed a similar (but not statistically significant) trend in the frequency of *GJB2* mutations in this group, as shown in Table 3.

The genetic epidemiology of *GJB2* deafness in Turkey and other countries also appears to support our contention that assortative mating, along with relaxed selection during the last 100–200 years, has resulted in increased frequency of *GJB2* deafness. In Turkey, it seems quite likely that the appearance of an indigenous sign language might well have had a positive effect on the survival of genes for deafness throughout human history by creating "negative bottlenecks," or limited periods during which the frequency of the most common genes for deafness in the population were amplified by assortative mating and relaxed selection.[30] Archeological evidence[32] indicates, for example,

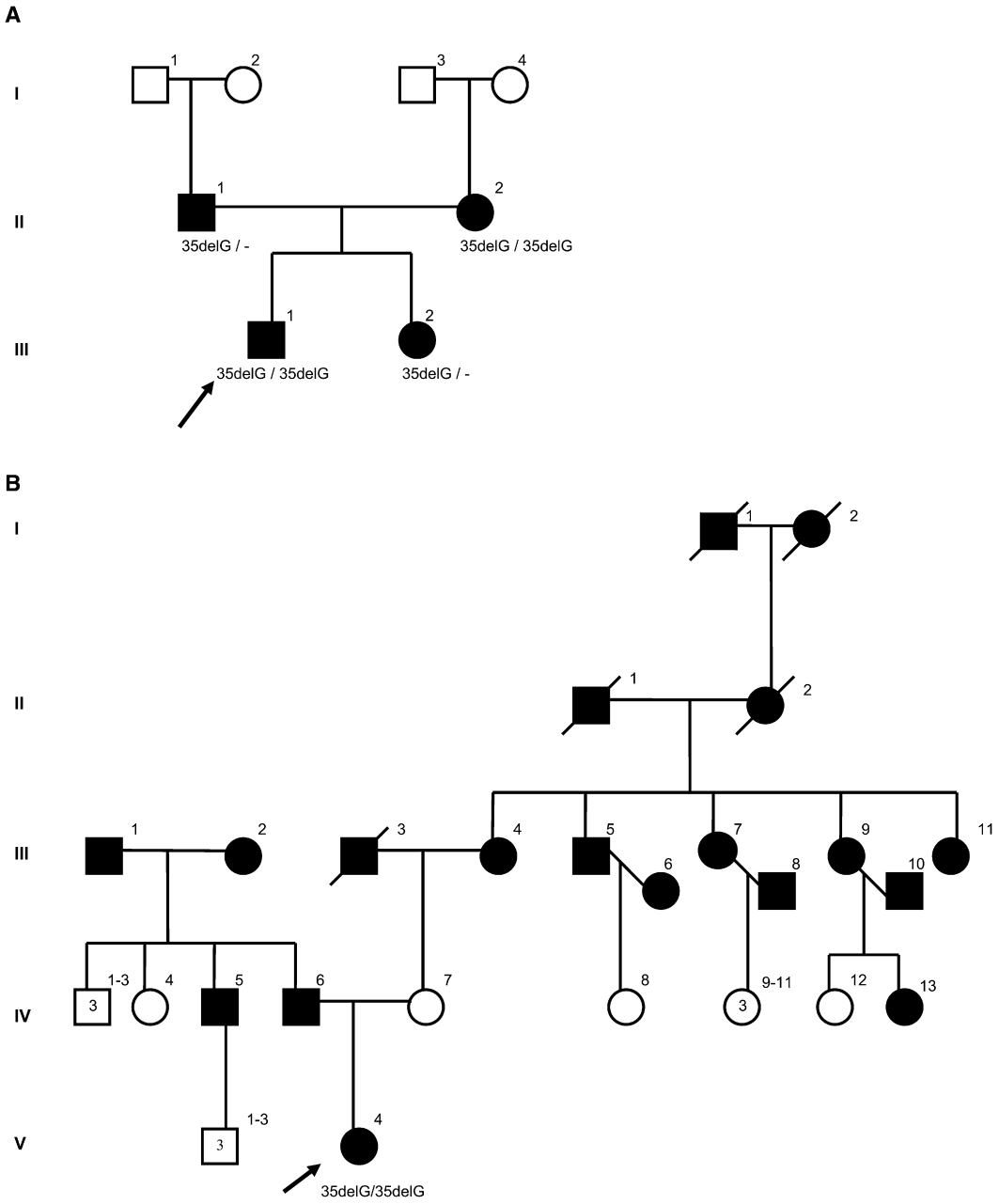

Figure 1. Pseudodominant Transmission of Deafness and Linguistic Homogamy
Pedigrees illustrating pseudo-dominant transmission of *GBJ2* mutations in a deaf by deaf mating (A) and a deaf by hearing mating (B) and an example of linguistic homogamy (B).

that at one time a deaf community was patronized by rulers of the Hittite Empire nearly 3500 years ago. If so, it is conceivable that, along with religious tolerance and the art of diplomacy, the 35 del G mutation might be the most conspicuous contemporary legacy of that Empire. In Western regions of Turkey, where the marriage patterns of the general population are similar to those of developed Western countries, with low rates of consanguinity and high rates of assortative mating between deaf individuals, the frequency of *GJB2* deafness was significantly higher than that in Eastern Turkey, where consanguineous marriages are the norm and D × D matings are not encouraged.[30] In Mongolia, where sign language was not introduced until 1995 and assortative mating was infrequent until recent years, *GJB2* is not a common cause of deafness (Nance et al., American Society of Human Genetics meeting 2000, Philadelphia, USA, Abstract 224). Finally, the observations of Friedman et al. on the high frequency of MYO15 deafness in the village of Benkala on the island of Bali, where an indigenous sign language has been in use for generations, clearly shows that the response of deafness genes to relaxed selection and assortative mating is not limited to DFNB1 but can affect the commonest recessive gene for deafness in any population.[33]

In the United States, 80%–90% of individuals with profound deafness currently marry a deaf partner;[39] however, the introduction of cochlear-implant technology is profoundly altering the mating structure of the deaf population. By facilitating oral communication and educational mainstreaming, substantially all of the deaf children of hearing parents will be redirected into the hearing mating pool. Even if all of the deaf children of deaf parents eschewed implants, continued to learn sign language, and mated assortatively, the size of the pool would decrease dramatically and would be increasingly composed of individuals with DFNB1 mutations. Under these assumptions, the ultimate size at which the mating pool stabilizes might well be influenced by the extent to which genotypic mate selection replaces phenotypic selection in the interim (Nance et al., American College of Medical Genetics meeting 2006, San Diego, USA, Abstract 52). On the other hand, if deaf couples begin to embrace cochlear-implant technology for their children, the pool size will continue to decrease, eventually resulting in the substantial disappearance of the deaf culture. Thus, the collection and analysis of data on marriages of deaf individuals might represent a vanishing opportunity to understand the factors that have contributed to secular changes in the genetic epidemiology of deafness in this country since Fay's landmark study.

Acknowledgments

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Web Resources

The URL for data presented herein is as follows:

Online Mendelian Inheritance in Man (OMIM), http://www.ncbi.nlm.nih.gov/Omim/

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