ELSEVIER

International Journal of Pediatric Otorhinolaryngology
35 (1996) 155 163

INTERNATIONAL JOURNAL OF
Pediatric
Oto
Rhino
Laryngology

Database for sensorineural hearing loss

Andrew J. Fishman*, Nancy Sculerati

Department of Otolaryngology, New York University School of Medicine, 550 First Avenue, New York, N.Y. 10016, USA

Received 8 June 1995; revised 16 November 1995; accepted 18 November 1995

Abstract

We are creating a bank of EBV immortalized lymphoblast cells and extracted DNA taken from the blood of deaf children and their relatives, in order to study the molecular basis of hereditary deafness. We have established a corresponding database for sensorineural hearing loss that records clinical data for each entered specimen. The purpose of this paper is to present the content and design of the computerized relational database. The data model is designed first to identify known etiologies of deafness, either acquired or syndromic, and then to characterize the clinical features of the deaf individual, and both their affected and non-affected family members. The application operates in a graphical environment of visual prompts and message panels. The database is organized by sections which record demographic data, presenting complaints, otologic history, birth and perinatal history, developmental history, symptoms of chronic airway obstruction, family history, neurologic history, congenital infections, hospitalizations and surgical history, medication history, vestibular findings, audiometry, radiology, medical conditions and syndromes and physical examination. The database was developed on a commercially available software product. Our database is presented as a model for use by other clinicians and investigators.

Keywords: Database; Computer; Deafness; Genetics; Molecular biology; Hearing Impairment; Hereditary deafness; Non-syndromal deafness; Children

1. Introduction

We are creating a bank of EBV immortalized lymphoblast cells and extracted DNA taken from the blood of deaf children and their relatives, in order to study

* Corresponding author, Tel.: (212) 263 6344.

SSDI 0165-5876(95)01318-0

the molecular basis of hereditary deafness. We have established a corresponding database for sensorineural hearing loss that records clinical data for each entered specimen. The purpose of this paper is to present the content and design of the computerized relational database. Our data model was chosen to identify known features of acquired and syndromic deafness and to help distinguish these from non-syndromic hereditary deafness, which is the most prevalent form of deafness. The data model describes, in detail, the clinical features of a deaf individual and both affected and non-affected family members, thereby defining the phenotype for the banked DNA genotype. The specific datafields were derived from a review of the current literature concerning the genetics of hereditary deafness, and the authors' experience treating hearing impaired individuals. The computer can permanently store information that is logically archived, and easily searched and retrieved.

2. Background and significance

Deafness is the most common clinical entity interfering with the acquisition of speech and language in childhood. At least one of every 1000 children has hearing loss severe enough to interfere with the acquisition of normal speech [1,6]. Though many cases of early onset deafness are the result of meningitis or exposure to ototoxic drugs, at least 60% are hereditary in nature [3].

Deafness may be broadly classified as hereditary versus non-hereditary and syndromic versus non-syndromic. Further classification is based on time of onset (congenital versus those appearing post-lingually) as well as denoting progression or stability of hearing loss.

Hereditary deafness manifests as part of a definable syndrome in no more than 25% of cases. The associated phenotypic features, in these cases, aid in identifying the genetic aberration. The vast majority; however, are non-syndromic, present only with hearing loss and display significant genetic diversity [6]. Advances in gene localization and identification of hereditary syndromes have occurred when the recognition of phenotypically variant subgroups suggests the presence of different genes. A database identifying distinctive clinical patterns may help guide investigation of non-syndromic hereditary deafness on the molecular level. Our database is presented as a possible model for use by other clinical centers. The specific datafields comprise a formalized history and physical evaluation that provides a model for the clinical evaluation of a child with hearing loss.

3. Materials and methods

Programming was done in the ObjectPAL™ language provided with Paradox for Windows™ version 4.5 distributed by Borland International (Borland International, P.O. Box 660001, Scotts Valley, CA 95067. Windows is a registered trademark of Microsoft Corporation). All work was done on a desktop PC

Table 1

Demographics
Name
Date of interview
Referral source
Chief complaint of referral
Date of birth
Address
Sex
Relationship of historian
Parent's primary language
Interpreter present
Interpreter comments
Patient's country of birth
Mother's country of birth
Father's country of birth
Religion
Race
Adoption status
Parental blood relation
Grandparental blood relation

Complaints
Complaint **Relational field options**
Articulation problems
Failed school screen
Cleft palate patient
Family history of hearing loss
High risk patent
Known hearing loss
Parent suspects hearing loss
Psychiatric in-patient
Speech delay
Suspected hearing loss
Description (*free text*)

Otitic history
Date of last ear infection
Rate of ear infections (*frequency/year*)
Age at first infection
Lifetime total
Chronic/recurrent rhinorrea (*y/n*)
Frequent pharyngitis/tonsillitis (*y/n*)

Birth and perinatal history
Gestational age at birth
Birth weight
Left hospital with mother (*y/n*)
History of intubation (*y/n*)
Treatment for jaundice (*y/n*)
Exchange transfusion (*y/n*)
UV lights (*y/n*)
Maximum bilirubin
Meningitis (*y/n*)
Type
Organism
Comments (*free text*)
Head trauma (*y/n*)
Comments (*free text*)

Developmental history
Roll over (*yrs*)
Sit-up (*yrs*)
Walk (*yrs*)
Unsteady (*y/n*)
Say words (*yrs*)
Use sentences (*yrs*)

Chronic upper airway obstruction (UAO)
Evidence of chronic UAO (*y/n*)
Symptoms **Relational field options**
Bed wets
Daytime somnolence
Hyperactivity
Mouth breather
Pauses
Snores
Stops breathing

Family history
Relative name
Relative ID #
Relation
Finding **Relational field options**
Auricular tags
Blindness
Brachial cleft cysts
Cleft palate
Congenital cardiac disease
Congenital cataracts
Craniofacial anomalies
Dystopia canthorum
Hearing loss
Heterochromia irides
Hearing loss in old age
Mental retardation
Microtia
Nystagmus
Patchy pigmentation
Polydactaly
Preauricular pit
Prolonged QT interval
Renal disease
Retinitis pigmentosa
Sudden death

Table 1 (Continued)

Syncope
Syndactaly
Thyroid disease
Uses hearing aid
Uses sign language
White streak in hair
Description (*free text*)
Address
Telephone number

Neurologic history
Finding **Relational field options**
Anoxia
Cerebral palsy
Hydrocephalus
Microcephaly
Non-febrile seizures
V-P shunt
Description (*free text*)

Congenital infections
Finding **Relational field options**
CMV
Herpes
HIV
Rubella
Syphillis
Toxoplasma
Description (*free text*)

Hospitalization and surgical history
Date
Institution
Procedure
Admitting diagnosis
Description (*free text*)

Medication history
Medication
Start date
Duration
Dose
Schedule

Vestibular data
Date
Examination
Findings (*free text*)

Radiology
Date
Exam (CT, MRI, X-Ray, 3-D Reconstruction)
Findings (*free text*)
Image (*graphic file*)

Audiometric data
Date
Shape in Left **Field options**
Residual low tone
Flat
U-shaped
Upsloping
Gradually downsloping
Steeply downsloping
Other
Other Shape
Shape in Right
Stable (*y/n*)
Progression (*y/n*)
Side
Frequency
Db drop
Time
Discrimination left
Discrimination right
Audiogram (*graphic file*)
ABR left (*free text*)
ABR right (*free text*)

Conditions and syndromes
Medical condition or syndrome **Relational Field Options**
Cardiac disease
Congenital cardiac disease
Congenital cataracts
Craniofacial anomalies
Dystopia canthorum
Diabetes
Interstitial keratitis
Mental retardation
Muscular dystrophy
Renal disease
Prolonged QT interval
Retinitis pigmentosa
Syncope
Syndactaly
Thyoid disease
Alport syndrome
Branchio-oto-renal syndrome
Cogan syndrome
Cornelia de Lange syndrome
Downs syndrome
Familial dysautonomia
Meniere disease

Table 1 (Continued)

Turner syndrome	Nose
Usher syndrome	Nare
Waardenburg syndrome	Exudate
Description (*free text*)	Comment (*free text*)
	Palate **Field options**
Physical examination	Cleft
Face	Submucous cleft
Ear (*left and right included*)	Bifid uvula
Pinna	Tonsil size (*right and left included*)
Helical pit	Pharynx comment (*free text*)
Prehelical pit	Nasopharynx comment (*free text*)
Ear tag	Larynx comment (*free text*)
Microtia	Frenulum
Stenosis	Tongue mobility
Atresia	Tongue comment (*free text*)
Tympanic membrane color	Cervical adenopathy (*free text*)
Mobility	Sinus tracts (*free text*)
Perforation	Neck comments (*free text*)
Otitis media	Fundoscopic examination report (*free text*)
Tympanosclerosis	General examination (*free text*)
Comment (*free text*)	

operating an Intel 80486 33 mHz processor, a SVGA monitor running at either 256 or 65 K colors and a high capacity fixed drive. The application is installed on a local area network in the N.Y.U. Medical Center. The application accepts the input of graphic files from digital scanners and fax-modems.

Paradox is a relational type database. This differs from the standard flat file database by the fact that multiple entries may describe a given datafield. Though somewhat more complex, this format is necessary to describe the dataset accurately.

A 'relational field' is a technical term used in database design. If a field on a database only allows the input of one item or a yes/no response, e.g. birthdate (which receives a single date input) or frequent pharyngitis (which receive a yes/no response) (refer to Table 1), it is a simple field. If a field allows the input of multiple items in the form of a list, where each item is independently searchable, then it is a 'relational field'. The options are presented to the user in the form of a 'pull down' menu off of which they may be chosen or an original entry not on the list may be entered manually. As an example, take the field 'medical condition or syndrome' (Table 1). A patient may have both craniofacial anomalies and syndactyly or even other distinct abnormalities which need to be recorded and individually detailed. A relational field allows the inclusion of each item and a search for any of the above would include this individual patient. This is the strength of a relational field. Relational field options are provided as prompts from a list. Relational field options which are listed in Table 1 are built into the program and presented to the user in the form of pulldown menus.

The informational content of the database, including individual and family history and otologic and medical findings are designed such that a junior otolaryngology house officer can complete the intake questionnaire during a 30 min patient interview.

4. Results

Sample identification is maintained through a unique pedigree coding determined by the following four elements: 1. Personal identification number (social security number when available); 2. Father ID #; 3. Mother ID #; and 4. Next oldest sibling (NOS) ID #. Affected individuals and available relatives are interviewed, and their blood is obtained. Each relative is also entered separately into the database. The four field identification system serves as the basis for an 'extract pedigree' function that generates a table of all related individuals from one selected individual.

The application operates in a graphical environment of visual prompts and message panels. The main screen contains a table of all included subjects for which a DNA sample has been obtained. A pull down menu leads to the various screens organizing the database. Table 1 is provided as an outline of the included datafields. Relational fields may contain multiple searchable entries. Data entry options are selected from a preset pulldown menu (denoted as *Relational field options* in Table 1) or typed in as original items.

Demographic data focuses upon country of origin and any history of consanguinity. A section on family history serves as a starting point from where listed family members can be contacted and then entered separately into the database. A section detailing presenting complaints is included so that ascertainment bias can be assessed when reporting incidence and prevalence data.

Information is acquired first for the affected individual because this is the natural process of presentation. In the recording of this data, there will be encountered, related individuals who possess significant historical findings. This data can be recorded as a prompt in the presenting patient's record to relatives who may be contacted and then be entered individually and fully. When the extract pedigree function is performed, a list of all related individuals is presented and the logic of familial relationships can be seen by the pedigree coding displayed i.e. same mother, same father etc. Follow-up data on individuals, such as serial audiograms are handled by the virtue that the database is 'relational' and 'multiple' items, e.g. medications, audiograms (with dates included) can be entered in an individual's record without having to start a whole new entry.

Otologic history focuses on otitis frequency, which is commonly and independently associated with speech delay secondary to conductive losses. Adverse neurologic history or a history of congenital infections may cause neurologic impairment including acquired sensorineural hearing impairment. Medical conditions and syndromes known to cause hearing impairment are also detailed individually (see Table 1).

The section on birth and perinatal history pinpoints events that make acquired ototoxicity or injury more likely. Included are hyperbilirubinemia, meningitis and prolonged intubation, which increases the likelihood of having received ototoxic medications. Items included in developmental history signal the possibility of more global neurologic impairment contributing to speech and language delay.

A detailed otologic, head and neck and general physical examination are recorded. A pertinent medication history is obtained. Radiographic evidence of cochleovestibular anomalies may be recorded, both in text and graphic image form, with the use of a digital scanner. Vestibular data are included when available. Audiometric findings for each ear are characterized by shape: U-shaped, upsloping, residual low tone, flat, gradually or steeply downsloping, or other. Scanned images of audiograms are maintained, when appropriate. Progression is denoted by a 10 dB drop in at least one frequency over the recorded time. Because the database is relational in format, appropriate datafields for audiology and other tests may be recorded and logged in relation to time as described above.

5. Discussion

Hereditary deafness is primarily caused by single gene defects that follow clear autosomal or sex-linked inheritance patterns. A small number of cases arise from major chromosomal anomalies, affecting many sequential genes, which can be characterized by cytogenetic staining techniques. Though rare, these sporadic chromosomal rearrangements are important because they can provide clues to the location of deafness genes, especially if they result in a recognizable syndrome.

Mitochondria possess a unique DNA that differs from nuclear DNA in both form and transmission pattern. It is recognized to be responsible for at least some forms of inherited deafness, including some syndromic cases, and one form characterized by extreme sensitivity to aminoglycoside ototoxicity [5].

Single gene defects causing deafness follow an autosomal dominant pattern in 10–20% of cases. 2–3% are X-linked. Greater than 70 percent; however, are recessive disorders and require the occurrence of two abnormal gene alleles, one from each parent. In the absence of consanguinity, recessive disorders appear as unique occurrences within a pedigree, typically from unaffected parents. Since the great majority are also non-syndromic and present only with hearing impairment, it is essential to rule out non-congenital factors to properly diagnose a case of hereditary deafness. Our database is designed to first identify known etiologies of deafness, acquired or syndromic, and then to characterize an affected individual's deafness by detailing clinical expression, radiographic findings and audiometric parameters. The computer database format allows for logical searches to extract individuals and their pedigrees that share study variables.

The inclusion of multiple family members is imperative, not only for gene localization studies, but also for diagnosing syndromic deafness. As an example, Waardenburg syndrome is characterized by great variability of phenotypic expression. It is an autosomal dominant disorder in which some affected family members may have only mild facial or pigmentary findings, few relatives may be deaf, and many may have unrecognized unilateral losses. A clinical diagnosis may be impossible without the examination of multiple relatives.

Audiometric data, though important in describing an affected individual's phenotype may serve as an example of variable expressivity in some instances, so care

must be taken not to assume genetic homogeneity based purely on extent of hearing loss. In Waardenburg syndrome for example, there is great variability in expression of hearing impairment even within families possessing the same gene defect, and predictions regarding the expression of hearing loss in future siblings cannot reliably be made. In the case of Usher syndrome, a recessive disorder, there seems to be a consistent pattern within affected families who possess the same gene. Related individuals with non-syndromic hearing loss whom have hearing loss of the same audiometric profile and mode of inheritance, are also likely to share the same specific abnormal gene [4]. Audiometric data is stored in both a descriptive format as outlined above, and in graphic image form so that intelligent analyses may be performed once study parameters are chosen.

Milestones in language development help time the onset of deafness to either pre- or post-lingual. This may denote a progressive disorder or help distinguish hereditary from acquired deafness in certain instances. For example, a child may demonstrate a history of exposure to perinatal toxins such as aminoglycosides. If this was responsible, it would likely be pre-lingual deafness. If this child displayed a pattern of normal, age appropriate language before the onset of deafness, then the deafness is likely not caused by the exposure and may represent a progressive inherited disorder in the absence of other factors.

Motor development is recorded because it provides insight, not only into vestibular dysfunction, but also into associated neuromuscular abnormalities. Genes for deafness have recently been localized near the genes for muscular dystrophy [2]. Though the relationship is still unclear, this is the subject of current investigation.

6. Conclusion

A human DNA bank associated with a database for sensorineural hearing loss should serve as a valuable research tool to aid in the understanding of the genetics of deafness. We have described our method for the collection of pertinent clinical data which describes affected individuals and their family members. The database was developed on a commercially available software product. The selected fields define the phenotype of included individuals. The relational nature of the database provides for the inclusion of follow-up and other time related data. Specific information has been provided so that it may be integrated into any database which aims to describe clinical features of deaf patients. Additionally, the data structure should prove useful to any clinician interviewing and treating hearing impaired individuals.

References

[1] Cremers, C.W.R.J., Graham, J., Parving, A. and Ruben R.J. (1988) Biology of sensorineural hearing loss in children. Int. J. Pediatr. Otorhinolaryngol. 15, 1–15.

[2] Guilford, P., Ben Arab, S., Blanchard, S. et al. (1994) A non-syndromic form of neurosensory recessive deafness maps to the pericentromic region of chromosome 13q. Nature Genet. 6, 24–28.
[3] Marazita, M.L., Ploughman, L.M., Rawlings, B., Remington, E., Arnos, K.S. and Nance, W.E. (1993) Genetic epidemiological studies of early-onset deafness in the US school-age population. Am. J. Med. Genet. 46, 486–491.
[4] Marres, H.A. and Cremers, C.W. (1989) Autosomal recessive nonsyndromal profound childhood deafness in a large pedigree. Arch. Otolaryngol. Head Neck Surg. 115, 591–595.
[5] Prezant, T.R., Agapaian, J.V., Bohlman, M.C. et al. (1993) Mitochondrial ribosomal RNA mutation associated with both antibiotic-induced and non-syndromic deafness. Nature Genet. 4, 289–294.
[6] Reardon, W. (1992) Genetic deafness. J. Med. Genet. 29, 521–526.