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# Genetic Studies of Questionnaire Data from a Residential School for the Deaf

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# GENETIC STUDIES OF QUESTIONNAIRE DATA FROM A RESIDENTIAL SCHOOL FOR THE DEAF

by

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Thesis

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FRB

April, 1981

Boston, Massachusetts

"Because as Galen says in his seventh book of the Method of the Art of Healing, a work in any science or art is propounded for three reasons. First, to satisfy one's friends. Second, that one may obtain a most useful exercise, that is by the mind. Third, so that one may be saved from forgetfulness, which comes with age. Hence it is that, moved by these three causes, I have proposed to put together a certain work in medicine for my scholars."

Mondino, Anathomia, 1316

GENETIC STUDIES OF QUESTIONNAIRE DATA FROM A RESIDENTIAL SCHOOL FOR THE DEAF

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A self-administered thirteen page Hearing Loss Questionnaire (HLQ) was designed in order to systematically collect medical and family history data on deaf children and their families. Data were collected from over 400 families with one or more children enrolled in September 1979 at the Maryland School for the Deaf (MSD). Almost 70% of the parents provided pedigree and family history information by completing the detailed HLQ. Computer analyses of the collected data allowed a thorough examination of almost 200 medical and family history variables, providing useful reference data on the MSD probands. Parental responses to a four-step rating scale of proband hearing ability were compared with actual audiometric data, allowing comparison with similar data from previous studies of hearing populations. Family history data on the non-respondents were available from school records, providing a unique opportunity to assess the potential response bias in questionnaire studies of genetic disease. Segregation analysis was performed on the informative sibships ascertained by incomplete truncate selection. The pooled estimate of the ascertainment probability, $\pi$, was 0.488, with no significant evidence of heterogeneity among the respondents and non-respondents. The hypothesis of fully penetrant dominant inheritance ($H_0$:p=0.50) was accepted in the Deaf by Hearing matings. However, the maximum likelihood estimate of the segregation

ratio ($\hat{p}$=0.257) was consistent with reduced penetrance in these families, as it also was in the Deaf by Deaf matings ($\hat{p}$=0.31). There were no significant differences in the maximum likelihood estimates of $p$ or of the proportion of sporadic cases, $x$, between respondents and non-respondents in the Hearing by Hearing matings. Among the non-consanguineous Hearing by Hearing matings with no family history of hearing loss, the maximum likelihood estimate of $x$ was 0.81. The removal of 46 sibships with probands born during the 1964-65 rubella epidemic reduced $\hat{x}$ to 0.71, indicating the potential value of segregation analysis for monitoring the secular trends in sporadic vs. genetic deafness. Among Hearing by Hearing matings with a family history of early onset hearing loss, a recessive hypothesis with no sporadic cases ($H_0$:p=0.25, x=0.00) fit the data well. However, the same hypothesis was rejected among the Hearing by Hearing matings with a family history of "presbycusis", where $\hat{x}$=0.59. Thus, although a family history of early onset hearing loss appears to be a much more reliable index of a genetic etiology that does a family history of "presbycusis", the results of this study suggest that the latter may also be a positive risk factor. The HLQ data implied that both parents and doctors may underestimate the extent to which genetic factors contribute to childhood hearing loss, even in the presence of a positive family history. Genetic factors were estimated to account for approximately 35% of the deafness in the MSD population. In the group with genetic deafness, the estimated proportions of recessive, dominant, and X-linked deafness were 57%, 39%, and 5% respectively. Comparison of the estimates in the respondent vs. the non-respondent groups revealed remarkable similarity between the two groups, indicating that the use of the HLQ did not further confound existing biases. This study has demonstrated the value and utility of using self-administered questionnaires in genetic research. Indeed, the HLQ may serve as a useful prototype for future large scale population based studies of deafness in man.

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# INTRODUCTION

# INTRODUCTION

Hearing impairment still remains one of the most, if not the most, prevalent chronic disabilities in the United States (Schein and Delk, 1974; Proctor, 1977). Over 14 million persons suffer sufficient hearing impairment to interfere with their ability to understand conversational speech and to affect their capacity to function in both the social and the vocational setting (Miller, 1976). Hearing problems in children not only interfere with their ability to communicate with others, but can have profound and often irreversable effects on their linguistic, cognitive, and psychosocial development, almost inevitably causing serious academic problems if the hearing loss is not identified early and managed appropriately (Whetnall and Fry, 1964; Vernon, 1967, 1969; Frisna, 1976).

A host of insults, both genetic and non-genetic, are known to contribute to the etiologic spectrum of deafness in man (Northern and Downs, 1978; Bieber and Nance, 1979). Although many earlier investigators ignored or were unaware of an hereditary component in the causation of deafness, more recent studies of the deaf and their families have provided ample evidence that genetic factors play a substantial role in the etiology of hearing impairment (Rose, 1975; Fraser, 1976).

Thus, for many compelling reasons relating to the diagnosis, treatment, and care of the hearing impaired it would seem desirable to conduct long term population based studies of the deaf. However, previous studies of deaf populations have relied almost exclusively on laborious or inefficient methods of data collection, which rarely used the deaf or their family members as a direct source of the survey data. Therefore, a goal

of this study was to design a self-administered Hearing Loss Questionnaire and test its utility for collecting medical and family history data on a large population of hearing impaired children and their families, paying particular attention to the presence and effects of any response bias in such a population study.

A Hearing Loss Questionnaire (Appendix I) was designed and mailed to all parents/guardians of one or more children enrolled as students at the Frederick, Maryland campus of the Maryland School for the Deaf during the 1979-80 school year. Computer analysis of the collected data allowed a thorough examination of almost 200 medical and family history variables, providing useful reference data on the MSD probands. Estimates were made of the proportions of sporadic and genetic hearing loss, of the proportions of inherited deafness due to dominant, recessive, and X-linked genes, and of the penetrance of the dominant genes. These estimates were also made in the non-respondent group, and were found to closely approximate those from the respondent group. Another goal was to evaluate the effects of a positive family history of "presbycusis" vs. a family history of early onset hearing loss on the segregation ratios in the proband sibships. Results indicate that a family history of early onset deafness or of presbycusis are positive recurrence risk factors although a majority of probands with a family history of presbycusis were estimated to be sporadic cases. Parental responses to a four-step rating scale of proband hearing ability were compared with actual audiometric data, allowing comparison with similar data from previous studies of hearing populations.

The results of this study demonstrate the value of self-administered questionnaires in survey and genetic research and indicate that the Hearing Loss Questionnaire may serve as a useful prototype for large-scale population based studies of deafness.

# GENERAL BACKGROUND AND OVERVIEW OF THE LITERATURE

## GENERAL BACKGROUND AND OVERVIEW OF THE LITERATURE

The following 104 pages of this dissertation present a synthesis and distillation of a wealth of information and research on the subject of hearing and hearing loss. Because of the enormous volume of material written on this general subject, an attempt was made to select that which would be most relevant to the present study. The overview begins with a consideration of the anatomy and physiology of the hearing organ, and with a review of our current understanding of the many types and causes of hearing loss, including an examination of some cogent animal studies, some data on the frequency of additional handicapping conditions, and a brief discussion of hearing loss in the adult. This review also describes the measurement of hearing, several relevant audiological studies of hearing impaired groups, and concludes with a section devoted to population studies of the prevalence and causes of deafness and a review of the genetic studies of hearing loss.

Hopefully, this general background and overview will serve to provide the reader with some insight into the marvelous complexity of the hearing organ and the extent to which untoward perturbations, both genetic and environmental, can lead to diminution or lack of hearing ability.

## THE NATURE OF THE HEARING PROCESS

Although in the adult the ear forms one anatomical unit, functioning as an organ of both hearing and balance, in the embryo it develops from three distinct parts. In humans the developing ear primordium can first be seen at about 22 days gestation as thickenings of the surface ectoderm, the otic placodes. These placodes invaginate to form otic vesicles which later divide into a ventral portion, forming the saccule and cochlear duct, and a dorsal part, forming the utricle and semicircular canals. The inner ear reaches its full adult size and form by the end of the fourth fetal month. The cochlear end organ is the last of the labyrinthine structures to develop and is therefore more subject to developmental anomalies than is the vestibular system.

The middle ear, or tympanic cavity, and the auditory tube are derived from the first pharyngeal pouch, an outpocketing of the pharynx. This pouch, of endodermal origin, appears in the embryo at about four weeks gestation. The malleus and the incus are derived from cartilage of the first pharyngeal arch and the crus of the stapes from the second arch.

The auricle develops from the fusion of mesenchymal swellings or hillocks surrounding the first pharyngeal cleft and the external auditory canal arises from inward growth of this cleft. The tympanic membrane consists of an ectodermal epithelium at the base of the auditory meatus, an endodermal lining in the tympanic cavity and intermediate connective tissue. Table 1 provides a chronological summary of major stages of ear development.

TABLE 1: SUMMARY OF EAR DEVELOPMENT

| Fetal Week | Inner Ear | Middle Ear | External Ear |
|---|---|---|---|
| 3rd | Auditory placode; auditory pit | Tubotympanic recess begins to develop | |
| 4th | Auditory vesicle (otocyst); vestibular-cochlear division | | Tissue thickenings begin to form |
| 5th | | | Primary auditory meatus begins |
| 6th | Utricle and saccule present; semicircular canals begin | | Six hillocks evident; cartilage begins to form |
| 7th | One cochlear coil present; sensory cells in utricle and saccule | | Auricles move dorsolaterally |
| 8th | Ductus reuniens present: sensory cells in semicircular canals | Incus and malleus present in cartilage; lower half of tympanic cavity formed | Outer cartilaginous third of external canal formed |
| 9th | | Three tissue layers at tympanic membrane are present | |
| 11th | Two and one-half cochlear coils present; nerve VIII attaches to cochlear duct | | |
| 12th | Sensory cells in cochlea; membranous labyrinth complete; otic capsule begins to ossify | | |
| 15th | | Cartilaginous stapes formed | |
| 16th | | Ossification of malleus and incus begins | |
| 18th | | Stapes begins to ossify | |
| 20th | Maturation of inner ear; inner ear adult size | | Auricle is adult shape, but continues to grow until age 9 |
| 21st | | Meatal plug disintegrates exposing tympanic membrane | |
| 30th | | Pneumatization of tympanum | External auditory canal continues to mature until age 7 |
| 32nd | | Malleus and incus complete ossification | |
| 34th | | Mastoid air cells develop | |
| 35th | | Antrum is pneumatized | |
| 37th | | Epitympanum is pneumatized; stapes continues to develop until adulthood; tympanic membrane changes relative position during first 2 years of life | |

Source: Northern and Downs, 1978

Sound waves entering the external auditory meatus cause the tympanic membrane to vibrate; these vibrations are transmitted to the inner ear by the auditory ossicles of the middle ear. At the inner ear, the sound energy is again transformed into wave motions which travel up the fluid-filled spiral chamber of the cochlea and stimulate the hair cells of the organ of Corti. Finally, nerve impulses are carried from the organ of Corti via the VIIIth cranial nerve to the auditory cortex where they are perceived as sound.*

As shown in Figure 1, the ear may be anatomically divided into three separate parts: the external ear, the middle ear, and the inner ear. The external ear includes the auricle, the external auditory canal and the tympanic membrane. The auricle (or pinna) is a flap of skin-covered cartilage, whose most proximal portion is the concha, the area leading to the opening of the external auditory canal. The cartilage of the auricle continues inward, becoming the supporting structure for the outer third of the ear canal while the inner two-thirds of the ear canal is formed by the temporal bone. The canal allows sound to enter the middle and inner ear, while preventing injury to the middle ear. Separating the external auditory canal from the middle ear is the tympanic membrane. This oval, semitransparent membrane is about 0.01 mm thick and is composed of four layers. The superficial epidermal layer is continuous with the lining of the external auditory canal. The inner layer is a mucous membrane which is continuous with the lining of the middle ear. Between the two outer layers is a double thickness of supporting connective tissue.

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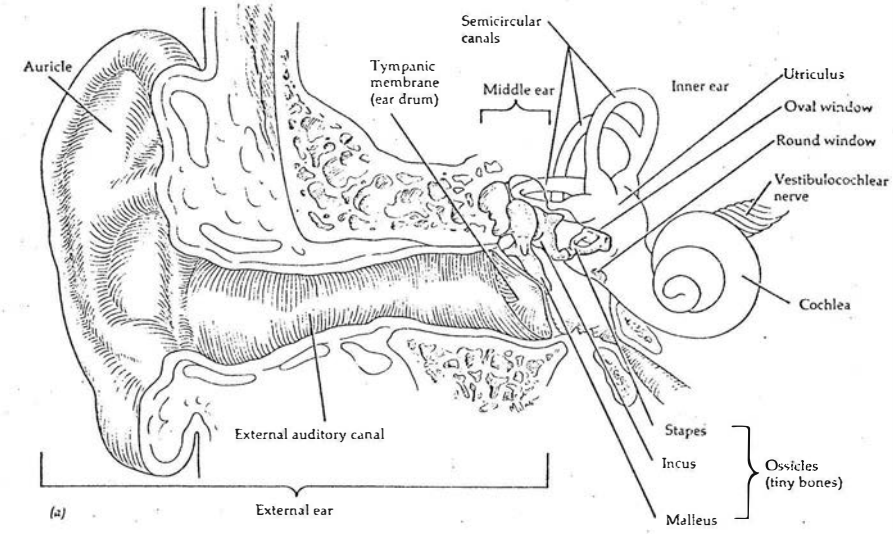
* A popular account of the mechanism of hearing appears in Appendix III.

The delicate structures of the middle and inner ear are housed within the temporal bone. The middle ear includes three ossicles contained within an air-filled enclosure (see Figure 1b). These three ossicles (the malleus, the incus, and the stapes) constitute an intricate lever system to transmit sound energy from the tympanic membrane to the oval window opening into the inner ear, or labyrinth. The manubrium of the malleus is connected by its lateral margin to the tympanic membrane, being embedded within the layers of the membrane in a position similar to the spoke of a wheel. The head of the malleus articulates with the body of the incus (biaxial diarthrosis or saddle joint), while the lenticular process of the incus articulates with the head of the stapes (enarthrosis or ball and socket joint). The base of the stapes, known as the foot plate, is attached by a fibrous tissue rim, the annular ligament, to the oval window of the inner ear. This attachment allows for both inward and outward movements of the footplate which correspond with the phase patterns of the incoming sound waves. The tympanic membrane receives energy over a relatively large area and delivers it via the ossicles to the small oval window. This reduction of surface area combined with the mechanical advantage of the ossicular chain allows the efficient transmission of sound energy from the low-density air of the middle ear to the high-density fluid of the inner ear, and thus results in an impedance matched system.

Within the bony capsule embedded in the temporal bone lies the membranous labyrinth, a series of communicating sacs and ducts. The capsule consists of (a) the central vestibule into which the oval window opens, (b) the three mutually perpendicular semicircular canals, also opening off the vestibule, and (c) the cochlea, which opens off the anterior portion of the vestibule. The semicircular canals, along with



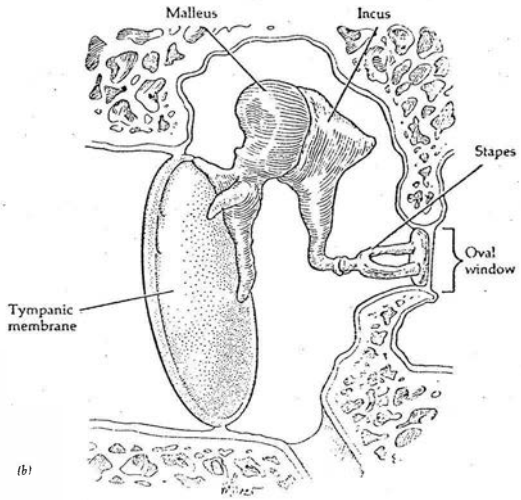



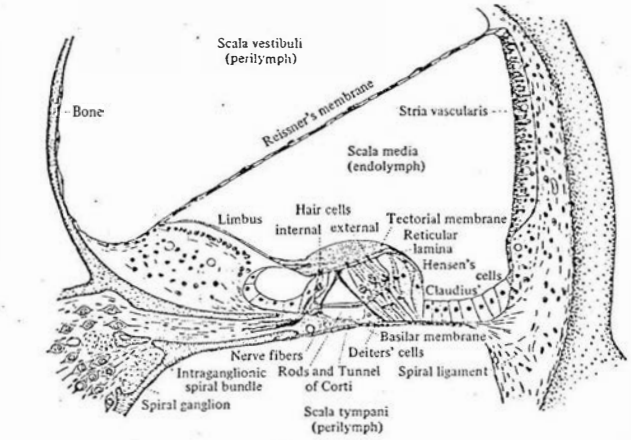

Figure 1
(a) The anatomy of the human ear.
(b) Structures of the middle ear.

Source: Luria et al., 1981

the utricle and saccule in the vestibule, are concerned with maintaining equilibrium. The membranous cochlear duct lies within the bony cochlear canal and makes 2 3/4 turns around the central bony modiolus. A basilar membrane stretches from the modiolus to the outer wall of the cochlear canal dividing it into two passages, the scala vestibuli and the scala tympani (see Figure 2). The sensory end organ, the organ of Corti, is located on the apical side of the basilar membrane, and lies beneath Reissner's membrane which helps form the partition between the perilymph, (thought to be an ultrafiltrate of plasma (Schnieder, 1974)), contained in the scalae vestibuli and tympani, and the central scala media. The scala media contains a fluid endolymph (produced by the secreting epithelium or stria vascularis of the cochlear duct), and is continuous with the membranous labyrinth. It is in the membranous portion of this system, the cochlear duct, that the sensory-epithelial structures of the organ of Corti are found. Acoustic nerve fibers extend from the spiral ganglion in the modiolus into the organ of Corti. Nerve fibers connect to the base of the inner and outer hair cells, whose apical stereocilia extend through the endolymph to the inferior surface of the proteinaceous tectorial membrane lying over the organ of Corti.

Auditory neural impulses are triggered by the development of receptor potentials resulting from relative movements of parts of the organ of Corti. It is thought that slight movement of the stereocilia by the relative motion of the tectorial and basilar membranes distorts the hair cell membrane allowing an influx of ions, thus initiating the partial depolarization of the hair cell membrane. Evidence suggests that this potential excites the cochlear nerves by acting directly upon the unmyelinated dendrites of the afferent neurons at the sides and bases of

FIGURE 2: CROSS SECTIONAL DRAWING OF THE COCHLEAR CANAL



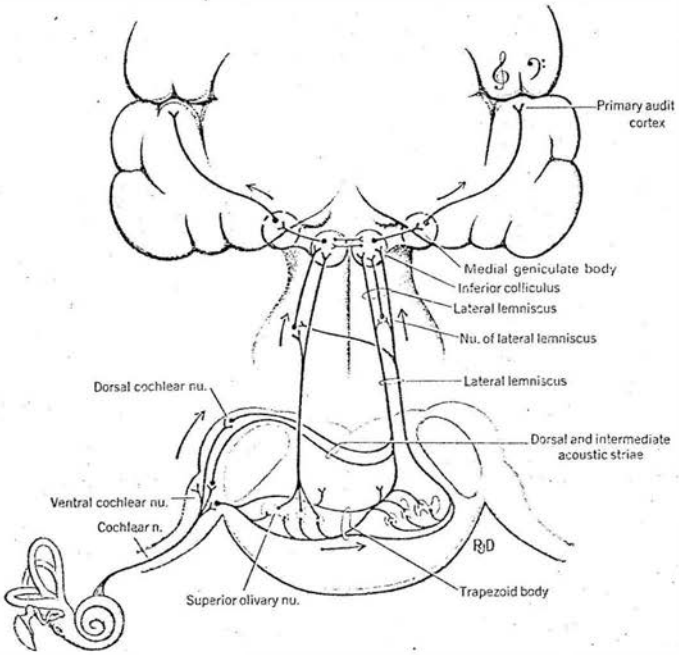

Source: Davis and Silverman, 1970

the hair cells (Gulick, 1971). As shown in Figure 3, axons from these nerve cells pass via the cochlear nerve to the dorsal and ventral cochlear nuclei located in the pons. Some fibers pass ipsilaterally to the superior olive, while others decussate to the contralateral side. Still other nerve fibers pass, with or without intermediate synapses, upward to the medial geniculate body en route to the auditory cortex in the temporal lobe. Several pathways of decussation exist such that stimuli received in both ears are synchronized at one or more levels. Thus, as the nerve impulses ascend the auditory pathways, there is an increasing interaction and integration of signals between the two ears. Figure 4 depicts the pathways of the descending efferent auditory nerve fibers, which convey inhibitory influences directly to the hair cells.

The human ear can perceive sounds from about 20 Hz to approximately 20000 Hz. Using elaborate microelectrophysiologic techniques, von Bekesy (1960) and others have demonstrated that, in accordance with principles of resonance, different sound frequencies act maximally on specific sites along the basilar membrane, which is narrowest and stiffest at its base and widest and most flexible at its apex. Thus, hair cells located at the basal turn of the cochlea are stimulated maximally by high frequency sounds; those at the apical turn by low frequency sounds; and those in between by sounds in the midfrequency range. However, the overlapping of nerve connections to the hair cells of the organ of Corti permits highly complex response patterns corresponding to subtle changes in tone pattern and intensity.

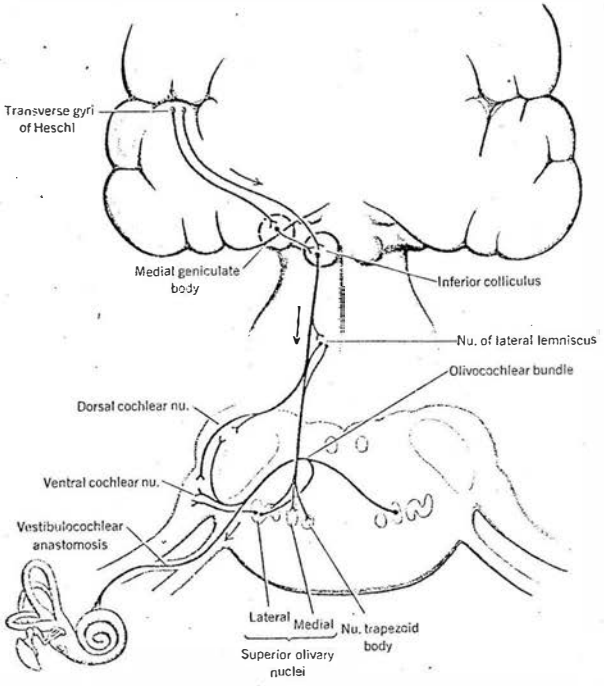
In higher animals hearing provides both sound perception and spacial orientation. While one ear alone permits the reception of sound, the presence of two facilitates the localization of sound and the discrimin a-

FIGURE 3: THE ASCENDING AUDITORY PATHWAYS
THE CROSS SECTION IS THROUGH THE UPPER MEDULLA




Source: Noback and Demarest, 1975

FIGURE 4: THE DESCENDING AUDITORY PATHWAYS




Source: Noback and Demarest, 1975

tion of meaningful signals in a noisy background. In addition, stimulation of the cochlear efferent fibers may reduce the activity of the afferent fibers, thus supressing unwanted neural activity or noise (Noback and Demarest, 1975). Loudness discrimination is possible because sounds of higher intensity cause a greater movement over a wider area of the basilar membrane than do those of low intensity. Thus, as more hair cells are stimulated, more auditory nerve fibers are excited and the frequency of nerve impulses in increased, leading to the sensation of greater loudness. Moreover, some hair cells (inner hair cells) have a greater threshold such that their recruitment may contribute to the sensation of loudness (Davis and Silverman, 1970).

The energetic processes involved in mammalian auditory transduction relate to the sound-evoked peripheral potential, termed the cochlear microphonic (CM). von Bekesy (1960) demonstrated that the energy of the CM greatly exceeds the energy contained in the incoming sound signals, and, in searching for a source of this energy, discovered a positive potential (80-90 mV) in the scala media, termed the endocochlear or endolymphatic potential (EP). Subsequent studies suggest that the stria vascularis (SV) is the main generator of this EP, perhaps through its role in providing the unique ionic composition of endolymph; extremely high $K^+$ concentrations and low $Na^+$ concentrations (Smith et al., 1954; Bosher and Warren, 1968; Johnstone, 1971; Thalman et al., 1980).

Several theories of cochlear transduction hold that biological batteries in the SV and hair cells cause a current to flow across the apical surface of the hair cells (Davis, 1965; Honrubia et al., 1976). The electrical resistance across the surface of the hair cells, when modulated by the sound waves, gives rise to the CM as an electrical

replica of the sound stimulus, but with a much greater energy content. The highly vascularized SV has a very high metabolic rate, and is thought to play an important role in the maintenance of the "ionic profile" of the endolymph. On the other hand, the organ of Corti is, per se, avascular and probably has a relatively low metabolic rate (Thalmann et al., 1980). However the organ of Corti does have a high total energy reserve (sum of high energy phosphate available from preformed ATP and phosphocreatine, and potentially available from the glycolytic breakdown of glucose and glycogen to lactate).

## THE NATURE OF HEARING DISABILITY

Early descriptions of hearing disorders and their treatment are found as early as about 1500 B.C. in the Ebers Papyrus (see Bryan, 1974). From this work it is clear that Egyptian medicine had reached a high degree of specialization, where one priest would specialize in deafness, another in running ears, etc. Remedies listed for "an ear whose hearing is poor" include red ochre (lead) and juice of tamarix (resin from the am tree), which were ground and mixed with fresh balanite (olive) oil and applied to the ear. In ancient Rome and Greece the treatment for running ears included such concoctions as goat's urine mixed with ashes of bat's wing, ant eggs or lizards (Bordley and Brookhouser, 1979). Similarly, those specializing in herbal medicine have long used the earwort (Dysophila auricularis) as a cure for deafness.

Hippocrates observed that discharge from the ears of children was a common occurrence, and believed that the discharge was a brain fluid that drained through the ear. Fifty years later, Aristotle dissected a number of animal ears, recognized the cochlea as part of the ear, and described the pharyngo-tympanic tube. However it was not until the first century A.D. that Celcus, a Roman physician, recognized and described disorders of the ear as entirely independent forms of disease (Lederer, 1960).

Andreas Vesalius (1514-1564), a Renaissance anatomist in Padua, made enormous contributions to medicine as a result of his careful dissections (Vesalius, 1555). His descriptions of the ear and its ossicles initiated the earliest theories of the physiology of hearing. The first publication devoted exclusively to the ear may be Eustacius' work entitled "Epistola de Auditus Organis", in which he described the tube that now

bears his name.

Willis (1621-1675), a British physician, described the seventh and eighth cranial nerves, and theorized that sounds produced vibrations in the tympanic membrane, which were then transferred to the inner ear and to the auditory nerve. Duverney (1683) reported postmortem examinations on children with middle ear infections and found no evidence of concomitant brain infection, thus dispelling the belief held for 20 centuries that discharge from the ear originated in the brain. Eighteenth century medicine saw the development of the tuning fork by Shore in 1711 as well as early attempts at ear surgery. The Italian, Valsalva (1741), divided the ear anatomically into three parts, and introduced the Valsalva maneuver to relieve negative middle ear pressure.

Flourens, a nineteenth century physician in Paris, described the action of the semicircular canals and introduced the idea that the auditory nerve had two branches, one each for hearing and balance (Flourens, 1828). Prosper Meniere, also a Parisian physician, reported case histories of patients with vertigo, nausea, and tinnitus, and described a alterations in their semicircular canals at autopsy (Meniere, 1861). Also in the nineteenth century advances in diagnostic hearing testing were achieved by Weber of Leipsig, Rinne in Gottingen, and Schwabach (Stevenson and Guthrie, 1949). During the present century surgical and medical advances in the treatment of hearing disorders have been the result of aseptic surgery and the use of antibiotics. Surgical advances including effective stapes mobilization, mastoid surgery, removal of eighth nerve tumors, and more recently, electrical cochlear prostheses, have been quite successful in improving hearing function in many individuals.

Along with the advances in treatment of some hearing disorders has come the recognition that deafness has many causes. Deafness may be genetic, of congenital or postnatal onset, or it may be acquired as a result of trauma or environmental effects in the pre-, peri-, or postnatal periods (Brown, 1969; Eagles, 1975; Bess, 1977; Bieber and Nance, 1979). Recognized environmental causes of hearing loss include prenatal rubella infection, meningitis, toxic drugs, viral infections, prematurity, otitis media, erythroblastosis fetalis, and congenital venereal disease (Northern and Downs, 1978). As Jenkins (1891) observed,

> "Speaking popularly, I find that deafness may be caused by some malformation of the tubes, bones, muscles, membranes, or nerves of the ear; it may result from obstruction of the external ear; from thickening, perforation, or inflammation of the membrana tympani;... from an abnormal arrangement of the three thousand minute fibres lining the cochlea, which fibres are the terminations of the acoustic nerves... Of specific causes producing these various irregularities, we find that locality, consanguinity of parents, a strumous and delicate habit of body, accidents, and mental impressions on the part of the mother before the child is born, have all of them an undoubted influence in the propagation of deafness."

Genetic and developmental causes of hearing loss: More than 70 types of inherited hearing loss have been described which differ in their pattern of inheritance, audiologic characteristics, age of onset, clinical course, or associated anomalies (Nance and McConnell, 1973; Nance and Sweeney, 1975; Fraser, 1976; Konigsmark and Gorlin, 1976; Bieber and Nance, 1979). This heterogeneity should not be surprising when one considers the complexity of the hearing organ. The interaction of hundreds of genes must be involved in its normal development, and consequently defects in any one of many genes can give rise to genetically distinct forms of hearing loss which, when viewed superficially, may appear to

be homogeneous. Although many genetic forms of childhood hearing loss are not associated with any additional recognizable phenotypic features (Konigsmark, 1962), associated anomalies allow identification of a substantial proportion of deaf children (Konigsmark and Gorlin, 1976). Because the associated anomalies encompass virtually every organ system and include all three Mendelian modes of inheritance, numerous classification schemes have been used to organize lists of such conditions (see Konigsmark, 1969; 1971; Konigsmark and Gorlin, 1976; Proctor, 1977; Bergstrom, 1980).

Developmental aberrations resulting in external, middle, and/or inner ear malformations and deafness, with or without other abnormalities, have been reported by many authors (Sando and Wood, 1971; Lindsay, 1973; Makishima and Snow, 1975; Jaffe, 1976; Phelps et al., 1977; Melnick and Myrianthopoulos, 1979; Gorlin, 1980; Jahrsdoerfer, 1980; Saito et al., 1981). In man, gross malformations of the inner ear are often classified as belonging to one of four epynomic types. Michel (1864) reported total absence of the membranous labyrinths, otic capsules, eighth cranial nerves, stapes bones, and stapedius muscles in an 11-year-old congenitally deaf boy. The mallei, incudes, tensor tympani muscles, tympanic membranes and external auditory canals were present. This type of malformation is not often reported, and was described in a patient exposed to thalidomide during the first month of gestation (Jorgensen et al., 1964).

The so-called "Mondini-Alexander" defect was first described macroscopically by Mondini in 1791 and later by Alexander in 1904. Typically there is partial atresia of the cochlear modiolus resulting in 1½ coils instead of the normal 2½ to 2 3/4. Great variation in the degree of cochlear dysplasia has been described, with hearing ranging from normal

to profound deafness, depending on the degree of morphological aberration.

Siebenmann and Bing (1907) reported an aplastic membranous labyrinth in a well-developed bony labyrinth from a patient with hearing loss, retinitis pigmentosa, and mental retardation. The stria vascularis, organ of Corti, spiral ganglion cells and their peripheral fibers showed varying degrees of atrophy and degeneration. Scheibe (1892) described temporal bones from a 47-year-old man with well-developed bony labyrinths and abnormal development of the cochlear duct and saccule bilaterally.

Regrettably, clinico-pathological studies have not been performed in sufficient number to allow correlations to be appreciated between the cause of deafness and the concomitant pathophysiologic events or the resulting pathological findings in temporal bones. In this regard, Love stated in 1921 that,"... the thing most wanted from the pathologist at present is a series of postmortem examinations of undoubtedly deaf-born children." Thirty years later Kinney (1950) reported his dismay at the lack of such studies after carefully surveying all of the published volumes of the Cummulated Index Medicus, in which he found 42 articles on the subject of hereditary deafness. Much to his chagrin however, not one of these 42 articles contained a report of a human case in which there was an accurate history and acceptable audiologic studies combined with pathological study of the temporal bone and brain. According to Kinney, "... this is a very shocking condition, and I would urge that effort be put forth to obtain such specimens from cases that might be within our knowledge." Despite the establishment of Temporal Bone Bank programs in the United States, many with federal grant support, there is little evidence that this "shocking" situation has improved substantially. The late Bruce Konigsmark, an eminent neuropathologist, has

unfortunately been one of the very few to make significant contributions to our knowledge of temporal bone histopathology in cases of hereditary deafness (see Konigsmark and Gorlin, 1976).

Hereditary inner ear anomalies, associated with hearing loss, have been described in a number of animal species (Ruben, 1980). Shakleford and Moore (1954) reported deafness in the Hedlund white mink. Although these animals respond to sound for the first few weeks of life, onset of degenerative changes in the organ of Corti, tectorial membrane, and Reissner membrane leads to total deafness. These degenerative changes may be due to a decrease in the vascularity of the stria vascularis, leading to cell death (Sugiura and Hilding, 1970). Ibsen and Risty (1929) reported deafness in the waltzing guinea pig, with autosomal dominant inheritance and lethality in the homozygote. There is evidence that the organ of Corti in these animals develops normally and then degenerates (Ernstson et al., 1969).

Charles Darwin (1892) may have been the first to report deafness in the white cat. The hearing loss, which may affect one or both ears, is associated with pigmentary features including white (or partially white) coat color, and blue eyes or heterochromia irides. Darwin observed that;

> "white cats, if they have blue eyes are almost always deaf... In the present instance the cause probably lies in a slight arrest of development in the nervous system in connection with the sense organs... As however, the colour of the fur is determined long before birth, and as the blueness of the eyes and the whiteness of the fur are obviously connected, we must believe that some primary cause acts at a much earlier period."

As Darwin suggests, the common embryology of the tissues involved is probably responsible for the pleiotropic effects seen in these cats,

as well as in other species with similar phenotypes. Weston (1969) has demonstrated that the neural crest cells migrate and take part in the formation of all of the affected tissues in the "white cat" syndrome. A variety of degenerative changes have been described in the inner ears of these cats, including primary anterograde degeneration in the nerve fibers and acoustic ganglia (Pujol et al., 1977), and there is evidence that at least two different genes can produce the white cat phenotype (Brown and Chung, 1971). Degenerative changes leading to deafness have also been described in the Dalmatian dog (Johnson et al., 1973), with autosomal dominant inheritance and considerable variation in expression. A decrease in vascularity of the stria vascularis leads to eventual cochlea-saccule degeneration.

Inherited deafness in various murine species has been studied since the late 1800s. Yerkes (1907) first summarized data on these "waltzing mice", which were once bred as pets in Japan, but which are said to have originated in China, where references to them reportedly go back to the year 80 B.C. (Deol, 1974). Today, over 50 mutant genes are known to affect the inner ear of the mouse (Deol, 1968; 1980), and they can be classed into two main groups. The first group is characterized by defective morphogenesis of the inner ear, with gross or cytoarchitectural abnormalities appearing at various stages of development. The second group includes those in whom development of the ear proceeds normally until the organ is fully (or nearly fully) developed, with subsequent onset of degeneration of various inner ear structures.

The precise nature of the degenerative types of changes seen in inner ears of deaf individuals is not well understood. Animal studies suggest that retrograde degeneration of the first-order neurons of the

cochlear nerve occurs either when the end organ is destroyed or when the cochlear nerve is cut in the internal acoustic meatus (see Ylikoski et al., 1978). Factors that initiate retrograde degeneration after lesions to the organ of Corti may include direct damage to the cochlear dendrites, collapse of the supporting elements, or loss of the inner hair cells. Ylikoski et al. (1978) studied cochlear nerves from seven profoundly deaf humans with non-congenital, non-genetic etiologies and found a reduction in nerve fiber number, interfibrillar fibrosis, and disorganized material or degenerative changes in the myelin sheaths in three of the individuals. In the remaining four cases no great reduction in the nerve fiber population was noted, and ultrastructurally the nerve fibers appeared unremarkable.

In addition to anatomical approaches to the study of hearing loss, numerous biochemical studies have been performed in an attempt to elucidate the mechanisms responsible for normal and abnormal function of the auditory end organ (see Paparella, 1970; Thalmann et al., 1980). This research suggests that inherited defects in the ability to maintain the normal metabolic composition of the inner ear fluids may explain some types of hearing loss in which the morphology of the middle and inner ear structures is grossly normal. However, a series of as yet undefined developmental defects of the labyrinthine vasculature may be a more likely explanation for hearing loss in persons with malformations of the inner ear structures.

Environmental causes of hearing loss; A host of environmental insults, often unrecognized or unsuspected, can result in partial or total loss of hearing function. Fetal and neonatal sepsis of the inner ear can occur in a variety of ways; extension from the middle ear via the oval window (H. influenza); vascular spread (CMV); retrograde invasion from the CNS via the cochlear aqueduct (aseptic meningitis and labyrinthitis) or from the modiolus (cochlear hemorrhage) (Spector, 1976).

Rubella embryopathy is probably the most common prenatal cause of profound hearing loss, with as many as 10000-20000 children affected by the epidemics of the early and mid 1960s (Karmody, 1968; Gumpel et al., 1971; Stuckless, 1980). Cooper and Krugman (1967) studied data derived from a follow-up of 344 infants born to mothers who reportedly had rubella during pregnancy. Among 271 "abnormal" infants they found congenital heart disease in 142 (52%), hearing loss (confirmed or suspected) in 140 (52%), cataracts or glaucoma in 107 (40%), "moderate to severe" psychomotor retardation in 65 (24%) ("less severe" in 44 (16%)), and neonatal thrombocytopenic purpura in 85 (31%). More recent studies indicate that as many as 73% of those exposed prenatally to rubella have hearing loss (see Vernon, et al., 1980).

There are several reports of a temporal relationship between maternal rubella and specific congenital anomalies in the offspring (Gregg, 1941, 1945; Swan et al., 1943; Cooper and Krugman, 1967). Congenital cataracts and heart disease are more frequently associated with maternal rubella acquired at an early stage of pregnancy, usually less than eight weeks. On the other hand, deafness is often associated with a later period of gestational exposure (Manson et al., 1960; Lundstrom, 1962). However no such temporal relationship was found by Forrest and Menser

(1970) in studies of 41 Australian children 5-19 years of age who were considered to have had congenital rubella. While 31 (76%) of these children had a sensorineural hearing loss, only eight children had the classical rubella triad of eye, ear, and heart anomalies.

Serologic studies of children with congenital hearing loss suggest that the contribution of maternal rubella may be greater than suspected on the basis of clinical studies alone. Ojala et al. (1973) found that one-third of 57 rubella seropositive children (ages six months to five years, with moderate to severe congenital sensorineural hearing loss) did not have a maternal history of rubella exposure during pregnancy. Gumpel et al. (1971) found that 25% of 60 seropositive deaf children had no history of maternal rubella. Thus these probable subclinical cases of congenital rubella may form a considerable proportion of the group which is classified as congenital deafness of unknown etiology.

Peckham et al. (1979) measured rubella antibody titers in 568 children under four years of age who were referred to a hearing center for testing. A total of 83 (24%) of the 349 children with confirmed sensorineural hearing loss were seropositive, while only 19 (9%) of the 219 children in whom sensorineural hearing loss was excluded had rubella antibody ($p < 0.001$). Among the deaf children, only 40% of the seropositive children had a history of maternal rubella illness with rash in pregnancy. Mean birth weights of these seropositive children was significantly lower ($p < 0.05$) than those of the seronegative group. While 83% of the 83 seropositive deaf children reportedly had no relevant medical or family history and no additional defect in addition to the hearing loss, only 31% of the 266 seronegative deaf children had no relevant history nor additional defects. Approximately 13% of the

seropositive children had other defects compatible with the congenital rubella syndrome (congenital heart defects, cataracts, microphthalmia, mental retardation). While 20% of the seronegative children had additional defects, they were of quite a different nature from those among the seropositive group.

Overall, the number of congenital rubella syndrome cases appears to be declining. The National Congenital Rubella Syndrome Registry shows a decrease from 2.7 reported cases per 100000 births in 1969 to 0.6 per 100000 births in 1978. This decrease parallels the rates reported by the Birth Defects Monitoring Program, which shows a 32% decrease in rates of congenital rubella syndrome, from five infants discharged with such a diagnosis per 100000 births in 1970 to 3.4 per 100000 in 1978 (Center for Disease Control, 1980). However, part of the decline in recent years may be due to incomplete reporting, because many cases of congenital rubella syndrome are not even recognized or reported until months or even years after the child's birth.

Prenatal infection by other organisms in the TORCH complex of (Toxoplasma, Other, Rubella, Cytomegalovirus, and Herpes Virus II) can also result in various defects in the central nervous system and hearing organ (Wong and Shah, 1979). Maternal influenza and chickenpox have also been implicated as possible causes of childhood deafness (Keleman and Neame, 1960; Hardy, 1973).

There is ample evidence that ingestion of certain drugs during pregnancy may cause damage to the developing fetal ear (Brown and Feldman, 1978; Marlowe, 1978). Quinine, chloroquine phosphate and streptomycin (especially in the dihydro form) destroy various neural elements of the inner ear (Robertson and Cambon, 1964; Matz and Naunton,

1968), whereas thalidomide is known to cause developmental defects in the osseous structures of the middle and inner ear (Jorgensen et al., 1964). Jones (1973) reported a case of drug-induced ototoxic effects in both a mother and her fetus. The mother had received both kanamycin and ethacrynic acid in the 28th week of her pregnancy for the respective treatment of a Klebsiella infection and renal insufficiency. Within two weeks after the onset of therapy the patient reportedly had a complete loss of hearing. Her child was believed normal at birth but by the third year of life, when speech had not occurred, was found to have a profound hearing loss. This combination of ethacrynic acid and kanamycin seems to act synergistically in both man and other mammals to produce an extreme ototoxic effect (Mathog and Klein, 1969; West et al., 1973).

Several other maternal disorders have been implicated as prenatal causes of hearing loss in children. These include endocrine diseases such as pseudohypoparathyroidism (Hinojosa, 1958) and diabetes mellitus (Jorgensen, 1961).

Premature infants, because of their increasing survival rate, may become an increasingly large group with sporadic deafness. Wright et al. (1972) reported that significant hearing loss was suspected in as many as 2% of surviving premature infants with birth weights less than 1400 gm. Hearing loss in many premature infants (as well as term infants) may result from hemorrhage into the inner ear after intrapartum injury or stress. Damage to the organ of Corti may be due to the anoxic ischemic state produced by the hemorrhage, to infarction secondary to hemorrhage, or as postulated by Keleman (1963), to possible toxic effects of the extravasated blood. Traumatic obstetrical procedures (forceps delivery,

version followed by traction, etc.) may account for the inner ear hemorrhage in many of these cases (Buch, 1966).

Hearing loss can also result from the effects of intrapartum asphyxia and anoxia/hypoxia/ischemia on the cochlear nuclei (Hall, 1964). Many children suffering from such insults may also have associated neurologic damage, including cerebral palsy, mental retardation, optic atrophy, and epilepsy. Elevated blood levels of unconjugated bilirubin, leading to kernicterus, can result in toxic damage to the cochlear nuclei or central neural pathways, leading to deafness (Matkin and Carhart, 1968). Kernicterus has recently become relatively less common due to the advent of prophylactic treatment for blood group incompatibility disorders.

Infections during infancy and childhood probably account for the largest proportion of deafness of postnatal onset in the non-genetic category. Such infections are actually quite common in the United States, as shown in Table 2, which summarizes results from a study of pediatric medical history data from the 1966-70 National Health Survey (Roberts, 1973). Data from this study show that the most frequently reported childhood infectious disease was measles of unspecified type. Among children, the proportion reported to have had measles was 73% in six year olds and increased to more than 90% by ten years of age, with about half of the children reported to have had measles between four and six years of age. Data indicated that 4% had a fever longer than one week. Although no data were available on incidence rates of chickenpox in children, 84% of youths reportedly had chickenpox.

The percentage having mumps increased throughout childhood from 38% in six year olds to over 55% by the age of ten. When it occurred, mumps was most frequently present at five or six years of age, with

Table 2

Percentage of U.S. Children, Aged 6-11 years (1963-65), and Youths, Aged 12-17 Years (1966-70), with History of Selected Illness or Other Medical Condition

| | Child (n=7119) | Youth (n=6768) |
|---|---|---|
| Infective diseases | | |
| Chickenpox | ---- | 84.1 |
| Measles | 85.8 | 92.5 |
| Mumps | 48.8 | 64.6 |
| Scarlet fever | 3.8 | 5.0 |
| Whooping cough | 9.4 | 14.5 |
| Accidents | | |
| Broken bones | 7.8 | 17.3 |
| Knocked unconscious | 3.4 | 8.9 |
| Scars from burns | 4.5 | ---- |
| Other accidents | 4.2 | 12.3 |
| Allergies and related conditions | | |
| Asthma | 5.3 | 6.0 |
| Hay fever | 4.6 | 9.2 |
| Other allergies | 11.4 | 13.6 |
| Kidney conditions | 3.9 | 4.6 |
| Heart conditions | 3.7 | 4.9 |
| Respiratory conditions | | |
| Sore throat | 11.7 | ---- |
| Colds | 21.0 | ---- |
| Coughs | 10.7 | ---- |
| Bronchitis | 15.7 | ---- |
| Chest colds | 6.2 | ---- |
| Pneumonia | ---- | 11.2 |
| Sensory-neurological conditions | | |
| Convulsions or fits | 3.3 | 3.1 |
| Eye trouble | 14.0 | 6.8 |
| Trouble hearing | 4.3 | 3.7 |
| Earaches | 26.8 | 15.1 |
| Running ears | 11.9 | 9.4 |
| Injury to ear | 2.4 | 3.6 |
| Eardrum perforated | 3.0 | 3.0 |
| Other ear operation | 0.7 | 0.9 |
| Other ear trouble | 4.8 | 3.6 |
| Trouble talking | 8.4 | 4.3 |
| Trouble walking | 2.3 | 2.0 |
| Arm or leg limitation | 1.3 | 1.7 |
| Operations | 30.8 | 39.2 |

Adapted from Roberts, 1973; Roberts and Ahuja, 1975a,b; Roberts and Federico, 1976.

two-thirds having onset of illness between four and seven years of age. Approximately 2% of children reportedly had mumps with a fever lasting more than one week. Whooping cough history was present in 9% of children and in 14% of youths. The proportion reported to have had whooping cough rose from 7% in six year olds to 18% by the age of 17 years. A history of scarlet fever was reported in almost 4% of the children, increasing from 3% at the age of six years to 5% at the age of ten years.

The proportion of six year old examinees who had suffered from fractured bones, loss of consciousness, or other accidents (excluding scars from burns) were 5.5%, 2.2%, and 3.3% respectively. Asthma was reported in 4% of six year old children, hay fever in 3.5%, and "other allergies" in 11%. Renal or cardiac conditions were present in six year olds by history in 4% and 3.5% respectively. The frequency of various respiratory conditions in the histories of six year olds ranged from a low of 7% for chest colds to 26% for common colds.

As shown in Table 2, sensorineurological conditions were a fairly common finding in the childhood medical histories. Almost 4% of six year olds reportedly had "some trouble hearing", 28% had a history of one or more earaches, and over 12% had a history of "running ears". Almost 25% of six year olds had had one or more operations, and about 4% were taking medicines regularly. As expected, those children with a history of hearing trouble had significantly poorer hearing in all tested frequencies than those children who had no history of hearing trouble (Roberts and Federico, 1976). Children with a history of ear discharge or earaches showed similar patterns of reduced hearing sensitivity, but the average difference between them and the control group was not statistically significant.

The most common cause of severe hearing loss acquired in the post-natal period appears to be meningitis, either pyogenic or tuberculous, although the incidence of this infection as a cause of hearing loss may be decreasing in affluent societies (Wong and Shah, 1979). From 5 to 35% of survivors of meningitis reportedly suffer from hearing loss (Sell et al., 1972). Nadol (1978) reported a retrospective review of 547 cases of meningitis treated over a 14 year period at the Massachusetts General Hospital. Among the 110 living patients who had bacterial meningitis, 5% of those under 30 months of age and 21% of those over 30 months of age had a sensorineural hearing loss which was bilateral in 77% of the cases. The isolated organism in these cases was Neisseria meningitidis. Hearing loss was found in three of seven persons who had fungal meningitis but was not found in 303 survivors of aseptic or viral meningitis. The latter finding is somewhat surprising in that viral infections (most commonly rubella, measles, mumps, and Herpes zoster) are commonly implicated as causes of hearing impairment. However, as Nadol points out, hearing loss was also absent in several other large studies of aseptic meningitis (Adair et al., 1953; Ritter, 1958; Meyer et al., 1960; Lepow et al., 1962) which included over 2200 cases of viral meningitis. As an explanation of these findings, Nadol suggests that either the incidence of hearing loss in acute viral meningitis is extremely low and thus is not detected even in large surveys, or that viruses do not cause acquired postnatal hearing loss. Another explanation may be that the relationship between viral invasion of the inner ear and hearing loss is more complex, perhaps requiring other factors, such as cellular damage resulting from virus induced delayed hypersensitivity (Hotchkin, 1962).

Measles and mumps reportedly cause hearing loss in children who are not fully immunized. Measles virus can enter the inner ear via the bloodstream or the CNS, or as a complication of purulent otitis media, causing suppurative labyrinthitis and destruction of inner ear struc - tures (Wong and Shah, 1979). Hearing loss after mumps occurs in about 5% of cases (Vuori, 1962) and may be the leading cause of unilateral sensorineural hearing loss in children. Although the hearing loss after mumps may be profound and permanent, Vuori et al. (1962) reviewed reports of less severe loss and at least partial recovery in 50 to 90% of cases. Other viral diseases which have been implicated as causes of deafness include chicken pox, western equine encephalitis, rubella, poliomyelitis, influenza, infectious mononucleosis, viral hepatitis, adenovirus, and the rare childhood case of herpes zoster oticus (Wong and Shah, 1979).

Although recurring episodes of acute otitis media increase the risk of permanent damage to the middle ear, the widespread availability and use of antibiotics should decrease the frequency of hearing loss in uncomplicated cases. Acute otitis media occurs most frequently in the first two years of life and the incidence declines steeply with age. Howie et al. (1975) reported that the initial episode of otitis media occurred in the first year of life in 49% of infants and in the second year of life in only 12%. They reported a 14-21% annual recurrence in children two to seven years old.

Exposure to ototoxic drugs in the postnatal period may also lead to hearing loss, and may be delayed as long as six months after ingestion (Shapiro, 1968). Although deafness is a more frequent complication of dihydrostreptomycin use than with streptomycin, idiosyncratic and famil- ial hypersensitivity to streptomycin has been reported (Prazic et al.,

1964). Neomycin, which shows nephrotoxic as well as ototoxic effects, can lead to profound hearing loss when administered parenterally, intrapleurally, intraperitoneally, orally, by aerosol, and even when used in solution to irrigate wounds (see Wong and Shah, 1979). In a remarkable case report, Banford and Jones (1978) described hearing loss in six infants after their burns were sprayed with a combination of neomycin, bacitracin, polymyxin B and colistin. Neomycin induced hearing loss is usually progressive, first affecting the higher frequencies with ultimate loss of the entire frequency range. Like kanamycin, neomycin penetrates inner-ear fluids slowly and is cleared slowly, leading to severe cochlear damage (destruction of inner and outer hair cells). Other drugs that may lead to hearing loss (which is sometimes reversible) include the aminoglycoside antibiotics, salicylates, and diuretics such as furosemide and ethacrynic acid (Brown and Feldman, 1978).

Numerous animal experiments indicate that ion transport, flow and resorption of endolymph, and activity of certain enzymes ($Na^+K^+$-ATPase, carbonic anhydrase, adenylate cyclase) may play an important role in normal auditory function (Thalmann et al., 1980). The perilymph, in addition to transmitting auditory vibrations, serves as the main medium of metabolic exchange of the organ of Corti. Certain substances such as the aminoglycoside antibiotics, have a tendency to remain in the perilymph for an extended time, long after serum levels have declined. This slow clearance may explain why the organ of Corti is particularly vulnerable to such substances (Stupp et al., 1973). Schacht's work in the guinea pig indicates that the polyphosphoinositides are *in vivo* receptors of aminoglycoside antibiotics, and that neomycin impairs the metabolism of this class of acidic phospholipids in the kidney as well

as the ear, with a parallel decline in the cochlear microphonic (Schacht, 1979). The binding of aminoglycosides to the polyphosphoinosidites displaces $Ca^{++}$ and inhibits turnover of these lipids, which may result in changes in membrane permeability. Disruption of cell membrane structure as a result of such binding may facilitate entry of neomycin into the cell, causing additional toxic effects.

Another major category of ototoxic drugs, the salicylates, have different modes of action, one of which is an uncoupling of oxidative phosphorylation. It has been proposed that the effect on hearing of the salicylates is due to an impaired energy metabolism in the nerve endings at the base of the hair cells, which are extremely rich in mitochondria (Thalmann et al., 1980).

The mechanism of action of the "loop diuretics" (ethacrynic acid, furosemide, bumetamide) appears to be through a depression of the endolymphatic potential (accompanied by edema of the stria vascularis and shrinkage of the intermediate cells). However the precise way in which this occurs is, as yet, unclear (Prazma et al., 1972).

Hearing loss in older children and adults; Numerous factors are known to be responsible for hearing loss in older children and adults. These factors include genetic disorders, trauma, ototoxic drugs, and noise exposure (Meyerhoff and Paparella, 1978; Summerfield, 1978). Several diseases including multiple sclerosis, diabetes, and VIIIth nerve tumors (acoustic neuromas) can also lead to significant hearing impairment in the adult, though estimates of the prevalence of hearing impairment caused by such diseases have not been made (Elliot, 1974).

The cumulative effect of occupational and/or environmental noise exposure is probably one of the more common but least appreciated fac -

tors responsible for hearing loss in older age groups (Henderson et al., 1976). In a fascinating historical vignette, Schuknecht (1979) reported on the probable noise-induced hearing loss in the infamous Siamese twins, Eng and Chang. These conjoined twins were born in Thailand in 1811 and moved to the United States at the age of 18 years. The many surgeons who examined them believed that it would be fatal to attempt to separate the twins. They subsequently married sisters and lived on a farm where they loved to hunt, using shotguns placed on their right shoulders. Sir James Simpson reported in the British Medical Journal that Chang, who was to the left of Eng, had bilateral hearing loss, while Eng had a greater loss in the left ear (Simpson, 1869). Schuknecht proposes that their hearing losses may have been the result of muzzle-blast injury from hunting, and speculates that the explanation for the hearing losses of different magnitudes may be that the hearing in Eng's right ear was less damaged due to the protective effect of head shadow. This theory seems intriguing and plausible, given that Eng and Chang were almost certainly monozygotic twins with identical genetic constitution, and also probably had very similar dietary and environmental exposures.

Although noise induced hearing loss may be the result of direct physical or mechanical damage to the inner ear structures, there has been considerable interest in the question of whether noise-induced hearing loss in mediated biochemically. Direct evidence for a biochemical basis of noise damage comes from several qualitative histochemical studies (Ishii et al., 1969) which demonstrate a reduction and redistribution of glycogen in the outer hair cells following moderate exposure to noise. This finding is of interest in view of the high glycogen levels in the organ of Corti and the finding that the susceptibility to

damage by sound is increased most markedly following application of iodoacetate, an inhibitor of glycolysis (Thalmann et al., 1977).

In addition to environmental causes of hearing loss, a number of genetic forms of hearing loss with onset in adult life have been described (Konigsmark, 1971b; Paparella et al., 1975; Konigsmark and Gorlin, 1976). One of the most common of the adult onset forms of hearing loss is the autosomal dominant disorder, otosclerosis. Affecting primarily the middle ear, otosclerosis typically leads to a conductive hearing loss, with onset typically in the teens and twenties and progression in varying degrees, often leading to stapes ankylosis due to bony overgrowth in the oval window area. Occasionally the pathologic process includes the inner ear as cochleosclerosis, adding a sensorineural component to the hearing loss (Cody and Baker, 1978).

Age related hearing loss of the sensorineural type has in the past been termed presbycusis (Gk. presbys, old, + akousis, hearing). Although undoubtedly an outdated "catch-all" term, it is still widely used to refer to a gradual, symmetrical, and progressive deterioration of hearing sensitivity, usually most marked in the higher frequencies (Gilad and Glorig, 1979). Variation is certainly present among individuals classified in the "presbycusis" group. Schuknecht (1964, 1974) described four histologic types of inner ear pathology in such patients, and there is some evidence suggesting that presbycusis may have a genetic compo - nent. Lowell and Paparella (1977) studied records of 120 clinic patients who had a symmetrical hearing loss with a minimal conductive component and with no history of trauma, ototoxic medication, ear disease, noise exposure, or ear surgery. In 14 of the 99 patients over 65 years of age, a positive family history of hearing loss was reported. However,

the authors did not specify the type or nature of the hearing loss in the other affected family members. As shown in Table 3, the proportion of adults with significant hearing impairment (thresholds greater than 26dB) increases steadily with age and approximates 30% in the 65-74 year age group (see Elliott, 1978). The data from which Table 3 was derived do not discriminate between presbycusis and other forms of adult hearing loss. Nevertheless, because hearing impairment is relatively infrequent below age 55, and because otosclerosis is almost always apparent before age 40, most of the hearing loss in the older age groups would be included in the "presbycusis" category.

Further evidence that genetic factors may be responsible for age-related hearing loss comes from several animal studies. Mikaelian et al. (1974) reported progressive hearing loss with age in the C57BL/6 laboratory mouse. The hearing loss was most pronounced at the high frequencies and was accompanied by degeneration of the organ of Corti, beginning at the basal end and progressing apically. When compared to the CBA/J mouse strain, Henry and Lepkowski (1978) found that the C57BL/6 mice showed progressive decreases with age in the amplitude of the cochlear microphonics and summating potentials in response to a click. Henry and Chole (1980) compared these two different inbred strains of mice (CBA/J and C57BL/6) utilizing volume-conducted auditory-nerve-evoked responses in order to determine electrophysiological "thresholds" from the auditory nerve throughout the lifespan of the mice. The auditory nerve thresholds in response to tone pips from five to 20kHz were similar in young mice of both strains, although the CBA/J mice had somewhat more sensitive responses from 30 to 80 kHz. The auditory anatomy, physiology and behavior did not change significantly with age in the CBA/J mice. In

Table 3

Percentage of U.S. Adults with Hearing Sensitivity Levels of 26 dB or Poorer (Adjusted to ANSI, 1969) by Age Group and Sex

| Age (yrs) | Men | Women |
|---|---|---|
| 18-24 | 1.2 | 0.4 |
| 25-34 | 1.4 | 1.3 |
| 35-44 | 3.7 | 2.2 |
| 45-54 | 4.1 | 4.6 |
| 55-64 | 10.6 | 10.1 |
| 65-74 | 30.5 | 26.2 |
| 75-79 | 48.7 | 47.4 |

From Elliott, 1978.

contrast, the C57BL/6 mice show a relatively rapid decline in hearing with age. At 200 days of age, the C57BL/6 auditory nerve responses are 30dB less sensitive at 5 kHz, and 55dB less sensitive at 30 kHz, than at adolescence. Additional research, utilizing more different inbred strains, with appropriate matings, combined with careful histopathologic study of the inner ear, auditory nerve, and brain, should provide further insight into the relationship between genotype and age-related hearing loss.

## POPULATION BASED STUDIES OF HEARING LOSS

Measurement, prevalence, and demographic considerations; In general, there are two types of hearing loss. Conductive deafness is a result of a block in sound transmission up to and including the stapedo-vestibular joint. Sensorineural deafness can result from a cochlear lesion (sensory) or from a lesion affecting the peripheral pathway or central projection of the VIIIth nerve (neural). In many persons, lesions of both types contribute to the hearing loss. From both the diagnostic and the therapeutic standpoints, it is important to determine whether the patient suffers from conductive and/or sensorineural deafness and to ascertain the degree and pattern of the hearing loss.

The most satisfactory way of measuring the severity of hearing loss is by audiometry. The pure-tone audiometer normally presents the subject with a range of pure tones through headphones at octave intervals between the frequencies of 125 and 8000 cycles per second (Hz). The reference point for normal hearing is represented by the zero decibel (dB) line on the audiogram, as established by the American National Standards Institue (ANSI, 1970). Hearing for an individual at the various frequencies is charted in relation to this zero reference point. Thus, the typical audiogram is constructed such that hearing poorer than normal is charted on a descending scale, and the individual's thresholds are charted in reference to the sound intensity required to elicit a response in a normal hearing individual. Sound may be presented by air or by bone conduction; the relative configurations of air and bone conduction audiograms can aid in the differential diagnosis of a given hearing problem (Davis and Silverman, 1970).

Speech audiometry employs a source of speech which presents a spondee or a phonetically balanced list of words in calibrated volume. The result is recorded on a chart as the percentage of phonetically balanced words heard correctly and repeated for each intensity employed. The intensity at which 50% of the spondee words are heard is called the Speech Reception Threshold (SRT). Because there is an interdependence between the average pure tone hearing deficit in the speech frequency range (500-2000 Hz) and the SRT, one can assume confirmation of the test results when the two thresholds are in close agreement. Another aspect of hearing function is speech discrimination - the clarity with which one hears speech when it is made comfortably loud. When the intensity of sound in phonetically balanced speech lists is increased by 20 dB over the SRT, a person with normal hearing or conductive deafness will score 90% or better (Jerger, 1960). In addition to those tests described above, many additional procedures are available which can in many cases provide information about the nature of the particular hearing disorder in an individual (see Katz, 1978).

Several investigators have published data which support the concept that the degree of hearing loss or even the shape of the audiogram may be genetically determined. Ciocco et al. (1939) compared average differences in auditory acuity between 40 pairs of siblings and between 40 control children (age and sex matched to the younger member of the sibling pair). Their analysis revealed that auditory acuity (pure tone air-conduction thresholds at seven octaves between 128 and 8192 Hz) differed significantly less between siblings than between non-siblings.

Previous studies of hearing in twins include several individual case reports of one or several twin pairs, most of whom were concordant

for deafness or had remarkably similar audiograms (Macfarlan, 1927; Rodin, 1933; Shambaugh and Shambaugh, 1933; Gedda et al., 1953), although Luchsinger and Hanhart (1949) and Post and Hopkins (1956) reported twin pairs in which the twins had dissimilar audiometric patterns. Sank and Kallman (1963) studied 37 twin pairs with early total deafness in at least one member of each twin pair. The clinical concordance rates for early total deafness (prior to audiometric analysis) were 59% for the 17 MZ and 19% for the 20 DZ twin pairs. Audiometric testing demonstrated that in eight of the 23 discordant pairs, the co-twins actually had a considerable hearing loss (at least 30 dB at three or more frequencies in one or both ears). When these eight pairs were reclassified as concordant, the deafness concordance rates for MZ and DZ twin pairs increased to 88% and 35%, respectively. Horiuchi (1976) reported audiometric studies of 25 pairs of twins, one or both of whom exhibited early severe deafness without a known exogenous (acquired) cause. Twin pairs were considered concordant when the "difference of hearing loss between the co-twins" was less than 30 dB. The method of calculating this difference of hearing loss between the co-twins was not stated, but thus defined, the concordance in the 17 MZ pairs was 88% and in the 8 DZ pairs was 50%.

Fisch (1955) examined case records and audiograms of 250 children with "congenital deafness" in a British clinic population. He found a statistically significant, but not absolute association between a history of disease in pregnancy (mainly rubella) and a flat type of audiogram ($p=0.001$), between a history of a pathological condition during the immediate prenatal, natal, or immediate postnatal periods and the sloping types of audiograms ($p=0.001$), and a less significant association between the residual type of audiogram (exaggerated degree of the

sloping type) and hereditary deafness (p=0.01).

Wildervanck (1957) and Fraser (1964) reported that conventional pure tone audiometry cannot identify carriers of genes causing recessive deafness. However Nance (1971b) reported on several kindreds in which carriers of genes causing autosomal or X-linked recessive deafness had minor audiologic abnormalities. Anderson and Wedenberg (1968, 1976) reported that normal-hearing carriers of genes causing recessive deafness could be identified using Bekesy audiometry. They found that 30% of suspected heterozygote carriers had small but distinct "dips" in their Bekesy audiograms. Parving (1978) used Bekesy audiometry to study 27 obligate and potential female carriers of Norrie disease, an X-linked disorder associated with congenital blindness and progressive deafness (Warburg, 1975). Parving found that 42% (3/7) of known carriers and 15% (3/20) of potential carriers showed "dips" in their Bekesy threshold tracings. In Parving's study, the apparent lack of sensitivity of the Bekesy tracings could be due to the limitations of the technique or to variation in the subjects themselves. Because Norrie disease is caused by an X-linked gene, appreciable variation in female phenotypes, due to random X-inactivation (Lyonization), would be expected.

Taylor et al. (1975) studied audiometric data obtained from 86 children attending a school for hearing impaired children. They classified children according to probable etiology of their hearing loss and reported that the 12 children with "dominantly inherited" hearing loss had a flatter mean audiogram with better high frequency hearing than either the "recessive" (N=14) or "unknown" (N=25) groups. Their data did not confirm the report of Fisch (1955) of an association between a "residual" type of audiogram and hereditary deafness. Taylor et al.

observed that there was similarity between the mean audiograms of the "recessive" and "unknown" groups. However, the differences between the means of these two groups and the mean of the "dominant" group (N=22) were not statistically significant. Pure-tone thresholds were considerably greater in the "maternal rubella" group than in the hereditary or unknown groups, although the sample size in the rubella group was very small (N=7). Bekesy audiometry failed to demonstrate a dip, corresponding to those described by Anderson and Wedenberg (1968, 1976), in any of the tested children or parents.

Self-report data on the degree of hearing loss would be of interest and value, if it were correlated reasonably well with actual audiometric measurements. Limited self-report data on persons with impaired hearing have been collected by the U.S. Bureau of the Census during calendar year 1971 for the Health Interview Survey of the National Center for Health Statistics (Gentile, 1975). Interviews were conducted in about 44000 households containing about 134000 persons living at the time of the survey. Table 4 summarizes results of responses to a four-step self-rating of hearing ability in each ear (good, a little trouble hearing, a lot of trouble hearing, deaf). About 48% of those who reported hearing problems reported problems with both ears. Hearing problems in only one ear were reported by about 47%, good hearing in both ears by 2.5%, and no answer in 2% of the total group. Of those with bilateral hearing problems 76% reported "a little trouble hearing", 20% reported "a lot of trouble hearing", and 4% reported that they were "deaf".

The National Center for Health Statistics has also evaluated the validity of the four-step self-rating scale (Schein, et al., 1970). The scale was first administered to adults attending 14 hearing and

Table 4

Number and Percentage of Persons Reported as Having Hearing Problems, by Responses to Self-rating Scale in the United States, 1971

| | Number in thousands | Percent | |
|---|---|---|---|
| Bilateral hearing problems | | | |
| Deaf | 273 | 2.1 | 4.2 |
| A lot of trouble hearing | 1270 | 9.6 | 19.8 |
| A little trouble hearing | 4871 | 36.8 | 75.9 |
| Total | 6414 | 48.5 | 100.0 |
| Trouble with one ear only | 6225 | 47.1 | |
| Both ears "good" | 336 | 2.5 | |
| No answer | 253 | 1.9 | |
| Grand total | 13228 | 100.0 | |

Adapted from Gentile, 1975.

speech clinics across the United States, and their responses were compared to actual audiometric data. The scale was then administered in household interviews of a representative sample of persons living in the Philadelphia Standard Metropolitan Statistical Area. Responses of those in the interview survey who reported some hearing impairment, in addition to those of a subsample of persons who reported no hearing loss, were compared with audiometric test results. As seen in Table 5, data from the clinic sample show that audiometric better-ear-averages (BEAs)* increase as the ratings for the worse ear increase. It is somewhat surprising that the BEAs are not approximately the same for the same better-ear rating. However, there may be a tendency to judge the hearing in one ear in relation to the other ear so that when the hearing in one ear is poor, hearing in the better ear may be somewhat overrated. For the same given rating, those who reported that they presently use a hearing aid have more severe hearing losses than those who have never used an aid. Schein et al. also examined the actual difference in hearing levels between the ears in relation to the respondents' estimates for each ear. As shown in Table 6, there is almost no audiometric difference when the respondents rate each ear the same (1-1, 2-2, 3-3, 4-4). As the ratings for each ear differ increasingly, the corresponding audiometric differences increase as well. Table 7 summarizes the audiometric BEAs associated with each rating, and demonstrates that an increase in pure-tone threshold is associated with an increase in the self-rating of hearing loss. These data on the self-rating of each ear point to

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* Better-ear-average (BEA) refers to the arithmetic average of pure-tone air-conduction thresholds at 500, 1000, and 2000 Hz in the better of the two ears.

Table 5

Mean Better Ear Average in Decibels and Number of Persons, by Self-Rating for Each Ear, According to Hearing Aid Use

| Hearing aid use | Respondents' rating for better/worse ear* | | | | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1/1 | 1/2 | 1/3 | 1/4 | 2/2 | 2/3 | 2/4 | 3/3 | 3/4 | 4/4 | |
| All persons | | | | | | | | | | | |
| Mean better-ear average in dB | 12.6 | 17.7 | 19.4 | 26.2 | 31.5 | 39.1 | 38.9 | 52.4 | 61.2 | 87.2 | |
| Number of persons | 200 | 217 | 194 | 36 | 374 | 274 | 50 | 277 | 73 | 41 | 1736† |
| Never used aid, all ages above 18 | | | | | | | | | | | |
| Mean better ear average in dB | 11.5 | 16.6 | 17.0 | 21.1 | 30.0 | 35.3 | 31.8 | 45.6 | 52.6 | 84.5 | |
| Number of persons | 183 | 200 | 154 | 29 | 320 | 198 | 33 | 130 | 21 | 7 | 1275 |
| Now uses aid, all ages above 18 | | | | | | | | | | | |
| Mean better ear average in dB | --- | 41.2 | 43.1 | 72.0 | 45.5 | 51.9 | 60.5 | 60.9 | 65.5 | 87.1 | |
| Number of persons | --- | 3 | 7 | 4 | 18 | 46 | 8 | 104 | 38 | 27 | 255 |

* Rating Criteria: 1= My hearing is good; 2= I have little trouble hearing; 3= I have a lot of trouble hearing; 4= I am deaf.

† 21 records were excluded because the rating for one or both ears was missing and/or no information was available on hearing aid use.

Adapted from Schein et al., 1970.

Table 6

Mean Differences and Standard Deviations of Hearing Levels[a] by 1740[b] Respondents Rating of Hearing Ability for Each Ear

| Respondents' rating for each ear[c] (right/left) | Number of persons | Mean difference[d] of hearing levels | Standard deviation |
|---|---|---|---|
| 1/1 | 200 | 0.7 | 10.0 |
| 2/2 | 375 | 0.8 | 10.9 |
| 3/3 | 277 | -0.6 | 13.2 |
| 4/4 | 41 | -1.5 | 9.6 |
| 1/2 | 104 | -17.0 | 18.6 |
| 2/1 | 114 | 13.6 | 15.5 |
| 2/3 | 124 | -16.2 | 16.7 |
| 3/2 | 152 | 14.0 | 17.2 |
| 3/4 | 33 | -24.3 | 15.2 |
| 4/3 | 40 | 25.8 | 21.9 |
| 1/3 | 79 | -40.7 | 24.9 |
| 3/1 | 115 | 35.7 | 22.9 |
| 2/4 | 20 | -41.4 | 29.6 |
| 4/2 | 30 | 43.7 | 30.7 |
| 1/4 | 19 | -64.3 | 26.3 |
| 4/1 | 17 | 70.6 | 23.0 |

[a]Arithmetic average of hearing levels (db) at 500, 1000, and 2000 cycles per second.

[b]17 records were excluded because rating for one or both ears was missing.

[c]Rating criteria: 1 = My hearing is good; 2 = I have a little trouble hearing; 3 = I have a lot of trouble hearing; 4 = I am deaf.

[d]Hearing for right ear always substracted from that for leftear; therefore, negative values mean that hearing loss in the right ear is greater and vice versa for positive values.

Schein, et al., 1970.

Table 7

Mean Better-ear Average[a] and Standard Deviations by 1746[b] Respondents' Rating Scales of Each Ear

| Respondents' rating scale | Left ear | | | Right ear | | |
|---|---|---|---|---|---|---|
| | Number of persons | Mean better-ear average (db) | Standard deviation | Number of persons | Mean better-ear average (db) | Standard deviation |
| Hearing is good | 402 | 17.2 | 15.4 | 446 | 17.4 | 13.9 |
| Little trouble hearing | 635 | 35.5 | 16.5 | 663 | 36.0 | 17.5 |
| Lot of trouble hearing | 581 | 55.6 | 18.5 | 523 | 57.1 | 18.6 |
| Deaf | 128 | 89.4 | 16.1 | 113 | 87.6 | 16.4 |
| Total | 1746 | | | 1745 | | |

[a] Arithmetic average of hearing levels (db) at 500, 1000, and 2000 cycles per second.

[b] Excludes 11 left-ear and 12 right-ear ratings that were missing.

Schein, et al., 1970.

the accuracy with which individuals can assess their hearing in response to a simple four-step scale.

In addition to accurate assessment of the extent and type of hearing loss, early identification of hearing loss in considered very important, so that proper use can be made of residual hearing in subsequent training and education (Menegaux et al., 1978). Early screening seems especially important in light of studies showing that dissuasion and inappropriate advice from doctors delayed a diagnosis of hearing loss in 25% of cases (Upfold, 1978). The delay between consultation and diagnosis of hearing loss was an average of six months greater in those children whose parents were dissuaded from or given incorrect advice about seeking additional hearing testing. In a Canadian survey reported by Malkin et al. (1976), family physicians initially rejected the idea of hearing loss in 54% of cases of later confirmed childhood deafness.

Methods and procedures for screening infants for hearing loss have varied greatly and have been the subject of considerable controversy (Jones et al., 1977; Boothman and Orr, 1978; Chevrie-Muller, 1978; Greville and Keith, 1978). Among the stimuli used include clackers, cowbells, gongs, noisemakers, whistles, and crinkled onion-skin paper (Mencher, 1970). Equally controversial has been the question of what constitutes an acceptable response to a given stimulus. Current screening methods generally involve use of a "High-Risk Register", such as the one developed by the Joint Committee on Hearing Screening (see Bergstrom et al., 1971; Northern and Downs, 1978). These "risk registers" usually consist of about five factors, with infants having any one of the five in their history assumed to be at-risk for hearing loss. The five most commonly included factors are; 1. a family history of childhood deafness,

2. maternal rubella or other intrauterine viral infection during pregnancy, 3. hyperbilirubinemia in the neonatal period, 4. maxillofacial anomalies, 5. prematurity. Additional factors used in some screening programs include severe anoxia, acidosis, exposure to ototoxic drugs, and five minute Apgar scores less that five.

More recent newborn hearing screening protocols may include the use of the "Crib-O-Gram" (Simmons and Russ, 1974; Jones and Simmons, 1977), and use of brain-stem evoked response audiometry (Mokotoff et al., 1977; Galambos and Hecox, 1978). The former is a behavioral technique, measuring a neonatal reflex response to a narrow band noise. This measurement is accomplished by automated scoring of activity changes, measured by a motion-sensitive transducer placed beneath the crib mattress, coincident with the test sound. Evoked response audiometry employs computer averaging of brain stem potentials evoked by an acoustic stimulus. In a rather novel approach to neonatal hearing screening, Clements (1979) tested hearing in sleeping babies by observing their response to muted humming noises or "primal sounds", supposedly like those that reach the fetus through the amniotic fluid. She reported a delayed or absent response in 2% of 2000 tested neonates in a metropolitan hospital.

Neonatal hearing screening of large populations (over 10000 infants) using a variety of the above methods has yielded estimates in the range of 0.5 to 1.3 per 1000 for the prevalence of congenital hearing loss. The yield from screening high risk groups (e.g. "graduates" of special care nurseries) is approximately one in 50 (Poland et al., 1980). By one year of age the prevalence of hearing loss is between 1.2 and 1.5 per 1000 children. Based on census projections, which estimate that there will be approximately four million live births in the United

States in the year 1982, we would therefore expect about 4000 infants with severe to profound hearing loss in that one year alone. For this reason, high risk registries have been established at a number of centers throughout the world, in order to screen, by various methods and strategies, infants at risk of having or developing significant hearing loss.

Mahoney and Eichwald (1979) undertook a state-wide high-risk infant hearing screening program in Utah, using a questionnaire designed for maternal response during hospitalization. Those infants judged to be at high risk (by the maternal questionnaire responses) were followed using a second questionnaire and, if deemed necessary, were tested audiologically. Completed questionnaires were received on 52% of 50700 live births from 1/1/76 to 6/30/77, of which 4591 (17%) were categorized as high-risk. Among these high-risk infants, 181 (4%) were determined to actually be at risk after follow-up, and 54 (30%) of the high-risk infants were subsequently found to have hearing loss. Item analysis of the original questionnaires revealed that a positive family history was the most frequent high-risk factor reported by the mothers, with a positive response in 63% of the high-risk forms. Maternal exposure to rubella during pregnancy was the next most frequent positive response. Among the 54 high-risk infants who werelater shown to have a hearing loss, 32 (59%) had reported a close relative with a childhood hearing loss.

The National Center for Health Statistics conducted a household interview survey and obtained self-report data on the ability to hear and to understand speech (Gentile et al., 1967). As shown in Table 8, the estimated prevalence of bilateral hearing loss was 0.6% for those less than 45 years old, 2.9% for individuals between 45 and 64 years old,

Table 8

Prevalence (Percentage) of U.S. Persons with Self-reported Bilateral Hearing Impairment, by Age Group

| Age group (yrs.) | NCHS[a] | NCDP[b] | U.S. census[c] |
|---|---|---|---|
| <6 | - | 0.2 | - |
| ≤14 | - | - | 0.8 |
| 15-24 | - | - | 1.5 |
| ≥25 | - | - | 7.8 |
| 25-44 | - | 1.4 | - |
| <45 | 0.6 | 1.6 | - |
| 45-64 | 2.9 | 4.5 | - |
| ≥65 | 13.2 | 17.4 | - |

[a] National Center for Health Statistics: Gentile, et al., 1967.

[b] National Census of the Deaf Population: Schein and Delk, 1974.

[c] U.S. Bureau of Census: Jackson, 1971.

and 13.2% for persons 65 years of age and older. Using interview respon - ses, the National Census of the Deaf Population 1971 prevalence estimates indicate that bilateral hearing loss in the United States increases with age from 0.2% in children less than six years old to 1.4% in persons 25 to 44 years old (Schein and Delk, 1974). The estimates were 4.5% and 17.4% for those age groups 45-64 years old and over 65 years old, respec - tively. Household interview data collected by the Division of Health Interview Statistics in cooperation with the U.S. Bureau of Census yields prevalence estimates for hearing loss of eight per 1000 in children less than 15 years of age; 15 per 1000 in the 15-24 year old age group; and 78 per 1000 in persons over 25 years of age (Jackson, 1971).

Demographic data on hearing loss in the United States are shown in Tables 9 and 10. These self-report data were collected during an interview survey in 1971 by the National Center for Health Statistics (Gentile, 1975). In children aged three to 14 years there is a slightly higher prevalence of hearing loss in blacks than in whites. The rates are reversed however, in individuals older than 14 years. The prevalence of hearing impairment appears to be lowest in the Northeast (Jackson, 1973).

Data from studies based on actual measurement of hearing sensitivity have demonstrated that pure tone air conduction thresholds increase with age and that the degree of age-dependent hearing loss is greatest at 4000 Hz and least at 500 Hz (Glorig and Roberts, 1965). Males appear to have more hearing loss with increasing age than do females, with the sex difference being greater at 4000 Hz than at 500 Hz. However the higher prevalence of hearing loss in males can, in large part, be account- ed for by the greater incidence of certain diseases (e.g. meningitis)

Table 9

Prevalence (Percentage) of U.S. Persons with Self-reported Bilateral Hearing Impairment by Age Group and by Race

| Age group (yrs.) | Race | |
|---|---|---|
| | White | Black |
| 3-14 | 0.24 | 0.37 |
| 15-44 | 0.30 | 0.23 |
| 45-64 | 1.38 | 0.95 |
| ≥65 | 8.15 | 4.73 |

Adapted from Gentile, 1975.

Table 10

Prevalence (Percentage) of Hearing Impairment by Age Group and by U.S. Region

| Age group | Northeast | North central | South | West |
|---|---|---|---|---|
| All ages | 3.71 | 4.57 | 4.99 | 5.10 |
| <17 | 0.52 | 0.76 | 0.90 | 0.95 |
| 64-74 | 12.39 | 15.41 | 18.95 | 19.37 |

Jackson, 1973.

in males (Vernon, 1968).

As part of the Health Examination Survey of 1966-70, hearing threshold levels were determined among 6768 12-17 year old non-institutionalized youths in the United States (Roberts and Ahuja, 1975). The pure-tone audiometric test results showed that about 1.5% of 12-17 year old youths had a hearing handicap (defined as a mean BEA greater than 26 dB, ANSI-1969). However this does not include youths residing in special schools or in other institutions. The level of hearing sensitivity in youths showed a generally consistent relationship with family income. In families with less than $5000 annual income, youths had higher BEA thresholds (poorer hearing) than youths from families with an annual income exceeding $5000, with large statistically significant mean differences at all octave frequencies. Similar differences, though not statistically significant, were found between youths' hearing levels and educational level of parents.

As part of its 1974 Annual Survey the Office of Demographic Studies (ODS) at Gallaudet College collected data on various demographic and socioeconomic variables on almost 800 families with one or more children enrolled in special educational programs for the hearing impaired (Rawlings and Jensema, 1977). The mean family size (number of children under 18 years of age) was larger (3.2) in those families with hearing impaired children than in families from the general population, which had a mean of 2.09 children. Women with a hearing impaired child also tended to have more total births than did mothers in the general population. Whereas 26% of women in the general population had one child only, only 8% of women with at least one hearing impaired child had only one child. Fathers of hearing impaired children tended to be less well

educated than those in the general population. Approximately 21% of fathers with a hearing impairedchild had an elementary education or less. In the general population only 15% of fathers with school-aged children had less than an eighth grade education. In this study, mothers of hearing impaired children tended to be slightly better educated than females in the general population. Jensema (1975) found that among 1362 students in the Annual Survey population, the distribution of income among parents of hearing impaired students is lower than among the general population of parents in the United States. Students in "higher-income" families also were more likely to have congenital hearing loss, were more likely to be white, to attend pre-school programs, and to use hearing aids. Higher income was also associated with greater academic achievement in the hearing impaired students, as measured by the Stanford Achievement Test Battery.

The largest percentage of students reported to the ODS Annual Survey fall into the more severe hearing loss categories. For those students in whom a better ear average (BEA) could be computed, almost 50% had an hearing loss of 85 dB or greater (Voneiff, 1971). Age data indicate that increasing age is associated with an increase in the proportion of students with a BEA greater that 85 dB. Whereas 19% of students under three years old had a BEA greater than 85 dB, 41% of students aged 14-17 years old had a BEA greater than 85 dB. Data from the ODS Annual Survey indicate that students whose hearing loss is reportedly due to prenatal causes have higher hearing thresholds than students whose hearing loss is supposedly due to postnatal causes.

Only 5% of students in the "prenatal" group had pure-tone thresholds less than 45 dB, compared to 16% in the "postnatal" group; while

42% of the prenatal students had thresholds ≥ 85 dB, compared to 35% of the postnatal group. The prenatal causes with the highest proportion of cases with pure tone thresholds of 85 dB or greater were heredity (49%), trauma to mother during pregnancy (46%), and maternal rubella (41%). Prenatal causes associated with the highest proportion of children whose threshold range was between 45 and 84 dB were prematurity (41%), Rh incompatibility (41%), and "other complications of pregnancy" (38%). Among the postnatal causes of hearing loss, meningitis (50%) had by far the greatest percentage of children with hearing thresholds of 85 dB or more.

Additional handicapping conditions; Since 1968 the Office of Demographic Studies (ODS) at Gallaudet College has conducted an Annual Survey of Hearing Impaired Children and Youth who are enrolled in special educational programs for hearing impaired students in the United States. Among other data, this Annual Survey collects data on the frequency and type of additional handicapping conditions (AHC) in the students. Table 11 shows the distribution of specific reported AHC in 43972 students in the 1972-73 Annual Survey sample (Jensema and Mullins, 1974). Mental retardation, emotional/behavioral problems and visual problems were the three most frequently reported AHCs. One or more "educationally significant" AHC was reported in 29% of the students. Data from the 1970-71 Annual Survey show that 35-45% of children with prenatal, non-genetic causes of deafness had an AHC, compared to only 17% of the students whose deafness was thought to be due to hereditary factors (Gentile and Rambin, 1973). The proportion of students with AHC in the students whose deafness was due to "unknown" causes (18.5%) is close to that in the heredity

Table 11

Educationally Significant Additional Handicapping Conditions in 43,972 Hearing-impaired Students in U.S.

| Additional handicapping condition | Number of persons | Percentage |
|---|---|---|
| Unknown or none | 31226 | 71 |
| Mental retardation | 3361 | 8 |
| Emotional/behavioral disorder | 3438 | 8 |
| Visual problems | 3153 | 7 |
| Brain damage | 1528 | 3 |
| Cerebral palsy | 1290 | 3 |
| Epilepsy | 409 | 1 |
| Heart disorder | 1155 | 3 |
| Orthopedic condition | 773 | 2 |
| Perceptual/motor disorder | 1984 | 4 |
| Other | 1841 | 4 |

ODS Annual Survey, 1972-73: Jensema and Mullins, 1974.

group, suggesting that a substantial underreporting of heredity as a cause may be occurring. The reported causes of hearing loss most frequently associated with AHC were prematurity (45%), trauma during delivery (44%), and Rh incompatibility (44%). Maternal rubella, the most frequently reported cause of hearing loss, is associated with an AHC in 35% of the students in the Annual Survey.

Several studies have been performed on data derived from a nationwide sample of over 40000 students with hearing loss who were classified as either having or not having congenital rubella syndrome (Jensema, 1974; Trybus et al., 1980). Educationally significant AHC were reported in 37% of the 8478 children with congenital rubella syndrome, compared to 25% of 44558 children with deafness attributed to other causes. The prevalence of specific additional handicaps, almost without exception, is greater in children whose deafness is attributed to maternal rubella. The most commonly reported AHC in the rubella group was visual problems followed by emotional/behavioral problems and heart disease. Mental retardation is reported in about 8% of the rubella and non-rubella groups (Trybus et al., 1980). While 85% of children in the rubella group had BEAs greater than 70 dB, only 65% of the children deafened by other causes had BEAs greater than 70 dB. Table 12 presents a list of suspected causes of deafness in children from the Annual Survey, along with commonly reported AHCs. These relationships were noted either because the types of AHC constitute a large proportion for a particular cause of deafness, or because the distribution of AHC associated with a given cause is different from the distribution of types of AHC for all causes.

During the 1972-73 school year the ODS Annual Survey also collected academic achievement test data from a nationwide sample of 6873

Table 12

Suspected Causes of Hearing Loss by Types of Additional Handicapping Conditions in Hearing Impaired Children in U.S.

| Suspected cause of hearing loss | Associated handicapping conditions |
|---|---|
| Prenatal | |
| Maternal rubella | Visual defects, heart disease, emotional or behavioral problems |
| Trauma to mother during pregnancy | Emotional or behavioral problems, mental retardation, cerebral palsy |
| Medication during pregnancy | Emotional/behavioral problems, perceptual/motor disorders, mental retardation |
| Prematurity | Cerebral palsy, emotional/behavioral problems, learning disabilities, mental retardation, perceptual/motor disorders, visual defects |
| Rh incompatibility | Cerebral palsy, perceptual/motor disorders, brain damage |
| Heredity | Emotional/behavioral problems |
| Trauma during delivery | Brain damage, cerebral palsy, emotional/behavioral problems, mental retardation, perceptual/motor disorders |
| Postnatal | |
| Meningitis | Emotional/behavioral disorders, epilepsy, mental retardation, perceptual/motor disorders |
| Mumps | Cleft lip and/or palate, heart disease, learning disabilities, mental retardation, orthopedic problems, visual effects |
| Measles | Emotional/behavioral disorders, learning disabilities, mental retardation, visual defects |
| Otitis media | Brain damage, cleft lip and/or palate, emotional/behavioral disorders, mental retardation, perceptual/motor disorders |
| Fever | Emotional/behavioral disorders, learning disabilities, mental retardation, perceptual/motor disorders |
| Trauma | Brain damage, cerebral palsy, emotional/behavioral disorders, mental retardation, perceptual/motor disorders |

Gentile and Rambin, 1973.

students (Gentile and McCarthy, 1973). Students in whom hearing loss occurred after age three years have higher age-adjusted mean test scores in all academic areas (except mathematics, which is least dependent on language skills), than students in whom the hearing loss was thought to be present at birth of before the age of three years. Those with hearing loss present at birth had higher mean scores than those whose loss was thought to have occurred after birth but before three years of age. When achievement test scores were examined according to reported cause of hearing loss, it was clear that those with reported hereditary hearing loss had greater academic achievement than children with other reported causes, except for mumps and otitis media. However these two exceptions are both conditions that tend to occur at a later age, once the child has already had some language development. The effects of the degree of hearing loss on achievement were also studied by the Annual Survey, and results were similar to those in the literature, which indicate that hearing loss leads to delay in language skill acquisition and is directly related to the degree of hearing loss.

Causes of hearing loss; Population studies of the causes of deafness have resulted in estimates of the proportion of deafness attributed to various causes that vary considerably. Subjects have been ascertained in schools, clinics, and other institutions and tabulations have been based on medical histories from patients, hospital records and from clinical evaluations. Many of the early reports are flawed by the widespread idea that genetic hearing loss must be congenital and that a postnatal onset was necessarily acquired. In addition, an hereditary basis for hearing loss was rarely considered in the absence of a strongly

positive family history. Table 13 summarizes the estimated proportion of genetic deafness in reports on hearing impaired persons in the United States and in several foreign countries.

Best (1943) summarized the presumed causes of deafness in children attending schools for the deaf in 1928. Meningitis and scarlet fever topped the list of presumed causes, accounting for deafness in 15% and 7% of cases, respectively. In 1937 Beasley reported that the deafness in 61% of the children in schools for the deaf was labeled congenital and estimated that in 41% of these congenital cases the deafness was hereditary.

Bordley (1951) studied 485 deaf preschool children and found a positive family history of hearing loss in less than 4%. Bordley and Hardy (1951) also studied 296 children aged six months to 14 years who attended a hospital hearing and speech center in Baltimore. In their analysis of etiologic factors underlying hearing loss, they attributed 14 cases (5%) to genetic factors. Twelve cases (4%) were classified as congenital anatomical maldevelopment (three with congenital atresia of the external auditory canal), and in 104 cases (35%) the cause of hearing loss was undetermined.

Fowler and Basek (1954) studied the medical charts of 270 children under ten years of age who had become deaf before the age of five years. The cases were consecutively drawn from clinic and private files and were selected only when complete data were available. The authors grouped the cases into those whose hearing loss was presumably due to prenatal causes and into those with hearing loss from postnatal causes. They reported that 81 (30%) of the 270 deaf children were deaf due to prenatal causes, and among those 81, ten cases were ascribed to "causes

Table 13

Estimated Proportion of Genetic Deafness in Various Studies

| Reference by 1st author | Location | No. | Reported Genetic cases (%) |
|---|---|---|---|
| Shambaugh, 1930 | USA, schools | 5348 | 26 |
| Yearsley, 1934 | England, clinic | 4314 | 5 |
| Bordley, 1951 | Baltimore, clinic | 296 | 5 |
| Hay, 1953 | New Zealand, clinic | 358 | 5 |
| Fry, 1954 | England, clinic | 800 | 18 |
| Arnvig, 1954 | Denmark, schools | 512 | 29 |
| Fowler, 1954 | N.Y., clinic | 270 | 4 |
| Hopkins, 1954 | Massachusetts, school | 138 | 26 |
| Zonderman, 1959 | Boston, clinic | 328 | 5 |
| Harrison, 1959 | England, clinic | 254 | 9 |
| Livingston, 1961 | England, clinic | 100 | 14 |
| Barton, 1962 | England, school | 270 | 25 |
| Robinson, 1963 | British Columbia,clinic | 200 | 12 |
| Danish, 1963 | Pennsylvania, school | 499 | 51 |
| Sank, 1963 | N.Y. State survey | 688 | 50 |
| Feinmesser, 1963 | Israel, school | 161 | 39 |
| Lumio, 1966 | Finland | 1061 | 52 |
| Maran, 1966 | USA, clinic | 437 | 17 |
| Johnson, 1967 | Massachusetts, school | 118 | 13 |
| Vernon, 1968 | California, school | 1468 | 26 |
| Dar, 1969 | Israel, school | 430 | 49 |
| Ruben, 1971 | N.Y. City, clinic | 348 | 20 |
| Gamstorp, 1971 | Sweden, school | 112 | 31 |
| Brown, 1973 | Massachusetts, school | 1222 | 45-50 |
| Fishman, 1973 | Israel, school | 45 | 73 |
| Fraser, 1975 | G. Britain, South Australia | 3229 | 50 |
| Rose, 1975 | 3 U.S. populations | 20000 | 50-75 |
| Sellars, 1975-78 | S. Africa, schools | 1128 | 10-36 |

during Preconception". Seven of these ten were thought to be hereditary cases, one child reportedly had concomitant retinitis pigmentosa (perhaps a case of Usher syndrome), and two children reportedly suffered from congenital syphilis.

Arnvig (1954) reported an incidence of childhood hearing loss of 0.07% (1/1400) in Denmark. He classified 512 children between seven and 16 years of age who were pupils at state schools for the deaf during the 1952-53 school year. Based on histories obtained from parents and clinical and hospital files he found 29% to have congenital deafness (with 22% due to "sporadic recessive deafness"), 50% to have a variety of non-genetic causes, and the remaining 21% to be deaf from unknown cause. His error in equating congenital with genetic is quite common among earlier studies of this type. Zonderman (1959) reviewed the records of 328 children under ten years old referred to the Massachusetts Eye and Ear Infirmary in an effort to identify the probable etiologic factors. The cause of hearing loss in this group of children was attributed to heredity (5%), acquired prenatal and natal causes (35%), acquired post-natal causes (15%), and cause undetermined in 45% of cases. The low number of "hereditary" cases is no doubt due to the fact that only those with a hearing loss from birth or infancy who had at least one similarly affected sib or at least two successive generations in his direct line of descent with a history of hearing loss from birth or infancy, were included in this group.

Barton et al. (1962) studied medical and family records of 254 8-17 year old children attending schools for the deaf in England, and concluded that hereditary factors accounted for the hearing loss in 64 (25%) of the children. An affected first, second, or third degree

relative was reported in 54 students. Two students were products of first-cousin matings, and eight students had a recognizable genetic syndrome of which hearing loss was a part. A second group of students included 69 children in whom deafness followed an infective illness. The remaining group (121 children) had no history of hearing loss in the family nor a history of preceeding illness. By examining the distribution of birth-weights in the three groups it was evident that low birth weight could be an important factor in the etiology of childhood hearing loss. In the group whose hearing loss was of undetermined causes 21% weighed less than five and one-half pounds at birth, whereas less than 2% of children in the "hereditary" group weighed less than five and one-half pounds at birth. Although difficulties during delivery (forceps, breech presentation, etc.), neonatal jaundice, and anoxia at birth were also more common in the children with deafness of undetermined causes, many of these children were premature and had low birthweight as well. Danish et al. (1963) reviewed medical records of 467 four to 20 year old students enrolled in the Pennsylvania School for the Deaf during the 1960-61 school year. On the basis of the written records and verbal reports from the school headmaster and infirmary nurse, they classified the students as having acquired hearing loss (31%), congenital nonhereditary hearing loss (18%), and congenital hereditary hearing loss (51%). The last category was divided into a probable group of 25% where there was a report of deafness in the family, and a presumptive group of 26%, when there was no mention of deafness in the family.

Johnson (1967) interviewed 109 mothers of 118 deaf children under five years of age in Massachusetts, and a control group of 54 mothers with hearing children. They were questionned by interviewers about

the medical and family histories in an attempt to identify factors which may have been responsible for deafness in the children. Comparison of events in the medical histories revealed certain differences between the deaf and control groups. Events that were more common in the histories of the deaf children included absence of fetal movement in the 3rd or 4th month of pregnancy, maternal thyroid deficiency, breech delivery, body blueness in the neonatal period, maternal rubella in the first trimester of pregnancy, maternal bleeding in pregnancy, birth weight less than four and one-half pounds, and ingestion of mycin drugs during the first neonatal month. Deafness was attributed to maternal illness in the first trimester of pregnancy (rubella-33, influenza-3, chickenpox-1, scarlatina-1) in 38 (32%) cases. Other causes of hearing loss were heredity in 15 (13%), blood group incompatibility in five (4%), meningitis in four, and trauma in one case. The cause of deafness was undetermined in the remaining 55 cases.

Vernon (1968) reported on records of 1468 school-aged children with an average threshold of at least 65 dB in 250-4000 Hz frequency range, who had applied for admission to the California School for the Deaf over a twelve year period (1953-1964). Based on information derived from interview and medical history forms, heredity appeared to play a role in the etiology of the hearing loss in 384 (26%) cases. Other reported causes of deafness were prematurity in 257 (18%), meningitis in 128 (9%), maternal rubella in 139 (9%), Rh incompatibility in 54 (4%), other causes in 142 (10%), and undetermined causes in the remaining 447 (30%) cases.

Table 14 summarizes the reported causes of hearing loss in 43792 students surveyed by the 1972-73 ODS Annual Survey (Jensema and Mullins, 1974). A majority of the students (64%) were thought to be deaf from

Table 14

Reported Causes of Hearing Loss in 43,792 Students in U.S.

| | Number | Percentage |
|---|---|---|
| No known cause | 21301 | 48 |
| At birth | | |
| Maternal rubella | 7718 | 18 |
| Pregnancy complications | 1415 | 3 |
| Prematurity | 2259 | 5 |
| Rh incompatibility | 1369 | 3 |
| Birth trauma | 1001 | 2 |
| Heredity | 3708 | 8 |
| After birth | | |
| Meningitis | 2335 | 5 |
| Mumps | 269 | 1 |
| Measles | 899 | 2 |
| Otitis media | 715 | 2 |
| Trauma | 403 | 1 |
| High fever | 1012 | 2 |
| Infections | 653 | 1 |

ODS annual survey, 1972-73: Jensema and Mullins, 1974.

birth. The hearing loss was reportedly of postnatal onset in 20% of the students. Almost half (48%) of the students had undetermined causes of deafness. The single most frequently reported cause of hearing loss was maternal rubella infection, in 18% of the students. The large number of maternal rubella cases were due mainly to the 1964-65 rubella epidemic. In those two years rubella was reportedly responsible for the hearing loss in 44% and 38% of the students, respectively. Other commonly reported causes of deafness were heredity, prematurity, and meningitis. Although hereditary factors were reported as a cause of hearing loss for only 8% of the students, an additional 12% had one or more hearing impaired relatives. Meningitis was the most frequently reported postnatal cause of hearing loss, followed by measles and high fever.

Sellars et al. (1975) studied 366 Black and Indian children enrolled at a school for the deaf in South Africa. Using family history information and full clinical, otological and audiological examinations they classified the deafness as genetic in 20%, acquired in 36%, and cryptogenic in 44% of the children. Their survey of 499 deaf Black South African children yielded estimates of 10%, 22%, and 68% for genetic, acquired, and unknown causes of deafness, respectively (Sellars et al., 1977). A similar study of 240 deaf White children attending two schools for the deaf in South Africa resulted in estimates that 36% of the children suffered from genetic deafness, 34% from acquired deafness and 30% from undetermined causes. (Sellars et al., 1976). The authors attributed the greater proportion of genetic deafness among white children to the more accurate family histories they were usually able to obtain from that group. Sellars and Beighton (1978) reported results of their study of 223 White children with partial hearing loss in three special

schools in South Africa. Based on the medical and family histories, the hearing loss was inherited in 34%, acquired in 24%, and of undetermined cause in the remaining 42% of cases.

Genetic studies of childhood hearing loss; An awareness of familial predisposition to disease has undoubtedly been present since ancient times, and can be found in the texts of early Greek physicians and philosophers. With regard to hearing loss, it is interesting to note that almost 150 years ago Kramer (1838), in his book on the "Nature and Treatment of Diseases of the Ear", stated that;

> "Many persons are undoubtedly predisposed hereditarily to diseases of the ear. In some families, several, or even all the members suffer from difficulty of hearing in a greater or lesser degree...even deaf-dumbness often occurs several times in one and the same family..."

In the chapter devoted to the subject of deaf-dumbness, Kramer notes that;

> "Most frequently, the parents of deaf dumb children hear perfectly well... in the instances of deaf-dumb children of parents whose hearing is obtuse, it is still quite undecided whether the organic defects of the parents' ears have been transferred to the children."

Kramer also gave a lucid, and perhaps one of the earliest recorded descriptions of X-linked deafness in a family and even proposes a clinical genetic study of the kindred;

> "...A man and his wife,..., both of them healthy, and having no hereditary predisposition to any disease of the ear in their family on either side, have five daughters and six sons; the latter were all born deaf-dumb, whilst the daughters, without exception, hear perfectly well. The mother of these eleven children is not aware of any circumstance that distinguished her pregnancies from each other, though the children are so remarkably differently endowed... Interesting conclusions might probably be derived, had we an opportunity of examining, with the necessary accuracy, the organ of hearing, not only in all the six deaf-dumb children, but also in the girls, who hear perfectly, and of comparing the results with each other."

Other investigators in the mid to late nineteenth century no doubt witnessed the familial recurrence of hearing loss, and several recognized the increased occurrence of consanguinity among parents of deaf individuals (Mygge, 1879; Mygind, 1894). In examining records of 477 deaf-mutes admitted to the Royal Deaf and Dumb Institute in Copenhagen between 1858 and 1877, Mygge reported that almost 7% of the students had parents who were related, compared to less than 4% in the general population in Denmark. Although convinced of a relationship between consanguinity and deafness, the precise connection was not clear to these investigators.

Particular concerns arose over the question of whether the increasing marriage rate among the deaf would lead to an increase in the prevalence of deafness.* Mygind (1892) reported that although deaf-mutes in Denmark frequently intermarry, there was not one deaf offspring among the 183 children produced by 98 marriages with at least one deaf partner. On

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* This increase in marriage rate was, no doubt, due in part to the improvement in the education of the deaf. The first institutions for education of the deaf were founded in France, Germany, and England in the late eighteenth century. Gallaudet founded the first school for the deaf in the United States in 1817. In addition to providing the deaf with an opportunity to learn a trade and thus become independent, education in the residential schools led to increased communication and social contact among the deaf.

the other hand, A.G. Bell (1883)*, in his address to the National Academy of Sciences had argued that;

> "... if the laws of heredity that are known to hold in the case of animals also apply to man, the intermarriage of congenital deaf-mutes through a number of successive generations should result in the formation of a deaf variety of the human race."

Bell's hypothesis was the result of his study of school records of a number of institutions for the Deaf in the United States, including the American Asylum for Deaf-Mutes in Hartford, Connecticut as well as schools in New York, Ohio, Indiana, Illinois, and Texas. His finding of frequent recurrence of unusual surnames led him to the assumption "that in many cases the recurrences indicate blood-relationship among the pupils." Bell also found that almost 30% of 5823 pupils at six institutions had deaf relatives. Comparing the congenitally deaf with the non-congenitally deaf, he found that the percentages of pupils having deaf mute relatives were 55% and 14% respectively. Bell also presented data indicating that a substantial proportion of adult deaf-mutes in the United States were married, and that an increasing proportion of the deaf-mutes who married were choosing deaf partners. Bell tabulated the percentage of deaf children resulting from marriages with at least one deaf partner. His study of the 1877 report of the American Asylum revealed that deafness occurred

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* Alexander Graham Bell was a Scottish teacher of elocution who had come to America to train teachers of the Deaf in the method of "Visible Speech", a system devised by his father, Alexander Melville Bell. A.G. Bell's concern for the Deaf led to his efforts in sound amplification by electrical transmission, resulting in his invention of the telephone.

in 34 of 239 (15%) children with both parents deaf, and in 14 of 57 (25%) children who had only one deaf parent. In the deaf by hearing matings Bell found that deaf-mutes with deaf relatives produced a higher proportion of deaf children than the deaf parents who had no family history of deafness. He stated that;

> "a hereditary tendency towards deafness, as indicated by the possession of deaf relatives, is a most important element in determining the production of deaf offspring. ... it may be a more important element than the mere fact of congenital deafness in one or both of the parents."

Nevertheless, Bell believed that the intermarriage among the deaf was of greatest concern, and that remedial measures should be taken to lessen or check this "tendency to the formation of a deaf variety of the human race in America." Bell proposed that "the most promising method of lessening the evil appears to lie in the adoption of preventive measures", and urged that "the causes that promote intermarriages among the deaf and dumb (segregation of the deaf in residential schools, use of sign language, and employment of deaf teachers) be removed.*

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* Bell was not the first to propose such policy with regard to the deaf. More than 250 years earlier Paulus Zacchias (1584-1659), a Papal physician, offered similar views regarding marriages of the deaf, in his treatise Quaestiones Medico-legales (1621). In translation (see Cranefield and Federn, 1970), Zacchias states that; "The deaf and dumb ought to abstain from marriage not only because they do not understand the end of marriages, but also for the good of the commonwealth, because there is evidence that they beget children like themselves, and it profits the commonwealth that people sound and in every respect perfect are born, not such strikingly impaired ones." What is amazing is that such views

Naturally, Bell's address to the National Academy of Sciences met with a flood of criticism and set off much heated debate (Bell, 1890, 1891; Engelsman, 1890, 1891; Gallaudet, 1890; Gillett, 1890, 1891; Jenkins, 1890; Crouter, 1891; Fay, 1891; Williams, 1891). F.L. Seliney (1888), president of the Empire State Association of Deaf-Mutes at Rome, New York, drew attention to Bell's own data, which showed that deaf children of deaf parents comprised only slightly over one percent of the total enrollment of 17000 pupils admitted to 35 institutions between 1817 and 1883. Among these 215 deaf children, 83 had only one deaf parent, meaning that only 132, or less than one percent, of all deaf pupils were produced as a result of deaf-mutes marrying deaf-mutes. As a result of this and other criticisms of Bell's proposals E.A. Fay, editor of the American Annals of the Deaf, undertook a massive study of the marriages of the deaf in America in order to help resolve the controversy sparked by Bell's address (Fay, 1897, 1898). A survey form or marriage record was distributed to the deaf, their friends and relatives and to

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are still held today, as evidenced by the following passage by Newby (1979); "... there is good reason why deaf children should attend day schools rather than residential ones - the genetic implications of segregating the deaf. Some cases of deafness are due to heredity, and if the social contacts of the deaf are limited to others who are deaf the problem of hereditary deafness will not only be perpetuated, it will increase as the deaf intermarry. Thus, from the geneticists point of view (apparently Newby considers himself a geneticist), it is a mistake for deaf children to attend residential schools. It would be much more sensible from the standpoint of the future of the race if deaf children could be educated in public schools where they would mingle with hearing children both on the school playgrounds and at home." It is indeed

the principals of schools for the deaf in the United States. The questionnaire solicited information on the hearing status of the marriage partners, their parents, sibs and children as well as information on other deaf relatives. Information on causes of deafness, age of onset of hearing loss, and consanguinity was also collected and additional data were retrieved from school records or direct correspondence if deemed necessary.

Fay's data consists of records of 4471 marriages that took place between 1803 and 1894 in which at least one partner was deaf. Aside from 1393 marriages in which information on the offspring was unknown, or which were less than one year duration, 3078 marriages remained for study. Fay's first question dealt with whether marriages of deaf persons were more likely to result in deaf children than were marriages between two hearing individuals. He found that 300 (9.7%) of the 3078 such matings produced deaf children. Although Fay did not collect or have information on the outcomes of hearing by hearing matings, his data

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unsettling that such serious misconceptions are yet held by contemporary university professors and other potentates. Such persons apparently choose to ignore, or are ignorant of the now well-known vast etiologic heterogeneity of human deafness, and of the fact that most genetically deaf persons are, in fact, the offspring of hearing parents. Furthermore, in matings where one partner has dominant deafness, the hearing status of the spouse is irrelevant in terms of the risk of transmitting deafness to the offspring. The author of this dissertation believes that the deaf should be offered competent counseling about their chance of producing deaf offspring, and should be encouraged to exercise their legal rights in freely choosing their mate or marriage partner.

convinced him that " marriages of deaf persons, one or both of the partners being deaf ... are far more liable to result in deaf offspring than ordinary marriages." These 3078 marriages had produced 6782 children, including 8.6% who were reportedly deaf, 75% who were hearing, and 16% whose hearing status was not known. Thus Fay recognized that "marriages of the deaf are far more likely to result in hearing offspring than in deaf offspring."

Fay was also interested in whether deaf by deaf matings were more likely to produce deaf children than were deaf by hearing matings. He found that 12.5% of the deaf by hearing marriages produced deaf offspring, compared with 9.2% of the deaf by deaf marriages; and that 9.8% of children with two deaf parents were deaf, compared to 8.4% of children with only one deaf parent. Thus Fay argued that "in the majority of cases no intensification of the liability to deaf offspring seems to be caused by the union of two deaf persons." Without knowledge of Mendel's (1865) discoveries, but with remarkable insight, Fay explained that;

> "This conclusion is not, as it might appear at first sight, inconsistent with the general law of heredity that the liability to the hereditary transmission of any characteristic existing in the parent is increased by the union of "like with like;" for, when the deafness of the parent reappears in the offspring, the characteristic transmitted is not deafness, as has been generally assumed by writers who have discussed this subject, but it is some anomaly of the auditory organs or of the nervous system, or the tendency to some disease, of which deafness is but the result or the symptom. Inasmuch as these anomalies and diseases resulting in deafness are many and various, it is probable that in most marriages of deaf persons, and even of congenitally deaf persons, the pathological condition that results in deafness is not the same in one partner that it is in the other, and their marriage therefore is not, from a physiological point of view, a union of "like with like." On the other hand, where the pathological condition of the two partners is the same, as it probably is in the majority of consanguineous marriages of deaf persons, there is doubtless an intensification of the liability to deaf offspring;"

Fay also analysed his data by tabulating results of marriages between those who were deaf as a result of congenital versus adventitious causes, of marriages between those with and without deaf relatives, and of consanguineous marriages. He demonstrated that the proportion of marriages producing deaf children was much greater if one or both parents had congenital deafness. Likewise, there was a similar increase in the proportion of deaf children resulting from marriages where one or both parents had deaf relatives. Furthermore, Fay's data revealed that the highest proportion of deaf offspring were produced by marriages between related partners, one or both of whom were deaf. Fourteen of 31 such marriages (45%) produced deaf offspring. Of the 100 children born, 30 (30%) were deaf.

Fay's work was important in demonstrating that many factors, including mating type, cause (onset) of deafness, family history, and consanguinity contributed to the chances that deaf individuals or couples would produce similarly affected children. Moreover, his explanations for his observations point to his astute recognition of the etiologic heterogeneity of deafness. Unfortunately, Fay's insights were not shared by many of the individuals who later reanalysed his data or who studied deafness in other populations.

Schuster (1906) applied methods of correlation analysis, introduced by Francis Galton and Karl Pearson, to Fay's data. He reported that the mean value of the father-child correlation of deafness was 0.54 and for mother-child was 0.535. These values were similar to parent-child values obtained on stature (r=0.506) and eye color (0.495) in man, and to values for coat color in horses (0.522), Bassett hounds (0.524), and in greyhounds (0.507). These results suggested to Schuster that deaf-

ness is inherited to a similar degree as are other phenotypic traits.

Hammerschlag (1910) re-analysed Fay's data with knowledge of Mendel's (1865) experiments on plant hybridization. Having demonstrated by appropriate crosses that the deafness and circular whirling (dancing or waltzing) movements in an inbred strain of mice (the Japanese Tanzmaus) were inherited as Mendelian recessive traits, he examined the Fay data to determine whether human deafness was similarly inherited. He examined the results of 38 matings between individuals he considered to be genetically deaf, having discarded matings in which both partners did not have at least two affected sibs or in which the cause of deafness in either partner was acquired or undetermined. These matings had produced 112 children, 28 (23%) of whom were deaf. Expecting that 100% of the offspring of two deaf parents should be deaf if the trait were recessive, Hammerschlag reasoned that the observed discrepancy was perhaps the result of including some parents who were not genetically deaf. Therefore he removed any matings in which both deaf parents had only deaf sibs and no other deaf relatives. The remaining 24 matings produced 78 children, 27 (37%) of whom were deaf. He then considered only those matings in which both deaf parents had deaf sibs and other deaf relatives. Eight such matings produced 33 children, 15 (45%) of whom were deaf. Hammerschlag concluded that deafness in man, unlike that in the mouse, was not inherited as a recessive trait. He had, of course, mistakenly assumed that all human deafness represented a single genetic disorder, and despite his familiarity with Mendelian laws, seemed to have overlooked the hallmark of recessive inheritance (affected offspring of normal parents). In fact, his criteria for selecting matings for study had, almost assuredly, removed most cases of recessive deafness from his analyses.

Lundborg (1912), like Hammerschlag, reanalysed Fay's data in an attempt to demonstrate that human deafness was inherited as a recessive trait. His approach was to eliminate all families with less than four offspring, in order to have the best chance of finding agreement with Mendel's ratios. After determining the various mating classes possible with a monohybrid hypothesis, and after calculating the expected ratios of normal and deaf offspring of such matings, Lundborg then classified Fay's data in this scheme not by the hearing status of the parents, but according to the hearing status of the offspring of each mating. Thus, it is not at all surprising that this rather senseless analysis demonstrated that the proportions of deaf and hearing offspring in the various mating classes were almost exactly as he had predicted.

In 1920, Lundborg published further analyses of Fay's data, in defense of his theory that human deafness is a recessive condition. He grouped families with four or more children into those with all deaf and those with all hearing progeny. Then he examined Fay's record of the hearing status and onset of deafness of the parents. Lundborg expected the former group to contain only matings between congenitally deaf individuals, and the latter group to contain no marriages in which both partners were deaf from birth. As his theory predicted, all of the parents in the first froup were reported by Fay as being congenitally deaf. However in the second group of 409 matings there were 30 in which both partners were reportedly deaf from birth. His explanation for this discrepancy was that the parents in these 30 matings were not genetically deaf, but were either incorrectly identified as congenitally deaf or had acquired their deafness during fetal life (and thus may have been congenitally but not genetically deaf). Although Lundborg,

like others before him, overlooked the possibility that deafness might be genetically heterogeneous, and therefore did little to clarify our understanding of the genetics of deafness, he did make one very important contribution by recognizing the phenomenon of ascertainment bias (see Crow, 1965). In discussing the expected 25% affected descendants of matings between normal heterozygotes he states;

> "That would no doubt be the case if we were able outwardly to tell heterozygotes from normal homozygotes, but unfortunately we cannot do that... those heterozygotes ... who have only a small number of normal children ... escape our observation. Children of these marriages are not included in a calculation of the percentage of the genotypical deaf-mutes in relation to the healthy individuals and of the phenotypical deaf-mutes. The consequence is that we get more than 25% affected persons when making such comparisons... I discussed this very state of affairs with the well-known statistician Weinberg of Stuttgart, and he worked out a method of calculation ... and indicated a formula ... for the correction of this source of errors ..."

Kratz (1925) and Dahlberg (1931) also reanalysed Fay's data on marriages of the deaf; Kratz offering a two recessive factor hypothesis and Dahlberg a polygenic model of inheritance to explain deafness in man. Like so many others, each failed to consider that deafness may be genetically heterogeneous and thus struggled to find a single mode of inheritance that was consistent with all of the family data (see Rose, 1975). As will be discussed later, it was not until the 1970s that a proper genetic analysis of Fay's valuable data was performed.

Stevenson and Cheeseman (1956) analysed data on childhood deafness in Northern Ireland. Their ascertainment, which they believed was complete, included children who were born deaf and also those who became deaf before six years of age. The latter group was included because the authors felt that parents were more apt to state that adventitious rather than inherited factors were responsible for their

childrens' deafness. Deaf children were ascertained by consulting records provided by welfare and school medical officers, schools and school principals, and physicians in general practice in Northern Ireland. Individual and family histories were obtained on all deaf individuals ascertained and were verified by hospital records, family doctors, or relatives. Stevenson and Cheeseman's objective was to study the genetic aspects of profound congenital deafness. They classified a person as hereditary deaf (HD) if that person was said to be born deaf or was later recognized as deaf when speech did not develop and when no other cause of deafness was known. Excluded from the study were three groups: those whose deafness was acquired after birth (AD); those whose deafness was congenital but not hereditary; and those whose deafness was hereditary but not congenital. A person was classified as acquired deaf (AD) when there was a clear history, which was independently confirmed, that the child heard prior to the illness or accident which supposedly caused the deafness. Also excluded were (two) children whose deafness was attributed to maternal rubella, (two) to Rh incompatibility, (one) to cretinism, (one) to congenital syphilis, and others who had cerebral palsy. Eight families were excluded whose deaf members had early onset (not congenital) perceptive deafness. There were 613 living deaf mutes ascertained, yielding a prevalence estimate of 45 per 100000 individuals in Northern Ireland. Table 15 shows the classification of the data according to parental mating types. The first group included 308 hearing by hearing matings (U x U) and one mating between a hearing person and a person whose deafness was "acquired" (U x AD). The second group included 64 matings between hereditary deaf (HD) persons and either hearing (U) or acquired deaf (AD) spouses (HD x U, AD), and the third

Table 15

Classification of Matings in North Irish Families with One Deaf Member

| Mating type | Number of matings | Consanguinity | Number of matings with ≥ 1 deaf offspring |
|---|---|---|---|
| U x U | 308 | 36 | 308 |
| U x AD | 1 | | 1 |
| HD x U | 12 | 1 | 3 |
| HD x AD | 52 | | 3 |
| HD x HD | 48 | | 11 |

HD = hereditary deaf, AD = acquired deaf, U = hearing.

Adapted from Stevenson and Cheeseman, 1956.

group included 48 matings between persons with hereditary deafness (HD x HD).

Using Haldane's (1932) method Stevenson and Cheeseman calculated the probability of an affected offspring, p, in those matings with at least one deaf offspring. These estimates are shown in Table 16. Their estimate of p in the 36 consanguineous U x U matings was 0.269, in perfect accord with a recessive hypothesis. However they recognized that the low estimate of p in the U x U matings (overall), 0.179, was inconsistent with a single recessive-gene hypothesis and pointed out that there appeared to be an excess of simplex sibships, which could result from inclusion of a number of families whose offspring had congenital, but not hereditary deafness. Considering only the non-consanguineous simplex sibships, Stevenson and Cheeseman found an excess of isolated cases, and estimated that there were approximately 104 sporadic cases among the 424 living persons whose congenital deafness was thought to be hereditary. They believed that this estimate of the proportion of sporadic cases seemed rather high "in view of the few known cases of deafness of intra-uterine origin", pointing out that "in only six instances was exclusion of congenital cases from the data made possible by clinical distinction." They did not revise their estimate of p based on their estimate of the proportion of sporadic cases.

Stevenson and Cheeseman recognized that their estimates of p in the families in which one or both parents was hereditarily deaf were inconsistent with a single recessive gene hypothesis. Of the 32 HD x HD fertile matings, only five produced only deaf offspring. Six matings produced both deaf and hearing offspring and 21 matings resulted in all hearing offspring. The authors considered the possibility that in the latter

Table 16

Segregation Analysis of North Irish Families with One Deaf Member

| Type of mating | Number of matings with >1 deaf offspring | $\hat{p}$ |
|---|---|---|
| Neither parent HD[a] | | |
| All matings | 309 | 0.179 ± 0.012 |
| Consanguineous | 36 | 0.269 ± 0.038 |
| One parent HD[b] | 6 | 0.548 ± 0.119 |
| Both parents HD | 11 | 0.649 ± 0.089 |

HD = hereditary deafness, AD= acquired deafness, U= hearing.

[a]308 U x U; 1 U x AD

[b]3 HD x HD; 3 HD x U

Adapted from Stevenson and Cheeseman, 1956.

21 matings one of the mates was congenitally but not hereditarily deaf. However a history of consanguinity or of affected relatives was present in the families of both spouses in 12 cases and in families of one spouse in five cases. They noted that "In one of the twelve matings there was clinical evidence ... that the partners were homozygous for different genes", (one was "only deaf" and the other had deafness and retinitis pigmentosa). In addition there were six matings which had produced both deaf and hearing offspring. A history of consanguinity or HD relatives provided evidence that both partners were HD in five of these matings. Based on their estimate of p in the U x U matings, Stevenson and Cheeseman rejected a decrease in penetrance as an explanation for their findings. They also dismissed multiple allelism, as it failed to explain how some HD x HD matings produced deaf and hearing offspring.

Among the 45 HD x U or HD X AD matings 39 produced all hearing fertile offspring. However there were six matings that produced both deaf and hearing children. The authors proposed that the non-HD partners in these six matings were heterozygous for the gene causing the deafness in their HD mates. They believed that dominant genes causing deafness "are numerically unimportant", having found only six sibships containing deaf children and having one HD parent. The data from the HD x HD matings, and the increased consanguinity rate led Stevenson and Cheeseman to propose that independent recessive genes were responsible for hereditary deafness in Northern Ireland. Excluding the estimated 109 U x U matings resulting in sporadic deafness, the consanguinity rate was 18% and the first-cousin rate was 9.5%. This observed frequency of first cousin marriages in the U x U matings was much higher than that in the general population of Northern Ireland (0.1-0.4%) (Kilpatrick et al.,

1955), and also exceeded the theoretical frequency of first cousin marriages among heterozygotes producing homozygous deaf offspring. Thus, these results were considered incompatible with a single recessive gene hypothesis. Stevenson and Cheeseman reasoned that with n independent genes of equal frequency, the expected proportion of HD x HD matings that would produce only deaf offspring would be $100n^{-1}$. Therefore, because five of the 32 fertile HD x HD matings produced only deaf offspring, their estimate of the minimum number of independent recessive genes causing deafmutism was six to seven.

Slatis (1958) agreed that much of the hereditary deafness observed by Stevenson and Cheeseman was caused by recessive genes, and that more than one independent recessive gene was needed to explain their data. Nevertheless, he calculated, using Stevenson and Cheeseman's own estimate of six independent recessive genes, that one would expect only 0.6 heterozygotes among the 27 HD x HD matings not producing all deaf offspring, when in fact, six segregating sibships were produced. Slatis reasoned that Stevenson and Cheeseman's data could only be explained by assuming that some cases of deafness were present in persons not homozygous for a recessive gene, and proposed that dominant genes accounted for approximately 15% of the HD cases. Alternatively, Slatis proposed that while some of the deafness was due to homozygosity at certain loci, certain rare non-allelic synergistic recessive genes could result in deafness in persons heterozygous for two or more of them. He favored this hypothesis over the possibility that dominant genes occur, because it could explain the reduced segregation ratio in the U x U matings without relying on sporadic phenocopies.

Chung, Robison, and Morton (1959) reanalysed Stevenson and

Cheeseman's Northern Ireland data and concluded that 68% of the hereditary deafness was due to recessive genes, 22% to dominant genes, 9% was sporadic, and less than 2% was the result of X-linked genes. Chung et al. used a method of segregation analysis based on the method of maximum likelihood (Morton, 1958, 1959) to analyse 288 U x U matings which produced sibships containing at least two persons, one of whom was deaf. These U x U matings were analysed as two separate groups; (1) those multiplex sibships, containing two or more deaf sibs, assumed to be the result of fully penetrant recessive genes with no sporadic cases, and (2) simplex sibships, with only one deaf child and n hearing sibs, in which the deaf child could represent either a chance isolated case or a sporadic case. The maximum likelihood estimate of the segregation ratio, p, in the multiplex sibships was $0.270 \pm 0.026$, in close agreement with a single recessive gene hypothesis. In the total group of U x U matings their estimates of the segregation ratio, p, and of the proportion of sporadic cases, x, were $0.258 \pm 0.024$ and $0.221 \pm 0.041$ respectively. Among the segregating sibships from the HD x U and HD x HD matings the pooled estimate of p was $0.592 \pm 0.083$, which was intermediate between Stevenson and Cheeseman's estimates of p for each group alone. Chung et al. pointed out that these estimates of p in the HD x U or HD x HD matings were inconsistent with the synergistic recessive gene hypothesis proposed by Slatis. The estimates of h, the proportion of affected parents who can only produce hearing children, were $0.830 \pm 0.058$ for the HD x U matings, and $0.583 \pm 0.111$ for the HD x HD matings.

Chung et al. also estimated the mean number of recessive genes causing deafness (detrimental equivalents per gamete) per individual as $0.160 \pm 0.024$, and that as many as 36 independent recessive genes could cause

deafness. However these estimates depend on a number of assumptions about the gene frequencies, inbreeding coefficients, selection, and penetrance that may or may not be valid.

Chung et al. cited the fact that in eight of the U x U pedigrees reported by Stevenson and Cheeseman, 14 of the affected offsprings' uncles and aunts were also deaf, suggesting dominant inheritance with somewhat reduced penetrance. Using their previous estimate of h, and a selection coefficient of 0.68 (estimated from fertility data by Stevenson and Cheeseman), they estimated the proportion of dominant cases of deafness among all HD individuals to be $0.223 \pm 0.029$. The sex distribution of HD cases showed a slight but non-significant excess of males (219:205). They proposed that, even if all the male excess were the result of X-linked genes, the frequency of X-linked cases among all HD cases would still only be 0.012 (1.3%).

In 1946 Hopkins and coworkers reported their studies of extensive pedigree and medical history data collected over a ten year period on present and former students of the Clarke School for the Deaf in Northhampton, Massachusetts. In their attempts to estimate the proportion of sporadic deafness in the simplex sibships, they removed from consideration all sibships in which the deaf child reportedly heard before the onset of any illness which was said to be the cause of the hearing loss. They also removed sibships in which there was reasonable evidence that the hearing loss was an aftermath of meningitis, maternal rubella, or serious mastoid infection. They also removed all cases but those from the hearing by hearing matings. Among the 214 simplex sibships (resulting from hearing by hearing matings) there were 42 in which a remote family history of hearing loss was present. These were considered to be cases of hereditary deafness, as were 78 additional cases in which

the child was thought to be congenitally deaf and in which the parents made no attempt to attribute the deafness to other causes. In the remaining 94 children the hearing loss was not thought to be congenital, but was reported by the parents as being the result of some illness from which the child suffered during early infancy. In their attempt to derive an estimate of the proportion of these 94 children which suffered from inherited rather than environmental hearing loss, Hopkins et al. examined data from those D x D matings which had produced all deaf children. In nine such matings, 12 of the 18 deaf parents were said to have been deaf as a result of infection. The authors interpreted this finding to indicate that because the 18 parents had produced only deaf children, they must therefore all themselves have hereditary deafness. The authors believed that 66%(12/18) of the deaf parents had thus been misclassified as environmentally rather than genetically deaf, and that a similar proportion of the 94 affected children from the H x H matings were likewise misclassified as acquired rather than genetic cases.

Hopkins et al. examined their data from the Clarke School in an attempt to test the hypothesis that the hearing loss in the sibships with congenital nerve deafness represented inheritance of an autosomal recessive trait. Among 272 sibships from H x H matings, there were a total of 1039 children, 345 of whom were deaf. Using the binomial theorem, they calculated the expected number of deaf offspring to be 397, and explained the deviation from the expected value as being due to non-genetic deafness, and variations from single gene inheritance. When they examined 62 sibships in which there was a positive family history of hearing loss, they found a much closer agreement between expected and observed numbers of deaf offspring. These sibships produced

293 children, 88 of whom were deaf (expected = 95.7). When the authors examined the outcomes of 16 consanguineous matings they found almost perfect agreement with their theory. Of 62 children born in these sibships 22 were deaf (expected = 23.52).

Hopkins et al. proposed that at least two types of hereditary nerve deafness were present in the Clarke School population, based on their data from one of the pedigrees. In that kindred (Pedigree 234), two unrelated deaf persons (apparently hereditarily deaf) produced a child who was not congenitally deaf, but "hard of hearing". This hard of hearing child mated with a first cousin (hearing) and produced a deaf child. The authors suggested that the two original unrelated parents were deaf due to different recessive genes (D_ee x ddE_), and that their "hard of hearing" child was a double heterozygote (DdEe), who mated with a hearing carrier first cousin (DdEE or DDEe) producing a deaf child (D_ee or ddE_).

Chung and Brown (1970) updated the Clarke School data by contacting the school's alumni and/or their families by questionnaire, and in some cases by direct examination as well. They defined a person with "hereditary deafness" (HD) as one who became deaf without associated tangible pre- or postnatal factors and had not learned to speak before the time of entering grade school. Other deaf persons were classified as having acquired deafness (AD), and hearing persons as "unaffected" (U). Chung and Brown recognized that the HD cases would represent true hereditary deafness and deafness caused by unrecognized environmental factors. Probands were those who had ever attended the Clarke School. There were 432 U x U matings ascertained through an affected child by multiple selection. The maximum likelihood estimate of $\pi$, the probability of ascertainment, was $0.810 \pm 0.032$. Prior to segregation analysis, the

U x U matings were grouped as consanguineous, having a positive family history (if a parental sib or direct parental ancestor was HD), or as having a negative family history. However from the published data, it is not clear that these three subdivisions were strictly mutually exclusive. Each group was studied, using the maximum likelihood methods of segregation analysis (Morton, 1959), in order to obtain estimates of the segregation frequency, p, and of the proportion of sporadic cases, x, with a fixed value of $\Pi$ = 0.810 from the distribution of simplex sibships. Chung and Brown also estimated the value of p in the multiplex sibships within each group, assuming no sporadic cases (x=0.00). As shown in Table 17, the low $X^2$ values indicate a close fit to the hypothesis that p=0.25, x=0.00 in the consanguineous matings. Chung and Brown logically concluded that deafness in these families was due exclusively to fully penetrant autosomal recessive genes. In the groups of sibships with a negative family history of deafness, the hypothesis that p=0.25, x=0.00 was rejected ($X^2_p$=22.68; $X^2_x$=44.63). The alternate hypothesis, derived from the Northern Ireland data (Chung et al., 1959), that p=0.25;x=0.263 was accepted. The maximum likelihood estimate of x was $0.270 \pm 0.054$. As expected, the hypothesis that deafness in the multiplex sibships was segregating as an autosomal recessive trait (p=0.25) was accepted. In the families with a positive family history of deafness the hypothesis that p=0.25;x=0.27 was not accepted, as it was in the negative family history group. Also rejected was a hypothesis of dominant inheritance (p=0.5;x=0.00). The maximum likelihood estimates of p and x were 0.405 and 0.128 respectively. Chung and Brown reasoned that the deafness in these segregating families may be inherited as dominant traits, with a reduced penetrance (0.405/0.500=0.810). The

Table 17

Segregation Analysis of Unaffected by Unaffected Matings ($\pi$ = 0.810), Clarke School Survey

| Group | Number of informative sibships | $p$ | $x$ | $\chi^2_p$ | $\chi^2_x$ |
|---|---|---|---|---|---|
| Consanguineous | | | | | |
| All matings | 19 | 0.25 | 0.00 | 0.85 | 0.003 |
| Multiplex | 5 | 0.25 | ---- | 0.09 | ---- |
| Negative family history | | | | | |
| All matings | 335 | 0.25 | 0.00 | 22.68 | 44.63 |
| All matings | 335 | 0.25 | 0.263 | 0.26 | 0.02 |
| Multiplex | 55 | 0.25 | ---- | 0.65 | ---- |
| Positive family history | | | | | |
| All matings | 24 | 0.25 | 0.270 | 7.26 | 6.64 |
| All matings | 24 | 0.50 | 0.00 | 8.41 | 31.06 |
| Multiplex | 9 | 0.25 | ---- | 0.04 | ---- |
| Multiplex | 9 | 0.50 | ---- | 3.66 | ---- |

Adapted from Chung and Brown (1970).

authors also suggested that these segregation patterns could be explained by a mixture of dominant and recessive deafness.

Chung and Brown performed segregation analysis on 70 HD x U or HD x AD Clarke School matings under the hypothesis that p=0.50; that no matings would produce only affected offspring, y=0.00; and that the proportion of matings that would produce only hearing offspring, h, would be predicted by the estimates of the proportion of recessive (68%) and sporadic (9%) deafness among the HD cases in the Northern Ireland survey; that is, $h_{exp}$=0.778. Their data indicate that a segregation frequency of 0.5 cannot be excluded, although the maximum likelihood estimate of p was 0.350, consistent with dominant inheritance with a penetrance of 0.70. Chung and Brown also ascertained 87 HD x HD matings by complete selection (at least one parent was a proband in the study). The maximum likelihood estimate of p, h, and y, were 0.688, 0.636, and 0.159 respectively. Chung and Brown used the values of h and y to estimate the number of recessive genes, n, in the Clarke School population. The value of y was taken to represent the frequency of matings of persons whose deafness results from homozygosity at identical loci ($d_id_i$ x $d_id_i$). Similarly, the value of h was assumed to largely represent the matings of persons whose recessive deafness was due to homozygosity at different genetic loci ($d_id_i$ x $d_jd_j$; $i \neq j$). Assuming equal gene frequencies and random mating of HD individuals, h/y=n-1, where n equals the number of of distinct genes producing recessive deafness. Chung and Brown's estimate of the number of distinct recessive genes contributing to deafness in the Clarke School population was n=5 (n-1=0.636/0.159=4.0; $\therefore$ n=5.0).

Sank (1963) mailed questionnaires to the 8200 known deaf residents of New York State over the age of 12 years, in order to collect data on

multiple births among the deaf (discussed previously). In 1958, a second questionnaire, designed to collect family history information, was mailed to the 1700 persons who had responded to the initial questionnaire. Sank's genetic analyses were based on 688 respondents to the second questionnaire. This sample consisted of 92 probands who had deaf relatives in addition to any deaf sibs or offspring, 95 probands who had only deaf sibs, and 501 probands who were the only deaf member of their families. Sank used Haldane's (1932) method to test the hypothesis that the deafness in offspring of hearing by hearing matings was segregating as a recessive trait. Her estimate of p in the 254 sibships, $0.260 \pm 0.017$, is consistent with recessive inheritance, as were her estimates in the 95 multiplex sibships. There were 40 D x D matings that produced both deaf and hearing children. Sank used Finney's (1949) tables, based on the "doubly truncated binomial distribution" to derive an estimate of $0.235 \pm 0.46$ for the value of p in these sibships, suggesting dominant inheritance with reduced penetrance. Using various trial estimates of the frequency of consanguinity and of gene frequency, Sank estimated that between 45 and 6800 independent recessive genes cause deafness.

Furusho (1957) in a study of childhood deafness in Japan, ascertained eight HD x HD matings, all of which produced only deaf offspring. He interpreted this as evidence that hereditary deafness was the result of a single recessive gene. He was, however, ascertaining matings through an affected child, therefore missing deaf by deaf matings which produced all hearing children. In a later study of deafness in Japan, Furusho and Yasuda (1973) used a maximum likelihood scoring technique to perform segregation analysis on hearing by hearing and on deaf by hearing matings. Their results in the former group were consistent with

autosomal recessive inheritance ($\hat{p}$=0.23; $\hat{x}$=0.25), and in the latter group with dominant inheritance and reduced penetrance ($\hat{p}$=0.36; $\hat{x}$=0.09). Using the theory of detrimental equivalents, they estimated that genes at five to six separate loci could cause recessive deafness. The authors also mentioned some of their unpublished findings which supported the idea that recessive deafness could result from more than a single gene. They ascertained 24 D x D matings through a survey of graduates of schools for the deaf and found that the offspring of 23 of these sibships were all hearing. Similarly, Mori (1957) had ascertained 64 fertile HD x HD matings in Japan and found that 52 of these matings produced only hearing children (see Rose, 1975).

Deraemaeker (1960) also proposed that multiple genes were responsible for deafness, based on his studies in a Northern Belgian province. He calculated the expected frequency of an hypothesized single gene for deafmutism based on the frequencies of first cousin matings in the population and among parents of recessive deaf mutes. His estimate was considerably less than the value predicted by the observed frequency of deafmutism, and he proposed that homozygosity at one of several loci could result in a greater frequency of recessive deafness.

Dar and Winter (1969) reported a study of case records of 430 deaf children from 319 families in Northern Israel, and found that 209 (49%) of the children had an affected relative. These "familial cases" included those where the deaf child had a positive family history of deafness in the absence of a known acquired cause. Autosomal recessive inheritance was assumed in cases where there were (1) multiple deaf siblings, or where (2) there was a single deaf child with another deaf relative from a consanguineous mating. Based on the above criteria,

the recessive group included 153 deaf children from 65 sibships, or 73% of all familial cases (36% of the entire deaf population ascertained at the clinic). The 153 deaf children constituted 39% of the total number of sibs. The authors attempted to eliminate bias of ascertainment using the Weinberg simple sib method, which yielded an estimate of the segregation ratio of 34%. Autosomal dominant inheritance was inferred in 48 affected children from 27 sibships. Use of the Weinberg simple sib method, yielded a segregation ratio in these sibships of 29%, indicating reduced penetrance in these families, which constituted 23% of the cases of familial deafness and 11% of the total group of 430 children. Unclassified were eight deaf children born from six deaf by deaf parents.

Taylor et al. (1975) performed segregation analysis on selected sibships ascertained through students attending a special school for hearing impaired children in England. They classified students according to the probable etiology of the hearing loss. Sibships were classified as belonging to the "recessive" group if there were two or more children in the family who had sensorineural hearing loss and whose parents had no hearing loss. In addition, probands placed in the recessive category had no evidence on medical examination or in their history, of prenatal infection by rubella virus or of neonatal jaundice due to rhesus incompatibility. Sibships were classified in the "unknown" group if there was no indication that there were hereditary or environmental factors responsible for their hearing disability. Taylor et al. hypothesized that the group of children of unknown etiology were, in fact, isolated cases of recessively inherited deafness. They combined the sibships from the "recessive" and "unknown" groups

and, using the method of Li and Mantel (1968), computed a segregation ratio of p=0.260 for the 32 sibships. The authors concluded that the results of the segregation analysis, together with their audiological data (discussed previously), supported their hypothesis.

G.R. Fraser studied over 3500 persons with severe bilateral hearing defects in the British Isles and South Australia (Fraser, 1976). His data were gathered over a ten year period (1958-67) in order to estimate the extent to which various etiological entities, both genetic and environmental, contribute to profound childhood deafness. In general, case ascertainment was through large residential schools and welfare organizations, and the data were collected by either questionnaire or individual evaluation. The largest part of his data is from large residential schools with children between four and 15 years old. Fraser attempted to assign a tentative cause of deafness using a combination of family and medical history data and clinical evaluation. He was able to identify a syndromic form of deafness in 11.5% of cases. These included recessive deafness with goiter, with retinitis pigmentosa, with EKG abnormalities; dominant deafness with pigmentary anomalies; as well as several other known syndromes. Based on pedigree information, Fraser classified 19.7% of cases as autosomal dominant, autosomal recessive or X-linked recessive. He assigned a diagnosis of acquired deafness to 33% of the total population, and other complex etiology to about one percent of the cases. Thus, he was able to tentatively classify 65% of the cases as genetic, complex, or acquired using clinical, and family and medical history information. The remaining 1116 cases with undetermined causes of deafness were tentatively assigned to various categories, as shown in Table 18.

Table 18

Ascribed Etiology of Deafness from Unidentified Causes in 1116 Individuals in the British Isles

| Type of deafness | Males | | Females | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| Genetically determined | | | | | | |
| Autosomal recessive | 185 | 31 | 202 | 39 | 387 | 35 |
| Autosomal dominant | 91 | 15 | 82 | 16 | 173 | 15 |
| X-linked recessive | 33 | 6 | 0 | 0 | 33 | 3 |
| Acquired | 285 | 47 | 231 | 44 | 516 | 46 |
| Other | 4 | 1 | 3 | 1 | 7 | 1 |
| Totals | 598 | | 518 | | 1116 | |

Adapted from Fraser, 1976.

Table 19 summarizes Fraser's final "tentative" breakdown of the types of hearing loss in his study population. His estimates attribute the cause of deafness to genetic factors in 49.6%, acquired factors in 49.2%, and complex factors in the remaining 1.1% of cases. In the group with genetically determined deafness about 66% was estimated to be autosomal recessive, 31% autosomal dominant, and 3% X-linked recessive. Fraser performed segregation analysis on selected sibships from his study population, as summarized in Table 20. He calculated the segregation ratios using the methods introduced by Weinberg (1912a, 1912b) and Fisher (1934), which consist of removing the proband and calculating the ratio of the remaining deaf sibs to total sibs, counting each family the number of times it was independently ascertained. As expected, the segregation ratio in sibships in which the proband had a diagnosis of a recessive syndrome was close to the expected 0.25. Fraser proposed that the rather low value of 0.19 in the 36 sibships resulting from consanguineous H x H matings might be the result of factors such as illegitimacy, voluntary birth limitation, misdiagnosis, or mutation.

Fraser also discusses evidence that genetic factors may play a role in susceptibility to acquired hearing loss. He suggests that heterozygotes for mutant alleles causing autosomal recessive deafness may be more susceptible to ototoxic effects of exogenous factors such as rubella infection, streptomycin administration, and meningitis. Several families were ascertained in his survey in which probands with acquired hearing loss had relatives who suffered from profound childhood deafness, and in some cases the deafness in these relatives followed an hereditary pattern.

Table 19

Tentative Balance Sheet of Causes of Deafness in 3229 Subjects in British Isles and South Australia

| Type of deafness | Males | | Females | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| Genetically determined | | | | | | |
| Autosomal recessive syndromes | | | | | | |
| With goiter | 78 | 4.5 | 83 | 5.6 | 161 | 5.0 |
| With retinitis pigmentosa | 20 | 1.1 | 19 | 1.3 | 39 | 1.2 |
| With EKG abnormalities | 7 | 0.4 | 9 | 0.6 | 16 | 0.5 |
| Other | 6 | 0.3 | 4 | 0.3 | 10 | 0.3 |
| Non-syndromic, suggestive family history | 410 | 23.5 | 421 | 28.3 | 831 | 25.7 |
| Total recessive | 521 | 29.8 | 536 | 36.1 | 1056 | 32.7 |
| Autosomal dominant syndromes | | | | | | |
| With pigmentary abnormalities | 73 | 4.2 | 57 | 3.8 | 130 | 4.0 |
| Others | 11 | 0.6 | 5 | 0.3 | 16 | 0.5 |
| Non-syndromic | 178 | 10.2 | 166 | 11.2 | 344 | 10.7 |
| Total dominant | 262 | 15.0 | 228 | 15.3 | 490 | 15.2 |
| X-linked recessive | 55 | 3.2 | 0 | 0 | 55 | 1.7 |
| Malformations of complex etiology | | | | | | |
| Wildervanck syndrome | 2 | 0.1 | 18 | 1.2 | 20 | 0.6 |
| Other | 12 | 0.7 | 5 | 0.3 | 17 | 0.5 |
| Primarily acquired | | | | | | |
| Prenatally (mostly rubella) | 134 | 7.7 | 145 | 9.7 | 279 | 8.6 |
| Perinatally | 225 | 12.9 | 167 | 11.2 | 392 | 12.1 |
| Postnatally | 530 | 30.4 | 389 | 26.1 | 919 | 28.5 |
| Total acquired | 889 | 51.0 | 701 | 47.0 | 1590 | 49.2 |
| Grand total | 1741 | | 1488 | | 3229 | |

Adapted from Fraser, 1976.

Table 20

Segregation Data from Deaf Population in British Isles

| Type of family | Number of sibships | Segregation ratio[a] among sibs (deaf/total) |
|---|---|---|
| Hearing x hearing | | |
| Consanguinity | 36 | 0.19 |
| Positive family history | 55 | 0.22 |
| Syndromic deafness | | |
| Usher | 28 | 0.23 |
| Jervell and Lange-Neilsen | 14 | 0.25 |
| Pendred | 237[b] | 0.22 |
| Deaf x hearing | 42 | 0.28 |
| Deaf x deaf | 38[c] | 0.49 |

[a] Method of Weinberg (1912 a,b), as modified by Fisher (1934)

[b] Number of ascertainments; number of sibships not mentioned.

[c] Segregating sibships only.

Adapted from Fraser, 1976.

Rose (1975) performed segregation analysis on family data from three different deaf populations in the United States, using maximum likelihood methods developed by Morton (1959, 1962). Her analyses allowed estimates of the proportions of sporadic, dominant, and recessive deafness, the penetrance of genes for dominant deafness, and of the number of independent genes causing recessive deafness.

Rose analysed data collected by E.A. Fay (1898), on 4471 marriages of the deaf in America, in two parts: the "proband sibships" (the deaf probands and their sibs), ascertained through an affected by incomplete selection, where $\Pi = 0.455$; and the offspring of the "proband matings", ascertained through the affected parent(s) by complete selection, where $\Pi = 1$. The proband sibship data included 2082 informative non-consanguineous H x H matings. The maximum likelihood estimates of the proportion of sporadic cases, x, was 0.53, with deafness segregating consistently with a recessive hypothesis (p=0.25) in the remaining high-risk sibships. Her results of segregation analysis in the 164 consanguineous H x H sibships are not consistent with the hypothesis that the deafness in these sibships is segregating as an autosomal recessive trait with no sporadic cases (H:p=0.25,x=0.00). The hypothesis that p=0.31 (obtained from analysis of the 92 consanguineous multiplex sibships) and that $x=\hat{x}=0.09$ was accepted ($\chi^2_p=0.62; \chi^2_x=2.10$). However, removal of four matings with only deaf offspring permitted acceptance of the hypothesis that p=0.25, when x was fixed at its maximum likelihood value of 0.096 ($\chi^2_p=3.10$).

In Rose's analysis of the 41 D x H matings, the hypothesis of fully penetrant dominant inheritance of deafness was rejected. The maximum likelihood estimate of the segregation frequency, p, is 0.260,

indicating a penetrance of 0.520 for the genes causing deafness in these sibships. The hypothesis that p=0.260 was also accepted in the 48 D x D matings.

Rose's analysis of 65 D x D proband matings (where both partners were assumed to have recessive deafness) yielded values of 0.045 and 0.764 for the respective proportions of matings that could produce only deaf or hearing offspring. The relationship h/y=n-1 gave an estimate of ten independent recessive genes causing deafness in these families.

Rose also analysed data on 35285 deaf children collected by the Office of Demographic Studies at Gallaudet College as part of its 1969-70 Annual Survey. These family data were those abstracted from admissions records by clerical staff at the 433 collaborating institutions across the United States and reported to the ODS. In this survey, where $\pi$ =0.325, the 11986 H x H matings were divided into those with consanguinity, those with a negative family history of deafness, and those with a positive family history of deafness. Although an hypothesis of recessive inheritance fit the data well for all three groups, the respective proportions of sporadic cases,x, were 0.00, 0.605, and 0.203, indicating that there is a greater proportion of sporadic deafness among those with a negative family history. The D x H matings were divided into a group of 164 with, and a group of 90 without a family history of deafness. The hypothesis of fully penetrant dominant deafness with no sporadic cases (H:p=0.50;x=0.00) was rejected in both subgroups. Maximum likelihood estimates of p were 0.31 and 0.21 for those with and those without a positive family history, consistent with dominant deafness with reduced penetrance (P=p/0.50=0.62;0.42) in these families.

A third population of deaf families was analysed by Rose in her genetic study of profound prelingual deafness. This third group consisted of families that were incompletely ascertained by multiple selection ( $\pi$ =0.128) through deaf probands enrolled at Gallaudet College during the 1973-74 school year. Results of segregation analysis of the 399 H x H matings are consistent with recessive deafness, and yielded estimates of x of 0.162 for those sibships with a positive family history, and 0.370 for those without a family history of deafness. Segregation analysis of the deafness in the ten D x H matings with a positive family history was consistent with dominance and complete penetrance. A penetrance estimate of 0.410 was obtained in the 12 D x H matings with a negative family history.

Table 21 summarizes Rose's estimates of the proportions of sporadic, dominant, and recessive deafness in the three populations. These estimates indicate that over half of the deafness in the probands results from genetic factors, and that recessive deafness accounts for the majority in the genetic category. The higher proportion of genetic deafness in the Gallaudet College population may indicate that genetic deafness is less likely to be associated with additional handicapping conditions that would interfere with academic achievement.

Table 21

Comparison of Deafness Classifications Among Surveys

| Survey | Number of informative matings | Deaf offspring | | | % of genetic deafness | |
|---|---|---|---|---|---|---|
| | | Total | With sporadic deafness (% of total) | With genetic deafness (% of total) | Dominant | Recessive |
| Fay: Proband sibships | 2335 | 3483 | 45.1 | 54.9 | 12.0 | 88.0 |
| National survey | 12665 | 16482 | 49.3 | 50.7 | 14.0 | 85.6 |
| Gallaudet survey | 486 | 749 | 23.8 | 76.2 | 22.2 | 77.8 |

Rose, 1975.

# MATERIALS AND METHODS

## MATERIALS AND METHODS

The study population included all of the students enrolled in September, 1979 at the Frederick campus of the Maryland School for the Deaf (MSD). The parents/guardians of these students were asked to participate in the study by filling out a thirteen page Hearing Loss Questionnaire (Appendix I). Data from the completed questionnaires, along with audiological and family data obtained from school officials, formed the data base for this study.

Audiological data were obtained from school records. Many of the students had been tested several times, while all students had had at least initial admission testing in addition to other tests for hearing aid evaluation. Approximately 80% of the students had been tested by one of two clinical audiologists, and all had been tested by one of three audiologists. Hearing tests were performed using one of two Beltone CR 4000 audiometers, which were electronically calibrated weekly. Data on IQ test scores were also available on some of the students. These IQ data reflected scores on Hiskey-Nebraska and WISC-R tests administered by the MSD school psychologist.

The seven part Hearing Loss Questionnaire was designed to gather medical and family history data on the students (probands) and their families. Part A gathers basic demographic and socioeconomic status (SES) information. Part B gathers information about the family, including data on the hearing status of all close relatives. Data are also requested on any more distant relatives with hearing loss. Part C includes questions about the parents' knowledge of the onset, nature,

and etiology of the proband's hearing problem. In Part D, relevant data on the mother's pregnancy with the proband, including questions on illnesses and drug and medication use are obtained. Part E gathers data about the birth and delivery of the proband. Part F examines the health history of the child, and Part G gathers data on eye disorders and other medical conditions in the proband.

The methodological approach to the questionnaire survey was based on the "Total Design Method" (TDM) described in detail by Dillman (1978). This method attempts to maximize both the quantity and quality of responses by paying strict attention to every detail that could affect response behavior. Dillman's TDM relies on theoretically based views of why persons choose to or not to respond to questionnaires and on evidence that careful attention to pertinent administrative details and questionnaire design is essential to conducting a successful survey. In order to achieve maximum accuracy and reliability of responses, the questionnaire was carefully designed to avoid ambiguity and confusion. For the most part, questions are of the YES, NO, DON'T KNOW format, and where quantitative data are sought, questions are constructed to collect raw rather than categorical data. Comments and criticism were solicited from over 20 professionals who either worked with the deaf or who were familiar with questionnaire design. The comments were used to modify, delete or restructure some items contained in the questionnaire. In addition, the entire questionnaire was pretested on a sample of 30 adult women who had one or more children at least four years of age. Questions that were confusing or that led to unreliable or invalid responses were appropriately modified and retested. The questionnaire was then professionally typeset and printed on high quality ecru paper.

As part of the TDM, one or more items preceeded, accompanied, and followed the mailing of the Hearing Loss Questionnaire (see Appendix II). Ten days prior to the mailing of the questionnaire, a letter explaining the nature and purpose of the study was mailed to all parents/guardians by the superintendent of MSD. The parents were also informed of the study by an announcement in the school newsletter, SIGNPOST, about one month prior to the mailing of the questionnaires. Questionnaires were mailed to the parents over the course of a three day period. In addition to a copy of the questionnaire, the parents/guardians received a cover letter describing the study and asking for their participation, a Research Consent Statement, and a stamped manila envelope for their return of the completed form. Three weeks after the questionnaires were mailed, reminder postcards were sent to all parents whose completed questionnaires had not yet been received. Reminder letters were sent at six and ten weeks, and reminder notes were also published in two issues of the SIGNPOST. Families with published telephone numbers were called once as a final reminder. These procedures resulted in the receipt of completed questionnaires containing information on 228 sibships which included 243 probands (130 males, 113 females) and their family members. Family history, audiological, and IQ test score data were also available on the non-respondent group (106 families with 112 probands) and on the preschool and new student group (78 families with 79 probands).

Families were assigned sequential family numbers as their completed questionnaires were received. The data were then coded and keypunched. Keypunched data were verified by hand and through use of programs designed to identify coding errors. The verified and corrected data were then stored on disc as a sequential data file prior to analysis on an IBM 370/158 computer.

All data other than names were coded as numeric values in order to facilitate statistical analysis. Each of the 197 variables was coded using a general coding format procedure. For example,

blank = No answer
0 = No
1 = Yes
2-8 = Other responses
9 = Don't know

Most variables required a one or two column coding width. When coding multiple choice or short answer type questions, responses were assigned distinct numeric values. The coded data in the sequential disc file were used to create a data set for analysis using the Statistical Analysis System (SAS). SAS refers to a packaged computer system designed to allow a variety of statistical and computational operations to be performed on data stored in a SAS data set. (SAS Institute, 1979). Creation of a SAS data set involves use of input statements which assign appropriate SAS variable names to individual data items. The SAS data set was also stored on a disc file and backed up on magnetic tape. The SAS procedures (PROCs) used in the data analysis included ANOVA, CHART, CORR, DUNCAN, FREQ, GLM, MEANS, NPAR1WAY, PLOT, PRINT, SORT, SUMMARY, TTEST, and UNIVARIATE. These SAS procedures allowed a thorough investigation of the variation in the sample and a tabulation of reference data on the probands.

In addition to the above mentioned analyses, various genetic hypotheses were tested on the family history data, using two methods of optimization. In the Hearing by Hearing (H x H) and Deaf by Hearing (D x H)

matings, segregation analysis was performed using a version of N.E. Morton's computer program, SEGRAN (Morton, 1959; 1962; 1969). SEGRAN permits comparison of the frequency of deaf and hearing offspring of parents belonging to a given mating type and generates maximum likelihood estimates of the segregation frequency, p, and of the proportion of sporadic cases, x, in the population. In the Deaf by Deaf (D x D) matings, hypotheses were tested concerning the values of p, and of the proportion of such matings which could produce only affected offspring, y, using the Nelder-Mead simplex direct search method (Nelder and Mead, 1965; Walsh, 1975). Tested hypotheses and the specific equations used are discussed in the Results section.

# RESULTS

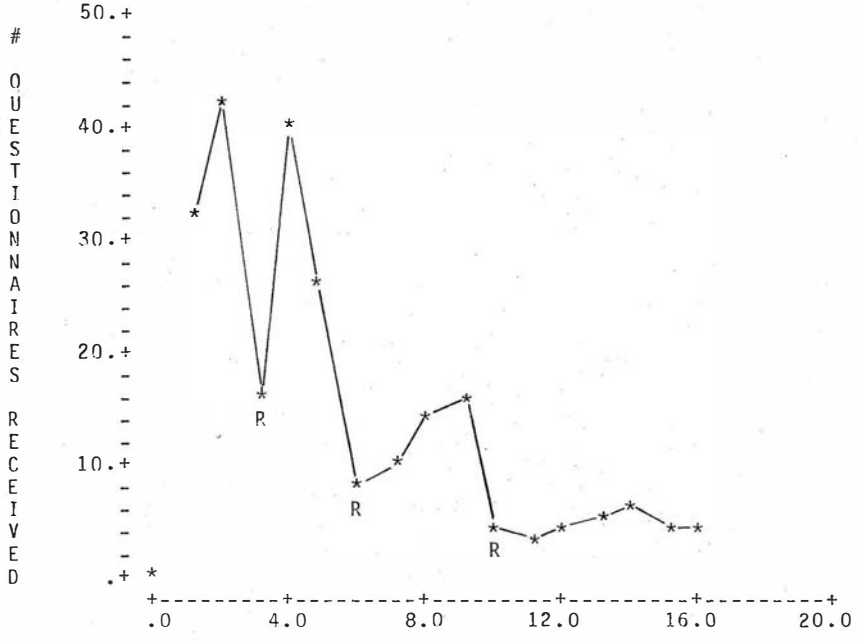
# RESULTS

Completed Hearing Loss Questionnaires were received over the course of 16 weeks. As shown in Figure 5, the use of reminder cards and letters seemed to effect spurts in the response rate shortly after they were mailed. Questionnaires were completed by the probands' parents in 92% of the cases (mother in 78%), guardian in 5%, and other relatives in the remaining 3% of the respondents. The average time needed to complete the Hearing Loss Questionnaire was 1.6 hours, with 78 % spending between one and two hours, and 6 % needing more than two hours. Of the forms received, 24 were considered of limited or marginal use due to incomplete or unclear responses. These respondents were contacted by telephone to clarify incomplete or incoherent responses. In eight cases there was little information on the family history due to early adoption or foster care placement of the proband. Other family situations (divorce, separation) contributed to poor family history data in ten cases and in six cases the family history section was left blank because the respondents thought the probands hearing disorder was environmental and "didn't think the family history information would be of value". In all but ten cases, parental mating types and other family history information were obtained either by telephone conversations with the respondents themselves or from school records. When school information on mating types of the parents were compared with questionnaire responses, discrepancies were evident in three families. School records were in error in two cases (where parents were not married and data on father was not complete), and in one case foster parents filled out the questionnaire as if they

FIGURE 5

SCHEDULE OF COMPLETED QUESTIONNAIRE RECEIPT

MARYLAND SCHOOL FOR THE DEAF SURVEY




R = REMINDER LETTER SENT.

were the parents, rather than including data on the biological parents. Responses to questions concerning the mothers' pregnancy history or the probands' childhood medical histories were limited or incomplete in 28 cases. Most of these questionnaires (23/28) were completed by someone other than the probands' mothers, and in the remaining five cases, the mothers reported that they could not remember details of their pregnancy with the proband or of the probands' medical histories. Pregnancy history data on eight of the former group were obtained directly from the mother or from school admission records.

Summary data on SES variables (parent/guardian education, occupation, family income) are shown in Tables 22-27, which compare the MSD families with families in the State of Maryland, and in the United States. As shown in Table 22, the MSD families are underrepresented in the white collar category. In terms of total family income, Table 23 shows that fewer of the MSD families fall into the highest income classes. About 34% of mothers of MSD children had not completed a high school education, which is virtually identical to the figures for the State of Maryland (Table 24). However, 97% of the former group had at least finished grade eight, compared with less than 90% of mothers in Maryland families. Data in Tables 25 and 26 show that although fewer MSD families with a deaf parent are classified as having white collar main wage earners, the total annual family income exceeds $20000 in 62.5% of families with both deaf parents, and in 37.5% of families with one deaf parent, compared to 32.5% of MSD families with both hearing parents. Table 27 shows that 44% of MSD mothers from D x D matings had attended college, compared to 29% of mothers from H x H matings.

Table 22

Occupational Status of Main Wage Earner

| Occupational status[a] | U.S.[b] (n=42,871,000) | Maryland[c] (n=833,000) | MSD (n=228) |
|---|---|---|---|
| | Percent | | |
| White-collar workers | | | |
| Professional technical | 16.51 | --- | 9.79 |
| Managerial, official, non-farm proprietors | 16.06 | --- | 14.89 |
| Clerkical, sales, kindred workers | 4.34 | --- | 9.36 |
| Total | 46.97 | 54.8 | 34.04 |
| Blue-collar workers | | | |
| Craftsmen, foremen, skilled workers | 20.60 | --- | 21.28 |
| Operatives, skilled workers | 16.67 | --- | 13.19 |
| Laborers, except farm and mine | 4.34 | --- | 9.36 |
| Total | 41.61 | 35.81 | 43.83 |
| Service workers | | | |
| Service workers, farmowners, tenants, managers | 10.52 | 8.05 | 17.87 |
| Farm workers | | | |
| Farm laborers, foremen | 0.87 | 1.32 | 4.26 |
| Grand total | 100.00 | 100.00 | 100.00 |

[a] Green, 1970.

[b] U.S. Bureau of Census, 1980.

[c] U.S. Bureau of Census, 1978.

Table 23

Distribution of Total Family Income

| Income last year (thousands) | Percentage | | |
|---|---|---|---|
| | U.S.A.[a] N=82,389,000 | Maryland[b] N=1,066,000 | MSD N=220 |
| <$5 | 8.3 | 7.2 | 10.1 |
| $5-10 | 15.8 | 15.3 | 15.9 |
| $10-15 | 16.6 | 18.1 | 19.4 |
| $15-20 | 16.9 | 18.5 | 19.8 |
| $20-30 | 19.5 | 19.6 | 22.0 |
| $30-50 | 19.3 | 18.6 | 11.5 |
| >$50 | 3.6 | 2.7 | 1.3 |
| Total | 100.0 | 100.0 | 100.0 |

[a] U.S. Bureau of the Census, 1980.

[b] U.S. Bureau of the Census, 1978.

Table 24

Mothers' Education

| Highest grade completed | Percent | | |
|---|---|---|---|
| | U.S.[a] (n=23,999,000) | Maryland[b] (n=1,182,000) | MSD (n=228) |
| <8 | 3.01 | 10.15 | 2.95 |
| 8 | 2.96 | 7.02 | 5.06 |
| 9-11 | 11.75 | 16.41 | 25.74 |
| 12 | 48.32 | 36.72 | 36.29 |
| 1-3 years college | 17.32 | 13.96 | 17.30 |
| ≥ 4 years college | 16.64 | 15.74 | 12.66 |
| Total | 100.00 | 100.00 | 100.00 |

[a] U.S. Bureau of Census, 1980.

[b] U.S. Bureau of Census, 1978.

Table 25

Occupational Status of Main Wage-earner in Families of Students at Maryland School for the Deaf, Classified According to Parental Mating Type

| Occupational status[a] | Parental mating type | | | | | |
|---|---|---|---|---|---|---|
| | D x D | | D x H | | H x H | |
| | No. | % | No. | % | No. | % |
| White-collar workers | | | | | | |
| Professional, technical | 4 | 25.0 | 0 | --- | 5 | 2.46 |
| Managerial, officials, non-farm, proprietors | 1 | 6.25 | 2 | 25.00 | 32 | 15.76 |
| Clerical, sales, kindred workers | 1 | 6.25 | 0 | --- | 20 | 9.85 |
| Total | 6 | 37.50 | 2 | 25.00 | 57 | 57.30 |
| Blue-collar workers | | | | | | |
| Craftsmen, foremen, skilled workers | 7 | 43.75 | 3 | 37.50 | 37 | 18.23 |
| Operatives, skilled workers | 0 | --- | 1 | 12.50 | 29 | 14.29 |
| Laborers, except farm and mine | 1 | 6.25 | 0 | --- | 40 | 19.70 |
| Total | 8 | 50.00 | 4 | 50.00 | 106 | 52.22 |
| Service workers | | | | | | |
| Service workers, farmowners, tenants, managers | 1 | 6.25 | 2 | 25.0 | 18 | 8.87 |
| Farm workers | | | | | | |
| Farm laborers, foremen | 1 | 6.25 | 0 | --- | 9 | 4.43 |
| Grand total | 16 | | 8 | | 203 | |

[a] Green, 1970.

Table 26

Distribution of Total Family Income Among Students at Maryland School for the Deaf Classified by Parental Mating Type

| $ income last year (thousands) | Parental mating type | | | | | |
|---|---|---|---|---|---|---|
| | D x D | | D x H | | H x H | |
| | No. | % | No. | % | No. | % |
| <$5 | 2 | 12.5 | 1 | 12.5 | 19 | 9.8 |
| $5-10 | 2 | 12.5 | 2 | 25.0 | 31 | 16.0 |
| $10-15 | 1 | 6.25 | 0 | --- | 41 | 21.1 |
| $15-20 | 1 | 6.25 | 2 | 25.0 | 40 | 20.7 |
| $20-30 | 9 | 56.25 | 3 | 37.5 | 36 | 18.6 |
| $30-50 | 1 | 6.25 | 0 | --- | 24 | 12.4 |
| >$50 | 0 | ---- | 0 | --- | 3 | 1.5 |
| Total | 16 | | 8 | | 194 | |

Table 27

Educational Background of Mothers of Students at Maryland School for the Deaf, Classified by Parental Mating Type

| Highest grade completed | Parental mating type | | | | | |
|---|---|---|---|---|---|---|
| | D x D | | D x H | | H x H | |
| | No. | % | No. | % | No. | % |
| <8 | 1 | 6.25 | 2 | 25.0 | 4 | 1.95 |
| 8 | 1 | 6.25 | 0 | --- | 9 | 4.4 |
| 9-11 | 0 | --- | 2 | 25.0 | 59 | 28.8 |
| 12 | 7 | 43.75 | 1 | 12.5 | 74 | 36.1 |
| 1-3 years college | 2 | 12.5 | 3 | 37.5 | 36 | 17.6 |
| ≥ 4 years college | 5 | 31.25 | 0 | --- | 23 | 11.2 |
| Total | 16 | | 8 | | 205 | |

## THE PROBAND'S HEARING LOSS

The proband's hearing loss was first recognized by one or both of the parents in 76% of cases (mother alone in 44%). Other relatives first recognized the proband's hearing problem in 13%, a doctor in 10%, and a teacher in 1% of reported cases. The average age of the proband at which the hearing loss was first recognized was 16.2 months (SD=13.24), and ranged from birth (zero months) to 96 months. Although hearing loss in probands from multiplex sibships was recognized slightly earlier (14.7 months) than in probands from simplex sibships (16.8 months), the difference was not statistically significant ($p=0.45$). As shown in Table 28, the hearing loss was recognized much earlier in probands when one or both parents also had a hearing deficit. As shown in Table 29, the reported age at which the proband began using sign language, spoke single words, or spoke words together was less when a member of a multiplex sibship ("multiplex proband") than when the proband was the only affected child ("simplex proband"). These differences were statistically significant for age when signing began, and for age when the proband first spoke words together. When the latter two ages are compared by the mating type of the parents, the difference is significant only for age when signing began, with an average age of 1.5 years in probands with two deaf parents, and 5.2 years in probands with two hearing parents, as shown in Table 28.

Table 30 shows the correlations between the age at which the hearing loss was first recognized, the age at which the proband began using sign language and spoke word(s), with the IQ test scores of the proband and with SES variables. Age at which hearing loss was first recognized

Table 28

Comparison of Selected Variables Among Students at Maryland School for the Deaf According to Mating Type of Parents

| Proband variable | Parental mating type | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | D x D | | D x H | | H x H | | | |
| | No. | Mean s.e. | No. | Mean s.e. | No. | Mean s.e. | $x^2$ | p |
| Age when hearing loss recognized (mos) | 8 | 5.00 ± 2.33 | 7 | 13.43 ± 2.11 | 196 | 16.32 ± 0.88 | 9.29 | 0.0096 |
| Age when began sign language (yrs) | 11 | 1.55 ± 0.31 | 7 | 3.29 ± 0.68 | 187 | 5.20 ± 0.20 | 25.99 | 0.0001 |
| Age when first word spoken (yrs) | 3 | 2.33 ± 0.67 | 5 | 5.60 ± 1.03 | 135 | 3.46 ± 0.22 | 4.40 | 0.11 |
| Age when words combined (yrs) | 3 | 4.33 ± 0.67 | 3 | 6.67 ± 1.45 | 86 | 5.23 ± 0.30 | 1.32 | 0.52 |
| IQ test score | 4 | 118.00 ± 2.55 | 1 | 80.00 ---- | 78 | 97.48 ± 1.71 | 8.24 | 0.02 |

Table 29

Mean Values of Selected Quantitative Variables Among Students at Maryland School for the Deaf

| Variable | Overall | | Simplex | | Multiplex | | $X^2$ | p |
|---|---|---|---|---|---|---|---|---|
| | No. | Mean ± s.e. | No. | Mean ± s.e | No. | Mean ± s.e | | |
| Age hearing loss recognized (mos) | 212 | 15.97 ± 0.83 | 180 | 16.2 ± 0.91 | 32 | 14.66 ± 2.08 | 0.56 | 0.45 |
| Age sign language begun (yrs) | 206 | 4.95 ± 0.19 | 174 | 5.23 ± 0.21 | 32 | 3.41 ± 0.34 | 11.74 | 0.0006 |
| Age first word spoken (yrs) | 143 | 3.52 ± 0.21 | 120 | 3.61 ± 0.23 | 23 | 3.09 ± 0.48 | 1.09 | 0.29 |
| Age words combined (yrs) | 91 | 5.26 ± 0.29 | 77 | 5.53 ± 0.31 | 14 | 3.79 ± 0.63 | 5.31 | 0.02 |
| No. cigarettes/day in pregnancy | 72 | 12.72 ± 1.00 | 66 | 12.18 ± 0.97 | 6 | 18.67 ± 5.21 | 1.70 | 0.19 |
| Oz. alcohol/day in pregnancy | 48 | 0.79 ± 0.08 | 44 | 0.82 ± 0.08 | 4 | 0.50 ± 0.00 | 2.69 | 0.10 |
| Length of labor (hrs) | 186 | 7.78 ± 0.47 | 156 | 7.63 ± 0.48 | 30 | 8.57 ± 1.47 | 0.01 | 0.94 |
| Gestational age of proband (wks) | 209 | 39.26 ± 0.19 | 175 | 39.23 ± 0.22 | 34 | 39.38 ± 0.40 | 0.07 | 0.80 |
| Proband's hospitalization after birth (days) | 214 | 9.74 ± 1.12 | 179 | 9.69 ± 1.16 | 35 | 10.00 ± 3.42 | 0.21 | 0.65 |

Table 30

Spearman Correlation of Selected Variables with Socioeconomic Status and IQ Test Scores of Students at Maryland School for the Deaf

| | Hearing loss recognized | Signing began | First word Spoken | Words first Combined |
|---|---|---|---|---|
| IQ Score of proband | | | | |
| r | -0.11 | -0.217 | -0.296 | -0.33 |
| p | 0.36 | 0.058 | 0.025 | 0.04 |
| n | 78 | 77 | 57 | 38 |
| Education of mother | | | | |
| r | -0.217 | -0.015 | -0.084 | -0.23 |
| p | 0.002 | 0.832 | 0.3135 | 0.0275 |
| n | 213 | 208 | 146 | 94 |
| Occupational status | | | | |
| r | -0.167 | 0.030 | -0.11 | -0.13 |
| p | 0.015 | 0.67 | 0.21 | 0.20 |
| n | 211 | 206 | 145 | 94 |
| Family income | | | | |
| r | -0.216 | -0.023 | -0.16 | -0.18 |
| p | 0.002 | 0.75 | 0.06 | 0.08 |
| n | 204 | 200 | 146 | 94 |

is significantly correlated with the SES variables. However, age at which sign language began correlates significantly with IQ test scores of the proband, but not with the SES variables, while age at first word correlates significantly with both IQ test scores of the proband and with family income. Age when words were used together was correlated with the IQ test scores of the proband, education of the mother, but not significantly with family income or parental occupational status.

When asked about the onset of the child's hearing problem, 65% of the respondents felt that the hearing loss was probably present from birth or within the first few months of life. Approximately 19% of the respondents thought the probands' hearing loss occurred after birth or after the first few months of life, and the remaining 16% were not sure when the probands' hearing losses occurred. A total of 7 of 208 (3.4%) believed that the probands' hearing was getting worse, 13.5% thought the hearing was improving, and 83% stated that there was no change in the proband's hearing ability over time. Eighty-three percent of the children were consistently using one or more hearing aids at the time of this study.

Mean values for audiological variables (pure tone average threshold, speech reception threshold, speech awareness threshold) are shown in Table 31. The mean right and left pure tone air conduction thresholds were approximately 100 dB, and ranged from 53 dB to 130 dB.* Pure tone average air conduction thresholds were highly correlated with the speech reception and awareness thresholds, as shown in Table 32. Data in Table 33

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* In cases where there was "no response" (eg 110 dB+, 120 dB+), 10 dB was added to the threshold at that frequency (see Hine, 1973).

Table 31

Summary of Audiological Data on Students at Maryland School for the Deaf

| | | Decibel level | | | |
|---|---|---|---|---|---|
| | N | Mean ± s.e. | S.D. | Min. | Max. |
| Pure-tone average air conduction threshold | | | | | |
| Right | 391 | 100.28 ± 0.69 | 13.64 | 53 | 130 |
| Left | 388 | 100.18 ± 0.70 | 13.79 | 53 | 130 |
| Speech reception threshold | | | | | |
| Right | 82 | 80.74 ± 2.00 | 18.08 | 35 | 130 |
| Left | 82 | 77.87 ± 1.96 | 17.73 | 35 | 130 |
| Speech awareness threshold | | | | | |
| Right | 350 | 82.14 ± 0.77 | 14.46 | 45 | 120 |
| Left | 351 | 82.51 ± 0.81 | 15.12 | 30 | 115 |

Table 32

Spearman Correlation Coefficients from Audiological Data on Students at Maryland School for the Deaf

| | Pure-tone air conduction | | Speech reception | | Speech awareness | |
|---|---|---|---|---|---|---|
| | Right | Left | Right | Left | Right | Left |
| Pure-tone air conduction | | | | | | |
| Right | 1.0 n=283 | | | | | |
| Left | 0.71 n=283 | 1.0 n=283 | | | | |
| Speech reception | | | | | | |
| Right | 0.80 n=69 | 0.59 n=69 | 1.0 n=69 | | | |
| Left | 0.56 n=69 | 0.81 n=69 | 0.74 n=69 | 1.0 n=69 | | |
| Speech awareness | | | | | | |
| Right | 0.73 n=283 | 0.57 n=283 | 0.79 n=44 | 0.59 n=44 | 1.0 n=283 | |
| Left | 0.55 n=283 | 0.75 n=283 | 0.62 n=44 | 0.83 n=44 | 0.68 n=283 | 1.0 n=283 |

All coefficients significant at 0.05 level.

Table 33

Comparison of Audiological Data in Simplex and Multiplex Families of Students at Maryland School for the Deaf

| Variable | Simplex | | Multiplex | | $\chi^2$ | p |
|---|---|---|---|---|---|---|
| | No. | Mean ± s.e. | No. | Mean ± s.e. | | |
| Pure-tone air conduction | | | | | | |
| Right | 313 | 100.69 ± 0.73 | 64 | 98.81 ± 1.95 | 0.19 | 0.66 |
| Left | 311 | 100.61 ± 0.77 | 63 | 97.87 ± 1.91 | 1.80 | 0.18 |
| Speech reception | | | | | | |
| Right | 65 | 82.69 ± 2.11 | 18 | 75.89 ± 4.95 | 1.03 | 0.31 |
| Left | 65 | 79.46 ± 2.14 | 16 | 72.19 ± 5.04 | 1.32 | 0.25 |
| Speech awareness | | | | | | |
| Right | 281 | 82.40 ± 0.79 | 57 | 82.46 ± 2.26 | 0.59 | 0.44 |
| Left | 282 | 83.16 ± 0.85 | 57 | 80.79 ± 2.03 | 0.86 | 0.35 |

demonstrate that there were no significant differences in the mean values of the audiological variables between probands from simplex vs. multiplex sibships.

In order to investigate the relationship between actual audiometric data and respondent ratings for the probands' hearing ability in each ear, better ear averages (BEAs) were used. BEAs represent the arithmetic average of the pure tone air conduction thresholds at 500, 1000, and 2000 Hz for the better ear (see Davis and Silverman, 1975). Each respondent was asked to check a statement giving their assessment of the probands' unaided hearing ability in each ear. Table 34 shows the mean BEAs for the composite rating of both ears (1=child's hearing is good in this ear; 2=a little trouble hearing in this ear; 3=a lot of trouble hearing in this ear; 4=deaf in this ear). Table 35 shows the mean differences in pure tone average decibel thresholds between the probands' ears compared with the respondents' assessment of perceived differences in hearing ability between the probands' ears. Table 36 is a condensed version of Table 35. With the exception of the three respondents who selected a 3-step difference in hearing level between ears (1-4,4-1), the respondents' perceived differences generally reflect actual mean differences measured audiologically. When the respondents rated each ear equally (1-1, 2-2, 3-3, 4-4), the actual mean differences ranged from 0 dB to 6.2 dB, with an average difference of 4.99 dB. When the ratings for each ear differ by one step (1-2, 2-3, 3-4), the average differences range from 2.5 to 10.5 dB, with an average of 9.3 dB. When the ratings differ by two steps (1-3, 2-4), the actual audiometric differences range from 12.7 to 14.9 dB (average 14.2 dB). Table 37 displays the proband mean BEAs associated with the respondent ratings of

Table 34

Hearing Thresholds of 208 Students at Maryland School for the Deaf, Classified by Respondent Rating

| Respondents' rating of unaided hearing ability * Better ear/worse ear | No. | Mean better ear average (dB) ± s.e. | Standard deviation |
|---|---|---|---|
| 1/1 | 1 | 110 | |
| 1/2 | 2 | 101 ± 9.00 | 12.7 |
| 1/3 | 3 | 88.3 ± 0.88 | 1.5 |
| 1/4 | 3 | 104 ± 4.58 | 7.9 |
| 2/2 | 5 | 79.6 ± 9.88 | 22.0 |
| 2/3 | 8 | 79.8 ± 5.24 | 14.8 |
| 2/4 | 7 | 87.4 ± 5.59 | 14.8 |
| 3/3 | 39 | 87.3 ± 2.26 | 14.2 |
| 3/4 | 27 | 95.5 ± 2.40 | 12.46 |
| 4/4 | 112 | 101.8 ± 0.93 | 9.80 |

* Rating criteria: 1 = child's hearing good in this ear; 2 = a little trouble hearing in this ear; 3 = a lot of trouble hearing in this ear; 4 = deaf in this ear.

Table 35

Mean Differences in Hearing Levels Between Ears of Students at Maryland School for the Deaf, Classified According to Respondents' Rating of Unaided Hearing Ability for Each Ear

| Respondents' rating of unaided hearing ability * for each ear | | No. | Mean differences of hearing levels ± s.e. (db) | Standard deviation |
|---|---|---|---|---|
| (1/1) | (1/1) | 1 | 0.00 | -- |
| (2/2) | (2/2) | 5 | 4.80 ± 2.63 | 5.89 |
| (3/3) | (3/3) | 39 | 6.21 ± 1.01 | 6.33 |
| (4/4) | (4/4) | 112 | 4.61 ± 0.65 | 6.87 |
| (1/2) | (2/1) | 2 | 2.50 ± 2.5 | 3.54 |
| (2/3) | (3/2) | 8 | 6.88 ± 2.79 | 7.88 |
| (3/4) | (4/3) | 27 | 10.55 ± 1.91 | 9.94 |
| (1/3) | (3/1) | 3 | 12.67 ± 5.36 | 9.29 |
| (2/4) | (4/2) | 7 | 14.86 ± 6.36 | 16.84 |
| (1/4) | (4/1) | 3 | 6.0 ± 4.58 | 7.94 |

* Rating criteria: 1= child's hearing good in this ear; 2= a little trouble hearing in this ear; 3= a lot of trouble hearing in this ear; 4= deaf in this ear.

Table 36

Mean Differences in Hearing Levels Between Ears of Students at Maryland School for the Deaf, Classified According to Respondents' Rating of Unaided Hearing Ability for Each Ear and Grouped from Most Balanced to Most Divergent

| Respondents' rating of unaided hearing ability for each ear* (Better/worse) | No. | Mean difference in in hearing levels (db) | Standard deviation |
|---|---|---|---|
| (1/1), (2/2), (3/3), (4/4) | 157 | 4.99 ± 0.54 | 6.7 |
| (1/2), (2/3), (3/4) | 37 | 9.32 ± 1.55 | 9.42 |
| (1/3), (2/4) | 10 | 14.2 ± 4.57 | 14.50 |
| (1/4) | 3 | 6.0 ± 4.58 | 7.94 |

* Rating criteria: 1= child's hearing good in this ear; 2= a little trouble hearing in this ear; 3= a lot of trouble hearing in this ear; 4= deaf in this ear.

Table 37

Hearing Levels of Students at Maryland School for the Deaf by Respondent Rating for Each Ear

| Respondents' rating scale | Left ear | | | Right ear | | |
|---|---|---|---|---|---|---|
| | No. | Mean BEA* ±s.e. (db) | Standard deviation | No. | Mean BEA* ±s.e. (db) | Standard deviation |
| 1, hearing is good | 4 | 109.3 ± 0.75 | -- | 7 | 96 ± 3.75 | 9.9 |
| 2, little trouble hearing | 15 | 84.5 ± 4.52 | 17.51 | 12 | 81.75 ± 5.18 | 17.96 |
| 3, lot of trouble hearing | 60 | 88.4 ± 1.74 | 13.5 | 59 | 89.3 ± 1.93 | 14.79 |
| 4, deaf in this ear | 129 | 100.9 ± 0.94 | 10.63 | 131 | 100.66 ± 0.92 | 10.6 |

* BEA= Better Ear Average Pure Tone Air Conduction Threshold in dB.

proband hearing ability in each ear. With the exception of those 11 respondents who checked that the probands' hearing was "good in this ear", there is an increase in the pure tone threshold (BEA) as the respondent rating of proband hearing loss increases.

The suspected causes of the probands' hearing losses are shown in Table 38. The most commonly suspected cause of hearing loss was maternal rubella infection, with meningitis and heredity following as the next two most frequently suspected causes. Doctors reportedly mentioned heredity as a possible cause of hearing loss in six percent of cases, whereas twice that many parents suspected heredity as a possible cause. Table 39 provides a breakdown by parental mating type of the perceived recurrence risk for another child with hearing loss. As expected, a large majority (80%) of the H x H parents suspected a very low recurrence risk, whereas 40% of the D x D parents suspected a recurrence risk of 75% or greater. When these responses were examined according to the probable etiology * of the probands' hearing loss, as shown in Table 40, 32% of parents of children whose deafness was presumably genetic felt that they had a very small chance of having another deaf child, compared to approximately 90% of parents of children whose deafness was attributed to maternal rubella, other, or unknown causes. Table 41 compares the

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* In several of the analyses, the probands were divided into four groups (genetic, maternal rubella, other, and unknown), based on the suspected etiology of their hearing disability. This determination was based on information provided in the questionnaires and by school officials. Those probands in the "genetic" group had deaf sibs, parents or two or more deaf blood relatives; those in the "maternal rubella" group were those born during the 1964-65 rubella epidemic and whose mothers reportedly had suspected or documented rubella infection during pregnancy with the proband. Many in the "maternal rubella" group reportedly had cataracts or heart defects. The "other" category consists primarily of probands whose hearing loss followed meningitis, and the "unknown" group includes all probands to whom no definite cause of hearing loss could be attributed with confidence.

Table 38

Parents' and Doctors' Reports of Hearing Loss Causes in Students at the Maryland School for the Deaf

| Suspected cause of deafness in proband | Parent | | Doctor | |
|---|---|---|---|---|
| | No. | % | No. | % |
| Maternal rubella | 77 | 35.81 | 79 | 38.16 |
| Genetic/heredity | 23 | 10.70 | 12 | 5.80 |
| Meningitis | 21 | 9.77 | 19 | 9.18 |
| Ear infection | 9 | 4.19 | 3 | 1.45 |
| Prematurity | 4 | 1.86 | 3 | 1.45 |
| Mumps | 2 | 0.93 | 1 | 0.48 |
| Rh problem | 5 | 2.33 | 3 | 1.45 |
| Measles | 7 | 3.26 | 9 | 4.35 |
| Tuberculosis | 1 | 0.47 | 1 | 0.48 |
| Birth trauma | 6 | 2.79 | 1 | 0.48 |
| Fever in pregnancy | 2 | 0.93 | 1 | 0.48 |
| Birth defect | 2 | 0.93 | 5 | 2.42 |
| Cerebral palsy | 2 | 0.93 | 1 | 0.48 |
| Nerve damage | 3 | 1.40 | 12 | 5.80 |
| Fever | 4 | 1.86 | 5 | 2.42 |
| Ear growth | 1 | 0.47 | 1 | 0.48 |
| Diabetes in pregnancy | 0 | ---- | 1 | 0.48 |
| Don't know | 46 | 21.40 | 50 | 24.15 |
| Total | 215 | 100.00 | 207 | 100.00 |

Table 39

Perceived Recurrence Risk of Hearing Loss in Next Child Classified by Mating Type of Parents of Students at Maryland School for the Deaf

| Mating type | Perceived Recurrence Risk | | | | | |
|---|---|---|---|---|---|---|
| | Very small | 10% | 25% | 50% | 75% | Don't know |
| Deaf x deaf (n=10) | 2 (20%) | 1 (10%) | 0 | 2 (20%) | 4 (40%) | 1 (10%) |
| Deaf x hearing (n=6) | 2 (33.3%) | 0 | 1 (16.67%) | 1 (16.67%) | 2 (33.3%) | 0 |
| Hearing x hearing (n=187) | 149 (79.68%) | 4 (2.14%) | 2 (1.07%) | 8 (4.28%) | 12 (6.42%) | 12 (6.41%) |

Table 40

Perceived Recurrence Risk of Hearing Loss in Next Child Classified by Probable Cause of Hearing Loss in Students at Maryland School for the Deaf

| Category | Perceived Recurrence Risk (%) | | | | | |
|---|---|---|---|---|---|---|
| | Very small | 10% | 25% | 50% | 75% | Don't know |
| Genetic (n=46) | 15 (32.61) | 2 (4.35) | 2 (4.35) | 8 (17.39) | 15 (32.61) | 4 (8.69) |
| Maternal rubella (n=62) | 57 (91.94) | 1 (1.61) | 0 | 1 (1.61) | 1 (1.61) | 2 (3.23) |
| Other (n=17) | 16 (94.12) | 0 | 0 | 0 | 1 (5.88) | 0 |
| Unknown (n=78) | 65 (83.33) | 2 (2.56) | 1 (1.28) | 2 (2.56) | 1 (1.28) | 7 (8.97) |

Table 41

Comparison of Perceived Recurrence Risk of Hearing Loss of Parents of Students at Maryland School for the Deaf when One Child and More than One Child is Affected

| Sibship | Perceived recurrence risk | | | | | |
|---|---|---|---|---|---|---|
| | Very small | 10% | 25% | 50% | 75% | Don't know |
| Simplex (n=172) | 145 (84.30%) | 4 (2.33%) | 2 (1.16%) | 8 (4.65%) | 4 (2.33%) | 9 (5.23%) |
| Multiplex (n=31) | 8 (25.81%) | 1 (3.23%) | 1 (3.23%) | 3 (9.68%) | 14 (45.16%) | 4 (12.91%) |

parents' perceived recurrence risks in the simplex and multiplex cases. About 84% of parents with a single affected child thought they had a very low recurrence risk and slightly over 10% thought they had some risk. Although over 60% of the parents who had more than one affected child thought they had at least a 10% recurrence risk, 25% of this group thought they had a very low risk of having another child with hearing loss.

## THE MOTHER'S PREGNANCY WITH THE PROBAND

Table 42 shows the frequencies of reported illnesses during the mothers' pregnancies with the probands and compares the presence of such illnesses in the mothers of the simplex versus the mothers of the multiplex sibships. As can be seen from this table, the frequency of mothers reporting rubella and rash during pregnancy was significantly greater in mothers of simplex sibships than in mothers of multiplex sibships. Table 43 contains a list of reported use of medicine by mothers during pregnancy with the probands and provides a breakdown of such use in the mothers of the simplex and multiplex sibships. The most commonly used medicines during pregnancy were aspirin (50%), unspecified medicine for nausea (14%), and antacids (11%). There was no significant difference in reported use of any specific drug or medicine between the mothers of multiplex and simplex sibships.

Table 44 shows the percentage of mothers who reportedly used tobacco or alcohol, or who had had surgery or X-ray exposure during pregnancy with the proband. Smoking during pregnancy was reported by 43% of the simplex mothers, compared to only 20% of the multiplex mothers.

Table 42

Frequency of Illnesses During Mothers' Pregnancy with Proband in Simplex Versus Multiplex Sibships of 243 Students at Maryland School for the Deaf

| Illness | Overall | | Simplex | | Multiplex | | p |
|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | |
| Rubella | 63 | 25.93 | 59/169 | 34.91 | 2/45 | 4.44 | 0.0001 |
| Measles | 2 | 0.82 | 2/177 | 1.13 | 0/47 | | 0.46 |
| Flu | 21 | 8.64 | 14/172 | 8.14 | 6/45 | 13.33 | 0.28 |
| Hepatitis | 0 | | 0/181 | | 0/47 | | ---- |
| Skin rash | 21 | 8.64 | 20/180 | 11.11 | 1/47 | 2.13 | 0.05 |
| Chicken pox | 2 | 0.82 | 1/181 | 0.55 | 1/47 | 2.13 | 0.30 |
| Diabetes | 2 | 0.82 | 2/180 | 1.11 | 0/47 | | 0.47 |
| Kidney disease | 18 | 7.41 | 13/180 | 7.22 | 5/47 | 10.64 | 0.44 |
| Anemia | 18 | 7.41 | 15/178 | 8.43 | 3/47 | 6.38 | 0.65 |
| Threatened abortion | 11 | 4.53 | 7/178 | 3.93 | 4/47 | 8.51 | 0.19 |
| Trauma | 9 | 3.70 | 7/181 | 3.87 | 2/47 | 4.26 | 0.90 |
| Rh problem | 5 | 2.06 | 3/179 | 1.68 | 2/47 | 4.26 | 0.28 |
| Thyroid problem | 2 | 0.82 | 0/179 | | 2/47 | 4.26 | 0.006 |
| Toxemia | 13 | 5.35 | 11/180 | 6.11 | 2/47 | 4.26 | 0.63 |

Table 43

Frequency of Reported Drug Use During Pregnancy with Proband in Simplex Versus Multiplex Sibships of 243 Students at Maryland School for the Deaf

| Medication | Overall | | Simplex | | Multiplex | | p |
|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | |
| Aspirin | 122 | 50.21 | 93/161 | 57.76 | 26/42 | 61.90 | 0.63 |
| Non-aspirin pain medicine | 16 | 6.58 | 13/174 | 7.47 | 3/43 | 6.98 | 0.91 |
| Nausea medicine | 33 | 13.58 | 17/176 | 15.34 | 6/44 | 13.64 | 0.78 |
| Allergy medicine | 9 | 3.70 | 9/176 | 5.11 | 0/43 | | 0.13 |
| Antibiotics | 10 | 4.12 | 6/166 | 3.61 | 4/44 | 9.09 | 0.13 |
| Insulin shots | 7 | 2.88 | 5/185 | 2.70 | 2/47 | 4.26 | 0.58 |
| Diabetes pills | 7 | 2.88 | 5/185 | 2.70 | 2/47 | 4.26 | 0.58 |
| Heart medicine | 1 | 0.41 | 1/180 | 0.56 | 0/45 | | 0.61 |
| Tranquilizers | 12 | 4.94 | 10/180 | 5.56 | 2/43 | 4.65 | 0.81 |
| Seizure medicine | 1 | 0.41 | 1/180 | 0.56 | 0/45 | | 0.61 |
| Antacid | 27 | 11.11 | 22/177 | 12.43 | 5/45 | 11.11 | 0.81 |
| Quinine | 4 | 1.65 | 3/177 | 1.69 | 1/45 | 2.22 | 0.81 |
| Hormones | 7 | 2.88 | 4/180 | 2.22 | 3/45 | 6.67 | 0.12 |
| Sleeping pills | 3 | 1.23 | 1/180 | 1.11 | 1/45 | 2.22 | 0.56 |
| Diuretics | 19 | 7.82 | 17/176 | 9.66 | 2/45 | 4.44 | 0.26 |
| Birth control pills | 7 | 2.88 | 5/180 | 2.78 | 2/44 | 4.55 | 0.55 |

Table 44

Frequency of Maternal Smoking, Drinking, Surgery and X-ray History During Pregnancy with Proband in Simplex Versus Multiplex Sibships of Students at Maryland School for the Deaf

| Maternal exposure | Overall | | Simplex | | Multiplex | | p |
|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | |
| Smoking | 86/227 | 37.88 | 77/181 | 42.54 | 7/35 | 20.00 | 0.01 |
| Alcohol | 55/227 | 24.23 | 49/180 | 27.22 | 5/33 | 15.15 | 0.14 |
| Surgery | 2/227 | 0.88 | 0/181 | | 2/34 | 5.85 | 0.001 |
| X-ray | 36/226 | 15.93 | 33/170 | 19.41 | 3/30 | 10.00 | 0.22 |

These mothers of simplex sibships also reported a greater frequency of alcohol use and X-ray exposure than did the mothers of multiplex sibships. Table 45 shows the number of mothers exposed to tobacco, alcohol, and X-rays during pregnancy classified according to probable cause of the probands' hearing losses. Only about 22% of mothers of probands whose hearing loss was clearly genetic reportedly smoked during pregnancy, compared to over 40% of mothers of probands whose hearing loss was attributed to other causes. Table 29 shows that the mean number of cigarettes smoked per day in the pregnant smoking mothers was 12.7. Average reported alcohol consumption was 0.8 ounces per day in those who reported drinking during pregnancy. Table 29 also shows a comparison of the amount of tobacco/alcohol consumption per day during pregnancy between the simplex and multiplex mothers. The data indicate no significant differences in alcohol/tobacco consumption among the users between the two groups. As shown in Table 46, the amount of reported maternal alcohol or tobacco use during pregnancy was not significantly correlated with the audiologic pure tone average decibel threshold or the better ear average threshold. Likewise, data in Table 47 demonstrate that the means of these audiologic variables do not differ significantly between probands whose mothers did or did not report tobacco, alcohol, or X-ray exposure.

## PROBAND BIRTH AND DELIVERY

Mean gestational ages were 39.23 (+/- 0.022) weeks and 39.38 (+/- 0.40) weeks, respectively, for probands from simplex and multiplex sibships. As shown in Table 29, the average reported length of labor

Table 45

Frequency of Maternal Tobacco, Alcohol and X-ray Exposure During Pregnancy Among Mothers of Students at Maryland School for the Deaf, Classified by Probable Cause of Probands' Hearing Loss

| Maternal exposure | Probable cause of deafness | | | | | | | | p |
|---|---|---|---|---|---|---|---|---|---|
| | Genetic | | Other | | Maternal rubella | | Unknown | | |
| | No. | % | No. | % | No. | % | No. | % | |
| Smoking | 11/49 | 22.45 | 8/19 | 42.11 | 26/63 | 41.27 | 39/85 | 45.88 | 0.05 |
| Alcohol | 12/47 | 25.53 | 5/19 | 26.32 | 22/62 | 35.48 | 15/85 | 17.65 | 0.11 |
| X-ray | 6/42 | 14.29 | 5/18 | 27.78 | 13/59 | 22.03 | 12/81 | 14.81 | 0.43 |

Table 46

Spearman Correlations of Maternal Tobacco and Alcohol Use During Pregnancy with Hearing Levels in Students at the Maryland School for the Deaf

| Variable | Maternal exposure during pregnancy | | | |
|---|---|---|---|---|
| | Tobacco | | Alcohol | |
| | r | p | r | p |
| Pure-tone air conduction thresholds (average) | | | | |
| Right | 0.02 | 0.85 | 0.05 | 0.75 |
| Left | -0.13 | 0.28 | -0.001 | 0.99 |
| Better ear average | -0.06 | 0.64 | 0.04 | 0.79 |

Table 47

Effects of Maternal Smoking, Alcohol, and X-rays During Relevant Pregnancy on Hearing Levels in Students at Maryland School for the Deaf

| Variable | No. | Threshold (dB) | No. | Threshold (dB) | $X^2$ | p |
|---|---|---|---|---|---|---|
| | Smoking | | No smoking | | | |
| Pure-tone air conduction | | | | | | |
| Right | 86 | 96.91 | 133 | 100.83 | 1.27 | 0.26 |
| Left | 85 | 97.72 | 132 | 100.97 | 2.74 | 0.10 |
| Better-ear average | 85 | 94.40 | 132 | 98.11 | 3.12 | 0.08 |
| | Alcohol | | No alcohol | | | |
| Pure-tone air conduction | | | | | | |
| Right | 55 | 97.22 | 161 | 100.51 | 0.92 | 0.34 |
| Left | 55 | 99.40 | 159 | 99.86 | 0.07 | 0.79 |
| Better-ear average | 55 | 94.38 | 159 | 97.52 | 1.69 | 0.19 |
| | X-ray | | No x-ray | | | |
| Pure-tone air conduction | | | | | | |
| Right | 60 | 102.43 | 165 | 98.72 | 2.32 | 0.13 |
| Left | 60 | 100.43 | 163 | 99.55 | 0.03 | 0.86 |
| Better-ear average | 60 | 98.20 | 163 | 96.20 | 0.16 | 0.69 |

did not significantly differ between probands from simplex sibships (7.6 hours) and multiplex sibships (8.6 hours). Approximately 85% of the probands were born after spontaneous labor with the remaining 15% after induced labor. Table 48 shows that while 12% of simplex mothers reported induced labor, over twice that many (27%) mothers of multiplex sibships reported delivering the proband after induced labor. Data in Table 49 show that 22% of the probands whose hearing disability was thought to be genetic were delivered after induced labor compared with less than 10% of probands whose deafness was the result of maternal rubella infection or "other" causes. Table 48 shows that the overall types of anesthesia and delivery did not differ significantly between probands from simplex or multiplex sibships.

Table 50 shows the numbers and percentages of mothers who reported various problems during the delivery of or shortly after the birth of the probands. There were no significant differences in the percentage of reported problems at delivery, of probands needing ventilatory assistance, or of probands needing oxygen at the time of delivery between the probands from simplex and multiplex sibships. Although almost twice the proportion of simplex probands went into an incubator at birth, the difference between the simplex and multiplex probands only approached statistical significance. A significantly greater proportion of multiplex probands (20.6%) than simplex probands (9.1%) were reportedly jaundiced at birth. About three percent of all probands required blood transfusions within the first few months after birth. The average postpartum hospital stay was approximately ten days for probands from both simplex and multiplex sibships, as shown in Table 29.

Table 48

Type of Labor, Delivery, and Anesthesia for Relevant Birth Among Mothers of Simplex and Multiplex Sibships of Students at Maryland School for the Deaf

| | Overall | | Simplex | | Multiplex | | p |
|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | |
| Type of labor | | | | | | | |
| Spontaneous | 173 | 85.64 | 143 | 88.27 | 24 | 72.73 | 0.02 |
| Induced | 29 | 14.36 | 19 | 11.73 | 9 | 27.27 | |
| Total | 202 | | 162 | | 33 | | |
| Type of anesthesia | | | | | | | |
| None | 35 | 17.58 | 30 | 18.40 | 4 | 11.43 | |
| General | 98 | 49.24 | 86 | 52.76 | 14 | 40.00 | 0.16 |
| Spinal | 49 | 24.62 | 36 | 22.09 | 13 | 37.14 | |
| Local | 17 | 8.54 | 11 | 6.75 | 4 | 11.43 | |
| Total | 199 | | 163 | | 35 | | |
| Type of delivery | | | | | | | |
| Vaginal, forceps | 65 | 30.09 | 55 | 31.25 | 9 | 26.47 | |
| Vaginal, no forceps | 83 | 38.43 | 67 | 38.07 | 15 | 44.12 | 0.78 |
| Vaginal, don't know | 56 | 25.93 | 43 | 24.43 | 9 | 26.47 | |
| Caesarean section | 12 | 5.56 | 11 | 6.25 | 1 | 2.94 | |
| Total | 216 | | 176 | | 34 | | |

Table 49

Type of Labor Classified by Probable Cause of Hearing Loss of Proband at Maryland School for the Deaf

| Cause of proband hearing loss | Type of labor | | | | No. |
|---|---|---|---|---|---|
| | Spontaneous | | Induced | | |
| | No. | % | No. | % | |
| Genetic | 35 | 77.8 | 10 | 22.2 | 45 |
| Other | 16 | 94.1 | 1 | 4.9 | 17 |
| Rubella | 56 | 91.8 | 5 | 8.2 | 61 |
| Unknown | 60 | 83.3 | 12 | 16.7 | 72 |

$X^2 = 5.45$, $p = 0.14$, d.f. = 3.

Table 50

Frequency of Neonatal Problems in Probands at Maryland School for the Deaf from Simplex and Multiplex Sibships

| | Overall | | Simplex | | Multiplex | | p |
|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | |
| Problems in delivery | 25/202 | 12.37 | 20/164 | 12.20 | 5/33 | 15.15 | 0.64 |
| Help breathing | 15/161 | 9.32 | 13/133 | 9.77 | 2/24 | 8.33 | 0.83 |
| Oxygen at birth | 19/176 | 10.80 | 17/142 | 11.97 | 2/29 | 6.90 | 0.43 |
| Incubator | 56/201 | 27.86 | 50/162 | 30.86 | 5/32 | 15.63 | 0.08 |
| Special care | 35/216 | 16.20 | 30/176 | 17.05 | 5/33 | 15.15 | 0.79 |
| Jaundiced | 24/218 | 11.01 | 16/176 | 9.09 | 7/34 | 20.59 | 0.05 |
| Blood transfusion | 6/221 | 2.71 | 4/181 | 2.21 | 2/33 | 6.06 | 0.21 |
| Baby medication | 16/197 | 8.12 | 13/161 | 8.07 | 2/30 | 6.67 | 0.79 |

Birth weights, current weights, current heights, and IQ test scores of the probands were appropriately adjusted for age, sex, race, or interactive effects, and were compared among probands from simplex and multiplex sibships, and among probands grouped by probable cause of their hearing disability. Table 51 shows that there were no significant differences in age and sex adjusted current weights between white and non-white probands, but that there were significant differences in adjusted birth weights, current heights and in IQ test scores between these two groups. White probands had higher birth weights (adjusted for sex and gestational age) and age adjusted IQ test scores. The non-white probands had greater age adjusted current heights. When these variables were compared in probands from simplex and multiplex sibships, adjusted birth weights were found to be significantly higher in the latter group. No significant differences were detected in current adjusted weights, current adjusted heights, or in adjusted IQ test scores between the simplex and multiplex groups.

Tables 52 and 53 show the results of covariance analysis of proband birth weights and current weights based on the probable cause of the probands' hearing loss. The covariance procedure adjusted birth weights for gestational age to current weights for current age. Probands in the maternal rubella and unknown groups had significantly lower mean adjusted birth weights than probands in the genetic and other (primary meningitis) groups. Likewise, the adjusted current weights in the maternal rubella group probands were significantly lower than in probands of the other three groups, which were not significantly different from each other. Mean current adjusted heights and adjusted IQ test scores were not signifcantly different among the four groups, as shown in Tables 54 and 55. However, the mean adjusted IQ test scores were highest in the "genetic" probands.

Table 51

Comparison of Mean Adjusted Birthweight, Current Weight, Current Height and IQ Test Score of Probands by Race and Family at Maryland School for the Deaf

| | No. | Mean ± s.e. | No. | Mean ± s.e. | p |
|---|---|---|---|---|---|
| | | White | | Non-white | |
| Current adjusted weight | 161 | -39.15 ± 1.54 | 39 | -37.72 ± 3.81 | 0.69 |
| Current adjusted height | 137 | 61.57 ± 0.53 | 27 | 65.15 ± 1.20 | 0.007 |
| Adjusted birth weight | 152 | 122.80 ± 1.54 | 32 | 115.49 ± 3.33 | 0.049 |
| Adjusted IQ test scores | 65 | 88.96 ± 2.01 | 19 | 72.62 ± 2.17 | 0.0001 |
| | | Simplex | | Multiplex | |
| Current adjusted weight | 167 | -39.13 ± 1.57 | 33 | -37.55 ± 3.68 | 0.69 |
| Current adjusted height | 132 | 21.98 ± 0.33 | 32 | 21.99 ± 0.90 | 0.99 |
| Adjusted birth weight | 153 | 128.99 ± 1.58 | 31 | 135.63 ± 2.54 | 0.031 |
| Adjusted IQ test scores | 77 | 102.48 ± 1.70 | 7 | 106.61 ± 6.20 | 0.49 |

Table 52

Covariance Analysis of Gestational Age Adjusted Birthweights of Probands at Maryland School for the Deaf by Probable Cause of Deafness

| | No. | Least square mean | Standard error | Prob >\|T\| $H_o$: $\bar{X}_i = \bar{X}_j$ | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | I/J | 1 | 2 | 3 | 4 |
| Genetic | 46 | 114.84 | 2.74 | 1 | . | | | |
| Maternal rubella | 56 | 92.89 | 2.41 | 2 | 0.0001 | . | | |
| Other | 15 | 115.93 | 4.74 | 3 | 0.8426 | 0.0001 | . | |
| Unknown | 79 | 105.74 | 2.06 | 4 | 0.0087 | 0.0001 | 0.0499 | . |

PROC GLM; SAS, 1979

Table 53

Covariance Analysis of Age Adjusted Current Weights of Probands at Maryland School for the Deaf

| | No. | Least square mean | Standard error | Prob >\|T\| $H_0: \bar{X}_i = \bar{X}_j$ | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | I/J | 1 | 2 | 3 | 4 |
| Genetic | 46 | 109.53 | 3.06 | 1 | . | | | |
| Maternal rubella | 59 | 95.81 | 2.71 | 2 | 0.0010 | . | | |
| Other | 16 | 114.56 | 5.18 | 3 | 0.4035 | 0.0016 | . | |
| Unknown | 79 | 109.70 | 2.33 | 4 | 0.9649 | 0.0001 | 0.3940 | . |

PROC GLM; SAS, 1979

Table 54

Covariance Analysis of Age Adjusted Current Heights of Probands at Maryland School for the Deaf

| | No. | Least square mean | Standard error | Prob >\|T\| $H_o$: $\bar{X}_i = \bar{X}_j$ | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | I/J | 1 | 2 | 3 | 4 |
| Genetic | 43 | 62.43 | 0.70 | 1 | . | | | |
| Maternal rubella | 47 | 62.20 | 0.66 | 2 | 0.8183 | . | | |
| Other | 11 | 61.28 | 1.37 | 3 | 0.4573 | 0.5429 | . | |
| Unknown | 63 | 62.10 | 0.57 | 4 | 0.7163 | 0.9036 | 0.5810 | . |

PROC GLM; SAS, 1979

Table 55

Covariance Analysis of Age Adjusted IQ Test Scores of Probands at Maryland School for the Deaf

| | No. | Least square mean | Standard error | Prob >\|T\| $H_o: \bar{X}_i = \bar{X}_j$ I/J | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|---|---|---|
| Genetic | 9 | 105.47 | 5.09 | 1 | . | | | |
| Maternal Rubella | 34 | 97.57 | 2.62 | 2 | 0.1773 | . | | |
| Other | 8 | 100.61 | 5.30 | 3 | 0.5107 | 0.6082 | . | |
| Unknown | 33 | 96.50 | 2.62 | 4 | 0.1177 | 0.7751 | 0.4893 | . |

PROC GLM; SAS, 1979

## HEALTH HISTORY OF THE PROBANDS

Table 56 provides a summary of the reported incidence of medical problems in the MSD probands. Comparing probands from simplex and multiplex sibships one notices a considerable, though not always statistically significant increase in the reported history of some of the health problems (including rubella, measles, whooping cough, meningitis, seizures, and asthma) in the simplex probands. As shown in Table 57, there were less than five reported ear infections in approximately 70% of both simplex and multiplex probands. Whereas 25% of the multiplex probands reportedly had more than 10 ear infections, only 11% of the simplex probands reportedly had more than 10. However, the overall pattern of ear infections did not differ significantly between the two groups. The reported number of non-ear infections was greater in the simplex probands than in the probands from multiplex sibships. Almost 10% of the simplex probands reportedly had more than 15 infections, whereas none of the probands from the multiplex sibships did. Over 90% of the probands from multiplex sibships had fewer than 5 infections, while only 75% of the probands from simplex sibships had less than five. Table 58 shows that there were no significant differences in the proportion of simplex versus multiplex probands who reportedly had specific surgical procedures.

Table 56

Frequency of Childhood Diseases in 243 Probands at Maryland School for the Deaf

| Illness | Overall | | Simplex | | Multiplex | | p |
|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | |
| Rubella | 25 | 10.3 | 22/177 | 12.43 | 3/47 | 6.38 | 0.24 |
| Measles | 68 | 27.98 | 59/180 | 32.78 | 9/47 | 19.15 | 0.07 |
| Mumps | 58 | 23.87 | 47/181 | 25.97 | 11/46 | 23.91 | 0.77 |
| Chicken pox | 155 | 63.79 | 123/180 | 68.33 | 32/46 | 69.57 | 0.87 |
| Scarlet fever | 3 | 1.23 | 3/183 | 1.64 | 0/47 | | 0.37 |
| Polio | 0 | | | | | | |
| Whooping cough | 8 | 3.29 | 8/183 | 4.37 | 0/47 | | 0.14 |
| Meningitis | 26 | 10.70 | 25/184 | 13.59 | 1/47 | 2.13 | 0.03 |
| Encephalitis | 1 | 0.41 | 1/183 | 0.55 | 0/47 | | 0.61 |
| Tuberculosis | 5 | 2.06 | 3/184 | 1.63 | 2/47 | 4.26 | 0.27 |
| Mastoiditis | 1 | 0.41 | 1/183 | 0.55 | 0/47 | | 0.61 |
| Seizure | 17 | 7.00 | 16/184 | 8.70 | 1/47 | 2.13 | 0.12 |
| Diphtheria | 1 | 0.41 | 1/185 | 0.54 | 0/47 | | 0.61 |
| Typhoid fever | 1 | 0.41 | 1/185 | 0.54 | 0/47 | | 0.61 |
| Kidney disease | 6 | 2.47 | 5/183 | 2.73 | 1/47 | 2.13 | 0.82 |
| Thyroid disease | 2 | 0.82 | 0/184 | | 2/47 | 4.26 | 0.005 |
| Headaches | 10 | 4.12 | 9/184 | 4.89 | 1/47 | 2.13 | 0.41 |
| Asthma | 46 | 18.93 | 40/182 | 21.98 | 6/47 | 12.77 | 0.16 |
| Head injury | 20 | 8.23 | 17/183 | 9.29 | 3/47 | 6.38 | 0.53 |

Table 57

Frequency of Ear and Other Infections in Probands at Maryland School for the Deaf

| | Overall | | Simplex | | Multiplex | | p |
|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | |
| Ear infections | | | | | | | |
| 0 | 83 | 37.56 | 68 | 38.20 | 13 | 40.63 | |
| <5 | 71 | 32.13 | 58 | 32.58 | 9 | 28.13 | 0.095 |
| 6-10 | 37 | 16.74 | 32 | 17.98 | 2 | 6.25 | |
| >10 | 30 | 13.57 | 20 | 11.24 | 8 | 25.00 | |
| Total | 221 | | 178 | | 32 | | |
| Other infections | | | | | | | |
| 0 | 89 | 40.64 | 66 | 37.71 | 17 | 50.00 | |
| <5 | 81 | 36.99 | 66 | 37.71 | 14 | 41.18 | |
| 6-10 | 24 | 10.96 | 22 | 12.57 | 1 | 2.94 | 0.086 |
| 11-15 | 7 | 3.20 | 4 | 2.29 | 2 | 5.88 | |
| >15 | 18 | 8.11 | 17 | 9.71 | 0 | 0.00 | |
| Total | 219 | | 175 | | 34 | | |

Table 58

Frequency of Selected Surgical Procedures in Probands at Maryland School for the Deaf

| | Overall | | Simplex | | Multiplex | | p |
|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | |
| Tonsillectomy | 74/242 | 30.58 | 56/184 | 30.43 | 14/47 | 29.79 | 0.93 |
| Adenoidectomy | 75/241 | 31.12 | 60/183 | 32.79 | 12/47 | 25.53 | 0.34 |
| Sinus surgery | 1/241 | 0.41 | 1/183 | 0.55 | 0/47 | --- | 0.61 |
| Mastoid surgery | 1/241 | 0.41 | 1/184 | 0.54 | 0/47 | --- | 0.61 |
| Ear tube placement | 26/241 | 10.79 | 21/184 | 11.41 | 4/47 | 8.51 | 0.57 |
| Myringotomy | 12/239 | 5.02 | 9/183 | 4.92 | 1/46 | 2.17 | 0.42 |

## OTHER MEDICAL CONDITIONS

Data on the probands' eyesight is shown in Table 59. Normal unaided vision was reported in 73% of the MSD probands. The pattern of reported eye problems did not differ significantly between probands from simplex versus multiplex sibships. Nearsightedness was reported in 16% of the probands and farsightedness in 4%.

Table 60 lists the number of positive responses to the questions about a history in the proband of each medical condition on pages 10 and 11 of the Hearing Loss Questionnaire (Appendix I), and compares the responses according to the probable cause of the probands' hearing loss. Almost 11% (7/64) of the probands whose hearing loss was thought to be the result of maternal rubella reportedly had cataracts, whereas none of the probands in the other three groups had cataracts. Over 14% (9) of these probands in the "maternal rubella" group reportedly had oligodontia. Approximately 45% (29) of the probands in the rubella group reportedly had a heart defect or murmur, and 15% (10) reportedly had severe behavioral/emotional problems. Almost 11% (7) of the rubella group probands were reported to have had "very slow growth". However, as reported above, the age-adjusted current heights were not significantly less than in the "genetic" or "other" groups, and the age and sex adjusted current weights were actually significantly greater in the rubella group than in the other three groups.

Because this study did not include clinical evaluation of the MSD students, no proper estimate can be made of the number of specific syndromic types of hearing loss present in this school population. Questionnaire responses and school officials did however identify several probands with recognized syndromic forms of hearing loss, including four

Table 59

Visual Status of Probands at Maryland School for the Deaf

| | Overall | | Simplex | | Multiplex | | |
|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | |
| Normal vision | 167 | 73.24 | 132 | 72.13 | 27 | 77.14 | |
| Nearsightedness | 38 | 16.67 | 30 | 16.39 | 6 | 17.14 | |
| Farsightedness | 10 | 4.38 | 7 | 3.83 | 2 | 5.71 | |
| Astigmatism | 2 | 0.88 | 2 | 1.09 | 0 | --- | p = 0.88 |
| Amblyopia | 2 | 0.88 | 2 | 1.10 | 0 | --- | |
| One bad eye | 9 | 3.95 | 9 | 4.92 | 0 | --- | |
| Total | 228 | | 182 | | 35 | | |

Table 60

Frequency of Reported Medical Problems in Probands at Maryland School for the Deaf, Classified by Probable Cause of Deafness

| | Overall | | Genetic | | Maternal rubella | | Other | | Unknown | | p |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | No. | % | |
| Cross-eyed | 7 | 3.02 | 2 | 3.28 | 3 | 4.69 | 0 | | 2 | 2.33 | 0.70 |
| Wall-eyed | 2 | 0.86 | 1 | 1.64 | 0 | | 0 | | 1 | 1.16 | 0.74 |
| Nystagmus | 4 | 1.72 | 0 | | 3 | 4.69 | 0 | | 1 | 1.16 | 0.17 |
| Cataract(s) | 7 | 3.02 | 0 | | 7 | 10.94 | 0 | | 0 | | 0.0003 |
| Glaucoma | 1 | 0.43 | 0 | | 1 | 1.56 | 0 | | 0 | | 0.46 |
| Unusual head shape | 4 | 1.72 | 1 | 1.64 | 1 | 1.56 | 1 | 4.76 | 1 | 1.16 | 0.72 |
| White forelock | 4 | 1.72 | 4 | 6.56 | 0 | | 0 | | 0 | | 0.06 |
| Twisted brittle hair | 1 | 0.43 | 0 | | 0 | | 0 | | 1 | 1.16 | 0.63 |
| Unusual facies | 2 | 0.86 | 0 | | 2 | 3.13 | 0 | | 0 | | 0.15 |
| Cleft lip/palate | 2 | 0.86 | 1 | 1.64 | 1 | 1.56 | 0 | | 0 | | 0.63 |
| Unusual shaped/missing teeth | 12 | 5.2 | 0 | | 9 | 14.06 | 1 | 4.76 | 2 | 2.33 | 0.002 |
| Unusual ear-shape | 5 | 2.16 | 0 | | 1 | 1.56 | 2 | 9.52 | 2 | 2.33 | 0.076 |
| Goiter | 2 | 0.86 | 1 | 1.64 | 0 | | 0 | | 1 | 1.16 | 0.74 |
| Other thyroid problem | 2 | 0.86 | 2 | 3.28 | 0 | | 0 | | 0 | | 0.13 |
| Heart defect/murmur | 39 | 16.81 | 2 | 3.28 | 29 | 45.31 | 2 | 9.52 | 6 | 6.98 | 0.0001 |
| Unusual nail shape | 2 | 0.86 | 0 | | 2 | 3.13 | 0 | | 0 | | 0.15 |
| Fused digits | 1 | 0.43 | 0 | | 1 | 1.56 | 0 | | 0 | | 0.45 |
| Absent MP/IP joints | 1 | 0.43 | 0 | | 1 | 1.56 | 0 | | 0 | | 0.45 |
| Clubfoot | 0 | | 0 | | 0 | | 0 | | 0 | | ---- |
| Scoliosis | 2 | 0.86 | 1 | 1.64 | 0 | | 0 | | 1 | 1.16 | 0.73 |
| Frequent bone fractures | 2 | 0.86 | 1 | 1.64 | 1 | 1.56 | 0 | | 0 | | 0.63 |
| Bony deformities | 2 | 0.86 | 0 | | 2 | 3.13 | 0 | | 0 | | 0.15 |
| Scaly or very dry skin | 12 | 5.17 | 3 | 4.92 | 3 | 4.69 | 2 | 9.52 | 4 | 4.65 | 0.83 |
| Absence of sweating | 1 | 0.43 | 0 | | 1 | 1.56 | 0 | | 0 | | 0.45 |
| Heavy freckling | 3 | 1.29 | 0 | | 1 | 1.56 | 0 | | 2 | 2.33 | 0.61 |
| Patchy skin color | 5 | 2.16 | 3 | 4.92 | 1 | 1.56 | 0 | | 1 | 1.16 | 0.36 |
| Fits, fainting spells | 3 | 1.29 | 0 | | 2 | 3.13 | 0 | | 1 | 1.16 | 0.43 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Severe behavioral/ emotional problem | 20 | 8.62 | 3 | 4.92 | 10 | 15.63 | 1 | 4.76 | 6 | 6.98 | 0.13 |
| Mental retardation | 2 | 0.86 | 0 | | 1 | 1.59 | 0 | | 1 | 1.16 | 0.76 |
| Diabetes | 1 | 0.43 | 0 | | 0 | | 0 | | 1 | 1.16 | 0.64 |
| Kidney disease | 1 | 0.43 | 0 | | 1 | 1.56 | 0 | --- | 0 | | 0.45 |
| Blood in urine | 2 | 0.86 | 0 | | 1 | 1.56 | 1 | 4.76 | 0 | | 0.15 |
| Poor balance, clumsiness | 22 | 9.5 | 5 | 8.20 | 5 | 7.81 | 5 | 23.81 | 7 | 8.14 | 0.14 |
| Dizziness | 7 | 3.02 | 4 | 6.56 | 0 | | 1 | 4.76 | 2 | 2.33 | 0.17 |
| Muscle problems | 10 | 4.31 | 2 | 3.28 | 4 | 6.25 | 0 | | 4 | 4.65 | 0.63 |
| Dysosmia | 1 | 0.43 | 0 | | 1 | 1.56 | 0 | | 0 | | 0.45 |
| Very slow growth | 8 | 3.45 | 0 | | 7 | 10.94 | 0 | | 1 | 1.16 | 0.002 |
| Total | 232 | | 61 | | 64 | | 21 | | 86 | | |

students with the Waardenburg syndrome, one with the Usher syndrome, and one with the Jervell and Lange-Neilsen syndrome.

## SEGREGATION ANALYSIS

Among the entire school population in this study there were a total of 318 sibships that were informative for segregation analysis (Table 61). These sibships were ascertained through an affected child by incomplete selection. All of these sibships contain at least one affected child (the proband), and were analysed separately according to the mating type of their parents. There were 186 informative sibships in the questionnaire respondent group, with 84 informative sibships in the non-respondent group. Family history information was also available on an additional 48 sibships from the preschool and new student groups.

The ascertainment probability, $\pi$, (defined as the probability that an affected individual is ascertained), was determined from the distribution of probands in the sibships under a model of incomplete multiple selection (Morton, 1959). In this situation, $\pi$ is uniform and $0 < \pi < 1$, and ascertainments are considered to be independent, the distribution of $\underline{a}$ probands among $\underline{r}$ affected individuals is described by

$$P(a/a>0) = \frac{\binom{r}{a}\pi^a (1-\pi)^{r-a}}{1-(1-\pi)^r}, \qquad (1)$$

when $1 \leq a \leq r$.

Table 62 shows the maximum likelihood estimates of $\pi$ in each of the four groups mentioned above, as well as in the group combining the respondents and non-respondents, and in all four groups combined. In each case,

Table 61

Summary of Family Data for Students at Maryland School for the Deaf

| Mating type | Sibships | Informative sibships | Among informative sibships | |
|---|---|---|---|---|
| | | | Affected children | Hearing children |
| Respondents | | | | |
| H x H | 200 | 169 | 199 | 376 |
| D x H | 7 | 6 | 9 | 13 |
| D x D | 13 | 11 | 23 | 10 |
| Undefined | 8 | 0 | - | - |
| Total | 228 | 186 | 231 | 399 |
| Non-respondents | | | | |
| H x H | 91 | 78 | 85 | 195 |
| D x H | 2 | 2 | 2 | 4 |
| D x D | 6 | 4 | 9 | 2 |
| Undefined | 7 | 0 | - | - |
| Total | 106 | 84 | 96 | 201 |
| Not queried | | | | |
| H x H | 61 | 42 | 48 | 92 |
| D x H | 1 | 0 | - | - |
| D x D | 14 | 6 | 11 | 4 |
| Undefined | 5 | 0 | - | - |
| Total | 81 | 48 | 59 | 96 |
| Grand Total | 415 | 318 | 386 | 696 |

Table 62

Maximum Likelihood Estimates of Ascertainment Probability ($\pi$) Among Students at Maryland School for the Deaf ($H_0: \pi = 0.50$)

| | Informative sibships | Overall | | Probands | $U_{\pi}$ | $K_{\pi\pi}$ | $\hat{\pi}$ | $X^2$ | $X^2_{het}$ |
|---|---|---|---|---|---|---|---|---|---|
| | | Affected Children | Hearing Children | | | | | | |
| 1. Preschool | 22 | 26 | 26 | 23 | -1.52 | 14.95 | 0.391 | 0.155 | |
| 2. New | 26 | 33 | 70 | 27 | -5.52 | 215.61 | 0.248 | 1.191 | |
| 3. Non-respondents | 84 | 96 | 201 | 90 | 7.28 | 45.24 | 0.647 | 1.17 | |
| 4. Respondents | 186 | 231 | 399 | 201 | 2.51 | 112.14 | 0.481 | 0.06 | |
| 5. 3 and 4 | 270 | 327 | 600 | 291 | 4.08 | 216.38 | 0.519 | 0.077 | 1.15 |
| 6. 1, 2, 3, and 4 | 318 | 386 | 696 | 341 | -2.97 | 256.95 | 0.488 | 0.34 | 2.54 |

the value of $\pi$ was not significantly different from the tested value of 0.50, as indicated by the low $X^2$ values. When the questionnaire respondents and non-respondents were analysed separately in a single computer run, there were no significant differences in the values of $\hat{\pi}$, as shown by the low $_{het}X^2$ value of 1.15. Furthermore, there was no significant difference in the value of $\hat{\pi}$ calculated in the entire group of 318 informative sibships ( $\hat{\pi}$ = 0.488, $_{het}X^2$= 2.54) when all four groups were combined. Therefore, the maximum likelihood value of 0.488 was used as the value of $\pi$ in the subsequent analyses, where hypotheses about the values of the segregation frequency, p , and of the proportion of sporadic cases, x , were tested.

Hearing by hearing matings; Because extended family history information was available only from questionnaire respondents, the non-respondent, pre-school, and new student groups were not included in some of the analyses. However, before analysing data on the questionnaire respondents as a separate group, 289 informative sibships from the H x H matings in all four groups were tested for any heterogeneity in the values of either $\hat{p}$ or $\hat{x}$. No significant heterogeneity was found among the groups for values of either $\hat{p}$ or $\hat{x}$ ($_{het}X^2_p$=1.71; $_{het}X^2_x$=1.07). Further analyses were then performed on the questionnaire respondent group alone.

The questionnaire respondent group was partitioned into several groups prior to analysis. Those sibships with no reported family history of hearing loss of any kind were separated from those with a positive family history (in a relative other than a parent or sib of the proband) of either early onset hearing loss of moderate to profound severity, or of later onset hearing loss of mild to moderate severity ("presbycusis").

This positive family history group was then further subdivided into those with a positive family history of either early onset hearing loss or of "presbycusis".

Simplex sibships (sibships in which only the proband is affected) in the H x H matings represent families who are either at "low risk" of having another affected child (their deaf child, the proband, represents a sporadic case), or families who are at the same a priori risk, p, as are the multiplex families (whose deaf child represents a chance isolated case). The segregation frequency, p, and the proportion of sporadic cases, x, among all deaf individuals were estimated from the distribution of the simplex families among all families, fixing the value of $\pi$ at its previously estimated value of 0.488, where

$$P(r=1/r>0) = \frac{sp\pi\,(x+(1-x)q^{s-1})}{xsp\pi+(1-x)(1-(1-p\pi)^{s})}, \qquad (2)$$

and where s is equal to the sibship size and q=1-p (Morton, 1959).

The multiplex families were assumed to contain no sporadic cases of hearing loss because of the very low recurrence risk for sporadic hearing loss. In these families, where

$$P(r/r>1) = \frac{\binom{s}{r} p^{r}q^{s-r}\,(1-(1-\pi)^{r})}{1-(1-p\pi)^{s}-\pi spq^{s-1}}, \qquad (3)$$

the segregation ratio, p, was estimated according to the distribution of affected individuals in the sibships.

Table 63 shows the results of segregation analysis in the 111 sibships with no reported family history of hearing loss. The null hypothesis of recessive inheritance with no sporadic cases ($H_0$:p=0.25; x=0.00) was rejected ($\chi^2_p$=49.42, $\chi^2_x$=53.13) in these negative family history sibships.

Table 63

Segregation Analysis of Informative Sibships from H x H Matings Among Parents of Students at Maryland School for the Deaf ($\pi = 0.488$)

| Hypothesis tested | Sibships | Overall | | $U_p$ | $U_x$ | $K_{pp}$ | $K_{xx}$ | $K_{px}$ | $\chi^2_p$ | $\chi^2_x$ |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Affected Children | Hearing Children | | | | | | | |
| Negative family history | | | | | | | | | | |
| $H_0$:p=0.25,x=0.0 | 111 | 125 | 251 | -218.08 | 84.59 | 962.33 | 134.66 | -348.85 | 49.42 | 53.13 |
| $H_1$:p=0.25,x=$\hat{x}$=0.807 | 111 | 125 | 251 | 13.36 | --- | 69.43 | --- | --- | 2.57 | --- |
| Family history of hearing loss (early-onset or presbycusis) | | | | | | | | | | |
| $H_0$:p=0.25,x=0.00 | 58 | 74 | 125 | -76.98 | 43.26 | 487.79 | 97.56 | -193.16 | 12.15 | 19.18 |
| $H_1$:p=0.25, x=$\hat{x}$=0.611 | 58 | 74 | 125 | 17.42 | --- | 84.52 | --- | --- | 3.59 | --- |
| Family history of early hearing loss | | | | | | | | | | |
| $H_0$:p=0.25,x=0.00 | 24 | 35 | 49 | -17.25 | 6.61 | 210.70 | 33.69 | -80.65 | 1.41 | 1.30 |
| Family history of presbycusis | | | | | | | | | | |
| $H_0$:p=0.25,x=0.00 | 40 | 46 | 91 | -70.51 | 41.03 | 334.06 | 72.30 | -133.79 | 14.88 | 23.28 |
| $H_1$:p=0.25,x=$\hat{x}$=0.60 | 40 | 46 | 91 | --- | -0.39 | --- | 46.99 | --- | --- | 0.003 |
| $H_2$:p=0.25,x=$\hat{x}$=0.59 | 40 | 46 | 91 | 5.21 | --- | 63.03 | --- | --- | 0.43 | --- |
| Multiplex sibships | | | | | | | | | | |
| $H_0$:p=0.25,x=0.00 | 34 | 77 | 43 | 14.10 | --- | 167.55 | --- | --- | 1.19 | --- |

When x was then fixed at its maximum likelihood estimate of 0.807, the revised hypothesis ($H_1$: p=0.25, x=$\hat{x}$=0.807) was accepted ($\chi^2_p$=2.57), despite the rather high maximum likelihood estimate of p ($\hat{p}$=0.287).

There were 58 informative sibships among the hearing by hearing matings with a positive family history (in a blood relative other than a parent or sib) of either hearing loss of early onset or mild to moderate hearing loss of late onset (presbycusis). The hypothesis that the hearing loss in these sibships was segregating as a recessive trait with no sporadic cases ($H_o$: p=0.25, x=0.00) was rejected ($\chi^2_p$=12.15; $\chi^2_x$=19.18). When x was allowed to assume its maximum likelihood value of 0.611, the hypothesis that p=0.25 was then accepted.

The positive family history group was further broken down into a group of 24 sibships with a positive family history of early onset hearing loss only, and into a second group of 40 sibships with a positive family history of presbycusis only. Table 63 shows that the hypothesis of autosomal recessive inheritance with no sporadic cases ($H_o$: p=0.25, x=0.00) was accepted in the subgroup with a positive family history of early onset hearing loss only ($\chi^2_p$=1.41, $\chi^2_x$=1.30). However the same hypothesis was rejected in the subgroup of H x H matings with a positive family history of presbycusis alone ($\chi^2_p$=14.88, $\chi^2_x$=23.28). In this group the maximum likelihood value of x was 0.59. When x was fixed at this value, a hypothesis of p=0.25 was then accepted ($\chi^2_p$=0.43). Table 63 also demonstrates that the segregation of the hearing loss in the 34 multiplex H x H families is consistent with the hypothesis of recessive inheritance with no sporadic cases ($\chi^2_p$=1.19).

In order to determine the effect of the 1964-65 rubella epidemic on the results of the segregation analyses, 90 sibships with probands born

during the period 7/1/64-3/30/65 were removed from the hearing by hearing mating groups. When this "rubella cohort" was analysed alone, the hypothesis of recessive inheritance with no sporadic cases ($H_0$:p=0.25, x=0.00) was, as expected, rejected ($\chi^2_p$=65.41; $\chi^2_x$=68.66), as shown in Table 64. When x was fixed at its maximum likelihood value of 0.85, the revised hypothesis ($H_1$: p=0.25, x=$\hat{x}$=0.85) was then accepted ($\chi^2_p$=0.0014). When the group of H x H matings with no family history of hearing loss was reanalysed after the removal of 46 sibships (each having a proband born during the epidemic period), the maximum likelihood value of x dropped from its previous value of 0.81 to 0.71, as shown in Table 64.

Deaf by Hearing Matings: The sibships resulting from the D x H matings were ascertained by incomplete selection through a deaf student at the school. Because of the very low chance that sporadic hearing loss would occur in two generations of the same family, the hearing loss in these families is assumed to represent the effects of dominant genes, with no sporadic cases. When these families were analysed using equation 2 above, the hypothesis of fully penetrant dominant inheritance was accepted, as shown in Table 64. When p was fixed at its maximum likelihood value of 0.257, an even better fit to the data was observed ($\chi^2_p$=0.00002); indicating that the reduction in the segregation ratio could be due to decreased penetrance (P=0.257/0.50=0.52) in these families.

Deaf by Deaf Matings: Hearing loss in the families with D x D matings is assumed to be genetic because each mating had at least one child (the proband) with a hearing loss. A proportion, y , of these sibships contained only deaf children and are termed non-segregating. The hearing loss in these children could be the result of homozygosity for recessive

Table 64

Segregation Analysis of Informative Sibships for H x H and D x H Matings Among Parents of Students at Maryland School for the Deaf ($\bar{H}$= 0.488)

| Hypothesis tested | Sibships | Overall | | $U_p$ | $U_x$ | $K_{pp}$ | $K_{xx}$ | $K_{px}$ | $\chi^2_p$ | $\chi^2_x$ |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Affected Children | Hearing Children | | | | | | | |
| H x H, including only sibships with proband born in 1964-65 rubella period | | | | | | | | | | |
| $H_0$:p=0.25,x=0.00 | 90 | 97 | 241 | -236.11 | 99.68 | 852.33 | 144.71 | -336.99 | 65.41 | 68.66 |
| $H_1$:p=0.25,x=$\hat{x}$=0.85 | 90 | 97 | 241 | 0.24 | --- | 39.75 | --- | --- | 0.0014 | --- |
| H x H, negative family history, excluding 46 sibships with proband born in rubella period | | | | | | | | | | |
| $H_0$:p=0.25,x=0.00 | 65 | 77 | 133 | -95.56 | 35.04 | 546.43 | 66.23 | -186.56 | 16.71 | 18.54 |
| $H_1$:p=0.25,x=$\hat{x}$=0.71 | 65 | 77 | 133 | 15.54 | --- | 63.78 | --- | --- | 3.78 | --- |
| D x H | | | | | | | | | | |
| $H_0$:p=0.50 | 8 | 11 | 17 | -10.86 | --- | 38.21 | --- | --- | 3.09 | --- |
| $H_1$:p=$\hat{p}$=0.257 | 8 | 11 | 17 | 0.034 | --- | 65.45 | --- | --- | 0.00002 | --- |

alleles in both parents, or to homozygosity for a completely penetrant dominant allele in one of the parents. The latter explanation should be dismissed because of its very low likelihood. The remaining families produced both affected and hearing offspring, and are termed doubly segregating. These sibships could be produced by matings which are a.) dominant by non-genetic or dominant by recessive, b.) dominant by dominant (heterozygous), or c.) homozygous recessive by heterozygous carrier (deaf from another cause). Although this last explanation, (c) is theoretically possible, it too should be dismissed from further consideration due to the low probability of a homozygote mating with a carrier who is coincidentally deaf from another cause.

In the D x D matings the distribution of $\underline{r}$ affected offspring is expressed by

$$P(r=s/r>0)=\frac{(1-y)p^s + y}{1-(1-y)(1-p\pi)^s}$$

in the non-segregating sibships, and

$$P(0<r<s)=\frac{\binom{s}{r}(1-y)p^r(1-p)^{s-r}}{1-(1-y)(1-p\pi)^s}$$

in the segregating sibships. The null hypothesis, that the proportion of families who could not segregate (because the parents were homozygous for recessive alleles for deafness) was zero ($H_o$: y=0.00), and that the segregating families consisted of dominant by non-dominant matings with a segregation ratio equal to that in the D x H matings (p=0.257) was rejected, as shown in Table 65 ($X^2$=28.32, p < 0.001). Using a version of the Nelder-Mead simplex direct search method of function optimization, the best estimates of the values of p and y were 0.31 and 0.18, respectively. This estimate of y can be used in the

Table 65

Nelder-Mead Simplex Optimization Estimate of p and y in D x D Matings Among Parents of Students at Maryland School for the Deaf

| Hypothesis tested | Sibships | Overall | | Likelihood | Log Likelihood |
|---|---|---|---|---|---|
| | | Affected Children | Hearing Children | | |
| $H_0$: p=0.257, y=0.00 | 21 | 43 | 16 | $0.23 \times 10^{-11}$ | -26.79 |
| $H_1$: $\hat{p}$=0.31, $\hat{y}$=0.18 | 21 | 43 | 16 | $0.33 \times 10^{-5}$ | -12.63 |

Likelihood ratio test for $H_0$:

$$X^2 = -2 \log \frac{\text{Likelihood } H_0}{\text{Likelihood } H_1}$$

$$X^2 = -2 [(-26.79)-(-12.63)]$$

$$X^2 = 28.32, \; p < 0.001$$

calculation of the proportion of deafness due to dominant genes, as shown in the next section.

## CLASSIFICATION OF HEARING LOSS

Table 67 provides summary breakdowns of the proportions of dominant, recessive, X-linked, and sporadic hearing loss in the MSD population and Table 68 provides a comparison of the summary estimates of such classification in the respondent and non-respondent groups. For each mating type, the number of sporadic cases was estimated by

$$n_i = x_i N_i ,$$

where $x_i$ is equal to the estimate of the proportion of sporadic cases among all cases in sibships of that mating type, and $N_i$ equals the total number of deaf children in sibships of that mating type. Thus, the pooled estimate of the proportion of sporadic cases among all cases would be

$$X = \frac{\Sigma n_i}{\Sigma N_i}$$

or

$$X = \frac{(0.774 \cdot 332) + (0.0 \cdot 11) + (0 \cdot 43)}{332 + 11 + 43}$$

$$X = 0.6658.$$

Estimates of the number of genetic cases resulting from dominant, recessive, or X-linked genes were made as follows. In the sibships resulting from D x D matings, an estimate of the number of offspring with recessive hearing loss, $R_r$ can be described by

$$R_r = y \left(\frac{R + C}{N}\right) N$$

Table 66

Excess of Sibships of Students at Maryland School for the Deaf that Include Only Male Deaf Sibs

| Deaf children in sibship | Sibships other than males only deaf | Sibships with only males deaf | | |
|---|---|---|---|---|
| | | Observed | Expected* | Excess |
| 2 | 11 | 11 | 3.63 | + 7.37 |
| 3 | 7 | 0 | 1 | - 1 |
| 4 | 0 | 0 | 0 | 0 |
| 5 | 0 | 0 | 0 | 0 |
| Total | 18 | 11 | 4.63 | + 6.37 |

* Expected = $N_k/2^k-1$ (Fraser, 1965).

Table 67

Summary of Estimated Classifications of Hearing Loss in the Families of Students at Maryland School for the Deaf

| Parental mating type | Estimated proportion sporadic cases | Overall deaf offspring | Offspring with | | | |
|---|---|---|---|---|---|---|
| | | | Sporadic deafness | Dominant deafness | Recessive deafness | X-linked deafness |
| H X H | 0.774 | 332 | 257 | 7 | 62 | 6 |
| D x H | 0.0 | 11 | 0 | 11 | -- | - |
| D x D | 0.0 | 43 | 0 | 32 | 11 | - |
| Total | | 386 | 257 | 50 | 73 | 6 |
| Percentage of all deafness | | | 66.58 | 12.95 | 18.92 | 1.55 |
| Percentage of genetic deafness | | | | 38.76 | 56.59 | 4.65 |

which reduces to

$$R_r = y\ (R + C),$$

where R equals the number of deaf offspring, C equals the number of hearing offspring, N equals the number of sibships, and y equals the proportion of non-segregating families with only deaf offspring. There were 43 deaf children and 16 hearing children produced by the D x D matings.

Thus

$$R_r = 0.18\ (59)$$

$$R_r = 11.$$

The estimates of the number of offspring from D x D matings with dominant and recessive deafness are therefore 32 and 11, respectively.

Although most of the hearing loss in the genetically deaf products of the H x H matings is due to homozygosity of recessive alleles, there is undoubtedly a certain proportion of deafness due to effects of incompletely penetrant dominant genes, and to X-linked genes. An estimate of the number of X-linked cases from the H x H matings was made, as shown in Table 66. This table shows the number of multiplex sibships from the H x H matings where causes of deafness in the proband other than X-linked recessive genes (acquired causes, suspected autosomal recessives due to parental consanguinity, autosomal dominant inheritance pattern, or autosomal dominant or recessive syndromes) could be ruled out. Shown for each sibship size are the expected number of sibships in which all deaf sibs are males. These numbers are estimates, based on the expected relationship between multiplex sibships containing only deaf females or both deaf females and deaf males, and those multiplex sibships containing only deaf males.

Thus,

$$\text{Exp} = \frac{N_k}{2^k - 1}$$

would represent the expected number of multiplex sibships containing only deaf males, where $N_k$ equals the number of multiplex sibships other than male only affected, containing $\underline{k}$ affected individuals (Fraser, 1965). Thus, because the numbers of "male only affected" and "female only affected" multiplex sibships would be expected to be roughly equal, the excess number of "male only affected" sibships was used as the estimate of the number of X-linked cases in the population. As shown in Table 66, there were an estimated six cases of X-linked deafness in offspring of H x H matings in the MSD population.

Although the hypothesis of fully penetrant dominant genes was not rejected in the D x H matings, the maximum likelihood value of p was less than 0.50 ($\hat{p}$=0.257). This estimate, combined with the rather high values of $\hat{p}$ in the H x H matings implies that some of the deaf offspring of the H x H matings are deaf due to dominant genes, with non-penetrance in one of the parents. An estimate of the actual number of such offspring, $R_D$, was calculated by

$$R_D = \left(\frac{N_1}{2p_1} - N_1\right)\left(\frac{R_2 + C_2}{N_2}\right) p_1,$$

$$R_D = \left(\frac{8}{2(0.257)} - 8\right)\left(\frac{199 + 85 + 48 + 376 + 195 + 92}{169 + 78 + 42}\right).257$$

$$= 7,$$

where $N_1$ and $N_2$ equal the number of sibships produced by the D x H and H x H matings, respectively; $R_2$ and $C_2$ equal the number of deaf and normal offspring produced by the H x H matings; and $p_1$ equals

the segregation frequency in the D x H sibships. There are, therefore, an estimated seven offspring with dominant deafness in the H x H sibships. The hearing loss in the remaining offspring was considered to be the result of homozygosity of recessive alleles for deafness.

As shown in Table 67, the above classification provides an estimate of approximately 35% for the proportion of deafness in the MSD population due to genetic factors. Among the group with genetic deafness, the estimated proportions of recessive, dominant and X-linked deafness were 57%, 39%, and 5% respectively. As shown in Table 68, the summary estimates of the proportion of dominant, recessive, X-linked, and sporadic deafness are very similar in the respondent and non-respondent groups.

Table 68

Classification of Hearing Loss in the Families of Students at Maryland School for the Deaf: Summary Estimates in Respondents and Non-respondents

| Type of deafness | RESPONDENTS (N=231) | | NON-RESPONDENTS (N=96) | |
|---|---|---|---|---|
| | Percent of total | Percent of genetic | Percent of total | Percent of genetic |
| Sporadic | 63.6 | -- | 68.7 | -- |
| Recessive | 21.2 | 58.3 | 17.7 | 56.7 |
| Dominant | 13.4 | 36.9 | 11.5 | 36.7 |
| X-linked | 1.8 | 4.8 | 2.1 | 6.6 |

# DISCUSSION

## DISCUSSION

There have been numerous previous studies of a variety of deaf populations in the USA and in other countries (see Table 13), many containing at least as many deaf individuals as the Maryland School for the Deaf. That discrepancies exist between the results of such studies is not surprising in view of the different populations studied. Deaf individuals have variously been ascertained from social groups for the deaf, schools or special educational programs for the hearing impaired, or from children or adults referred to hearing and speech clinics. In many surveys, those with postnatal onset or "acquired" deafness were excluded, which obviously leads to gross inconsistencies. As such, many of the various survey results are not strictly comparable to each other and one should therefore always consider the population from which a survey sample was drawn.

Unlike the ODS Annual Survey, which includes data on students enrolled in a variety of special educational programs for hearing impaired students, some with milder forms of hearing loss, the MSD population consists only of children with hearing loss of sufficient degree to warrant placement in a residential school for the Deaf. Careful audiologic screening at MSD refers many applicants with pure conductive hearing loss for possible surgery, and therefore most, if not all, MSD students suffer from a sensorineural hearing loss. Furthermore, few of the MSD students at the Frederick, Maryland campus of MSD suffer from severe additional handicapping conditions. As such, MSD is undoubtedly similar to and perhaps

representative of, many other state-supported schools for the deaf in the United States.

Although several previous studies of childhood hearing loss have, at least in part, utilized anamnestic data, none have attempted to make such extensive or primary use of a self-administered questionnaire as an instrument for data collection as has this study. Self-administered questionniares have been widely used to gather data for survey research, most commonly in the psychological and sociological areas, and are designed to be completed by the respondent without the help (or hindrance) of an interviewer. Several studies have documented that the use of self-administered questionnaires provided more information than the administered type (see Bennett and Ritchie, 1975). Over 30 years ago, studies using the Cornell Medical Index (one of the earliest and most widely used health history questionnaires) demonstrated that this carefully constructed, self-administered form yielded significantly more positive items of medical history than physicians recorded when interviewing the very same patients (Brodman et al., 1949). More recently, in a comparison of the traditional medical history obtained by interview, with a self-administered questionnaire, it was found that the latter obtained about three times as many symptoms. When relevant medical symptoms were classified as either "significant" or "non-significant", it was found that the self-administered questionnaire collected nearly twice as many significant symptoms (Young, 1971). Thus, as a method of data collection, the well-designed self-administered questionnarie appears to be at least comparable, if not in some cases superior, to the more traditional case history and administered questionnaire methods. The self-administered questionnaire method is especially useful when large amounts of data

need to be collected, as in the present study.

There are several distinct advantages and disadvantages in using the self-administered questionnaire survey approach. In terms of the advantages, the standardization of measurement is ensured, in that all potential respondents are asked the same questions in the same way. This method of standardization enhances test-retest reliability, which can be further improved by using "closed" rather than "open" questions. The presence of an interviewer, besides being extremely costly in time and expense, may introduce unwanted or unintentional biases (Cannell et al., 1968). In addition, self-administered questionnaires allow the respondents to work at their own pace, to consult with health records and other family members, and also provide for both visual and auditory recognition of technical terms, phrases, and checklist items, which are commonly found in medical questionnaires. There are, to be sure, certain disadvantages to this method of data collection. The questionnaire is not simply a collection of questions on a form to be filled out. Rather, in its proper form, the questionnaire is a scientific instrument for measurement and for the systematic collection of data, that therefore must be carefully designed and constructed, using simple and straightforward questions that can be understood by written instructions. Failure in this regard can lead to problems with data from respondents with very low intelligence or very poor reading ability. Thus, those with poor vision, including many elderly persons, are poor candidates for this approach to data collection.

Because the goal is to communicate with the respondent using the questionnaire as a medium, it behooves one to take great care in constructing questions that can be well understood, and to encourage the

respondent to reciprocate in this process by returning a properly completed questionnaire. Response in this context is not a simple stimulus response, but a rather more complex process in which the respondent actually selects from his total life experience, the portions that will become questionnaire data. The questionnaire, then, serves to focus attention on particular aspects of the life experience that may or may not be organized in the respondents' mind, and which almost certainly in some instances, will be vague or confused because of natural limitations of memory. Indeed, the type of data sought may alter the effects of memory on the response process. It has been shown, for example, that hospital episodes are remembered more clearly than physician visits (Cannell and Marquis, 1967), and that physician visits are better recalled than acute or chronic conditions (Madow, 1967). Other factors that may influence retention of medical information include impact and time. That is, the more recent the event(s) and the greater the impact of the experience on the life of the respondent, the better it will be remembered (Ley, 1972). Moreover, memory is selective, and may be influenced by coincidental psychic factors in addition to the continual elimination or extinction process. In some instances events may be recalled in an incomplete or distorted fashion which could magnify them out of all proportion. Thus, the response process is complicated by several factors, not the least of which frequently involves the respondent's own wishful thinking, or desire to please the doctor or research worker (Oppenheim, 1966). Added to the above considerations are the respondent's decisions about what he is actually prepared or willing to communicate. Many are, quite understandably, reluctant or unwilling to divulge information that may be embarrassing or be considered bizarre or otherwise socially

unacceptable. Some also are reluctant to provide information if they are unsure of or have misgivings about the purpose for which the data will be used, or the conclusions that might be drawn. Nevertheless, one can envision other forces which may counteract the censoring attitude and work in favor of rational, complete responses. Fortuneately (or perhaps unfortuneately), the complexities of the response process are probably not unique to questionnaire studies, and need not discourage us unnecessarily. However, it is nonetheless clear that some appreciation of the complexity of the response process is necessary prior to embarking on survey studies involving questionnaires (see Gordis, 1979). A number of excellent reference works are available on the subject of questionnaire design which can help one avoid many of the potential problems associated survey research using questionnaires (Oppenheim, 1966; Bennett and Ritchie, 1975; Berdie and Anderson, 1975; Dillman, 1978).

In this study, the high response rate and the relatively small amount of time needed to fill out the rather lengthy and detailed questionnaire indicate that the Hearing Loss Questionnaire, or others like it, can be a simple and efficient method by which to collect a large amount of data from a defined population (see also Cole et al., 1978; Pecoraro et al., 1979). Furthermore, as will be discussed later, it appears that the use of the Hearing Loss Questionnaire did not introduce additional or confound any existing response biases.

The parents of MSD students were much more likely to have had occupations in the Service and Farm worker categories than were parents in the US or Maryland populations (Table 22), and were less often reported as having White-collar jobs. These observations help explain the lower total family income reported by the MSD parents. Although the educational

levels of MSD mothers were roughly equivalent to mothers of US and Maryland families, MSD mothers were considerably better educated than were the 800 mothers of hearing impaired students reported by Rawlings and Jensema (1977) as part of the ODS Annual Survey. The higher educational level of MSD mothers may be, in part, the result of selective relocation to the State of Maryland. A number of MSD parents indicated that they had relocated to Maryland from elsewhere in the US, specifically so that their deaf child(ren) could attend MSD.* As Green (1970) has demonstrated, the overall family SES, and mother's educational level in particular, may be a major factor in family health behavior. In this regard, it would be of interest to study the proportion of environmental vs. genetic deafness according to family SES.

Within the MSD population itself, it is interesting to note that 25% (4/16) of main wage earners in the D x D matings held professional or technical jobs, compared to less than 3% (5/203) in the H x H matings (Table 25). Almost two-thirds of the former group had total annual family incomes of at least $20000, compared to less than one-third of the H x H group (Table 26). Consistent with these observations was the finding that deaf mothers of MSD probands were better educated than hearing mothers of deaf probands (Table 27). While the overall SES may not be quite as high in families with deaf children as in US families overall, it appears that MSD children of deaf parents were at least as well of (in terms of their family SES), if not better off, than their deaf peers with hearing

* The Maryland School for the Deaf is internationally known and recognized for its progressive teaching methods and, in particular, for its advocacy of the method of Total Communication.

parents. Data from this study indicate that the deaf probands may benefit in other ways when born to deaf parents. Not only was the proband hearing loss reportedly recognized earlier when both parents were deaf, but the probands began signing and speaking earlier than did probands with hearing parents. In addition, the mean IQ test scores were significantly greater (more than 20 points) in probands with deaf parents than the test scores of probands with hearing parents (Table 28), in agreement with earlier ODS Annual Survey findings. That the IQ test scores were higher in probands whose parents were deaf is consistent with the finding (Table 55) that mean adjusted IQ test scores were the highest in the probands whose hearing loss was thought to be the result of genetic factors. These are similar data to those from the ODS Annual Survey which revealed that the non verbal IQ scores were highest (102.5) in children in whom the probable cause of deafness was hereditary factors. Children whose hearing loss was said to be the result of maternal rubella had a mean non verbal IQ score that was six points less (96.5). The significant correlation of proband age when signing began with proband IQ test scores is consistent with reports of a correlation of age of speech with IQ test scores in hearing children. It is interesting to note that the proband age when the hearing loss was first reportedly recognized correlated significantly with SES variables, and that proband ages at signing and speaking correlated significantly with proband IQ test scores, but not with SES variables. The latter observations suggest that age at signing and speaking was not significantly influenced by those environmental factors relating to SES.

Audiometric data obtained from school records documented the serious hearing disability in the MSD probands (Table 31). The high

correlation between the pure tone air conduction thresholds and the speech reception and apeech awareness thresholds serves as an internal check on the consistency and accuracy of the audiometric test results (Table 32). The results of analysis of audiometric data with respondent rating of proband hearing ability in each ear extend the earlier studies of hearing self-assessment by Schein et al. (1970)(Tables 34-37). As would be expected, the range of audiometric thresholds was less in the MSD population than in the hearing clinic population studied by Schein. Nevertheless, the respondent rating of proband hearing ability in each ear was a useful indicator of actual proband hearing level, as measured by the Better Ear Average (BEA). Although the BEA alone is admittedly not a sufficient measure of overall auditory impairment, it is a very useful, and widely used and understood summary statistic.

The simplicity of the four-step rating scale of hearing ability belies the amount of information it yields. Combining the ratings of each ear results in a 10-step scale (Table 34). As the respondent assessment of proband hearing disability increased, the corresponding BEA threshold also increased. Also interesting is the finding that reported differences in the hearing ability between ears corresponded to actual differences in audiometric thresholds. When both ears were reportedly functioning equally well (or poorly), there was only a small difference in pure tone thresholds between right and left ears, and as the ratings increased from one to three step differences between ears, the difference in audiometric thresholds increased as well.

It is curious that a number of respondents checked that the hearing in one of the probands ears was "good", obviously contrary to fact. It may be that these respondents misinterpreted the intended meaning of

the questionnaire descriptions of relative hearing ability, or that these parents were displaying a form of denial with respect to their child's hearing handicap. Evidence for the latter possibility included the intriguing finding that almost 14% of questionnaire respondents stated that the proband's hearing was improving.

The finding that the parents most often first recognized the proband's hearing loss emphasizes the need for health workers to pay closer attention to parental concerns and questions about possible hearing difficulties in their children (see Fischer, 1981). Not surprisingly, maternal rubella, heredity, and meningitis were the three most frequently reported suspected causes of deafness in the MSD students by both their parents and doctors (Table 38). However it is noteworthy that twice as many parents as doctors suspected heredity as a cause of the child's deafness. In fact, according to the questionnaire responses, in only 12 (5.8%) cases did the doctor mention heredity as the probable cause of the child's hearing disability--a clear demonstration of the need to educate and inform health professionals about the extent to which genetic factors contribute to childhood deafness. This need is further evidenced by the data on parental perceived recurrence risks (Tables 39-41). Although these perceived recurrence risk responses are reasonably consistent with reality, it is nonetheless disconcerting that such a large proportion of parents (26%) with two or more deaf children, and 33% of parents whose deaf child's deafness was probably genetic, thought that their recurrence risk was very small. It would be of interest to know what recurrence risk estimates (or guesses) the probands' doctors would have made (or did make) for these families.

With the exception of a history of rubella or skin rash during

pregnancy, neither maternal illnesses nor maternal medication use during pregnancy were reported significantly more frequently by mothers with only one deaf child than by mothers with more than one deaf child (Tables 42, 43). Thus, these data provide little direct evidence that specific prenatal factors (other than maternal rubella) contributed heavily to deafness in this population. This is really not surprising since numerous studies support the current dogma that maternal rubella is (or was) the most common prenatal cause of deafness in current school aged children, and furthermore, the MSD population was probably not large enough to permit detection of less frequent factors. Similarly, meningitis was the only childhood illness that was reported significantly more frequently in the simplex probands than in the multiplex probands, (Table 56), in keeping with previously published data which indicate that meningitis is the most common postnatally acquired cause of childhood deafness (Jensema and Mullins, 1974; Fraser, 1976). Because genetic factors undoubtedly were responsible for deafness in some of the probands from the simplex sibships, perhaps a comparison of simplex and multiplex pregnancy histories with histories from a control group of mothers of hearing children may have been more enlightening in this regard.

Comparison of simplex with multiplex mothers did reveal that tobacco and alcohol use during pregnancy with the proband was over twice as frequent among mothers with one deaf child than mothers with more than one deaf child (Table 44). Furthermore, smoking during pregnancy was reported twice as frequently by mothers of probands whose deafness was due to maternal rubella, other (meningitis), and unknown factors, compared to mothers of probands whose hearing loss was probably genetic (Table 45). It is not clear how, or if, the physiological effects of

maternal smoking could result in any increased susceptibility of the hearing organ to infectious agents. Rather, perhaps smoking mothers themselves are more susceptible to infections which cause hearing deficits in the unborn fetus. If any such effects are present, the MSD data provide no evidence for a tobacco (or alcohol) dose-response relationship with degree of hearing loss in the probands (Table 46). It is curious that almost 30% of mothers with more than one deaf child reported induced labor with the proband, compared to 12% of mothers with only one deaf child (Table 48). The fact that the mean reported gestational ages of simplex and multiplex probands were essentially identical does not favor pre- or post- maturity as an explanation for this observation. To what extent the greater birthweights in the multiplex probands contributed to labor induction remains a matter for speculation. That twice as many simplex probands as multiplex probands were reportedly placed in incubators after delivery and that more of these incubator babies had deafness of "unknown" cause raises, once again, the concern about ambient noise levels in intensive care units. Such noise levels reportedly range from 56-75 dB, and are generally in the low frequency range (31-250 Hz) (Northern and Downs, 1978). Admittedly, infants placed into such incubators are often ill due to prematurity or systemic disease--however the noise exposure is continuous, often lasting for weeks. Thus, although it would seem highly presumptuous to attribute hearing loss to incubator noise levels with so many other well-known contributing (and often concomitant) factors involved, it would, nevertheless, be appropriate to attempt to attenuate noise levels in infant incubators as well as in special care nursuries themselves.

It is not surprising that the adjusted birth weights were significantly greater in the probands from multiplex sibships than from simplex sibships (Table 51). Likewise, the finding of significantly lower adjusted birth weights in the "maternal rubella" probands (Table 52) is consistent with lower birth weight in congenital rubella syndrome infants reported previously (see Peckham et al., 1979). The significantly lower age adjusted current weights in the rubella probands suggests that prenatal exposure to rubella virus has lasting effects, and confirms unpublished observations (Nance, personal communication) that children with congenital rubella syndrome have an asthenic habitus possibility with diminished subcutaneous fat. The finding that IQ test scores of rubella probands were not significantly lower than scores of the other probands implies that these children do not invariably suffer from significant intellectual impairment. However the MSD probands are a select group of deaf students in that many deaf children in Maryland with significant additionally handicapping conditions are not placed in the Frederick campus of MSD.

The most frequently reported medical problems or conditions in the maternal rubella probands were cataracts (11%), heart defect/murmur (45%), severe emotional/behavorial problems (16%), oligodontia (14%), and very slow growth (11%) (Table 60). The reports of unusual dentition (mostly oligodontia) deserve careful clinical followup and confirmation, as this particular trait has not been emphasized in previous descriptions

of congenital rubella syndrome patients. It appears that the MSD probands with congenital rubella syndrome have a wider variety of reported conditions than do probands whose deafness was not thought to be due to maternal rubella. It is important to note that reports of mental retardation were present in only two MSD probands (0.86%), compared to 8% of probands surveyed by the ODS Annual Survey (Trybus et al., 1980). Part of this discrepancy may result from the placement of multiply handicapped MSD applicants into other statewide special educational programs. In addition, it may be that few parents are willing or likely to believe, or admit, that their deaf child is retarded--which for most parents would be a subjective judgement, at best.

Although a variety of visual and eye problems were reported in the MSD probands, nyctalopia and tunnel vision (early signs of associated retinitis pigmentosa--Usher syndrome) were conspicuously absent from the list. It was assumed however that because a number of other visual problems were reported, and because almost all probands reportedly had had recent eye examinations, that the prenatal reports were reasonably accurate. About 10% of all MSD probands reportedly suffered from poor balance or clumsiness (presumably resulting from an associated vestibular dysfunction).

The group of probands whose deafness was considered to be of "unknown" etiology deserves more careful attention. Indeed probably several, if not many, of the children otherwise categorized perhaps

should have been classified into this group, since it might be argued that the probands were placed into the other groups using "post hoc; ergo propter hoc" reasoning. Without question, the assignment of a cause of deafness based on data from the medical or family histories is difficult, at best, in this type of investigation. This is especially true in individual cases in which there is more than one adverse factor in the medical or family history. As an example, in cases where the proband reportedly suffered from hearing loss after meningitis, it is not always (or ever) clear whether the child's hearing loss was a direct sequella of the disease itself or of the drugs used to treat the disease. Although a history of infection, trauma, or possible harmful perinatal events cannot be given undue weight, such data are nonetheless helpful in suggesting possible etiological relationships between early events and other variables of interest.

Population genetic study of human deafness makes sense for a number of reasons. First, hearing disability represents a relatively common group of underlying disorders, affecting as many as 1-2 per 1000 children in the United States. Second, assortative mating among the deaf is quite common, and therefore all three mating types (H x H, D x H, D x D) are available for study. Third, a high proportion of all deafness results from genetic causes. The results of this study confirm and extend more recent population surveys of human deafness, which have demonstrated the heterogeneous etiology of hearing disability (Stevenson and Cheeseman, 1956; Chung et al., 1959; Chung and Brown, 1970; Rose, 1975; Fraser, 1976). Most of the earlier investigators (with the notable exception of E.A. Fay) lacked this important insight. Thus, their

analyses suffered from oversimplified hypotheses and their attempts to explain all of congenital deafness as being the result of a single genetic cause were fruitless.

As in Rose's (1975) studies, the MSD sibships in this study were not separated by suspected cause of proband deafness prior to the genetic (or segregation) analyses. This practice is in contrast to some of the more recent surveys which attempted to classify cases of deafness into hereditary and non-hereditary causes prior to the segregation analyses (Sevenson and Cheeseman, 1956; Chung et al., 1959; Chung and Brown, 1970) Such procedures only serve to confuse matters by introduction of unwanted biases, the precise extent of which is difficult, if not impossible, to discern. Moreover, analyses performed on data from which certain sibships have been removed fail to capitalize on the ability of the modern methods of segregation analysis to separate high and low risk families, and to generate estimates of the proportion of sporadic cases. In contrast to the lower estimates of the proportion of sporadic cases in the U x U matings in the Northern Ireland (0.258) and Clarke School (0.270) populations, the maximum likelihood estimate of x in the non-consanguineous H x H matings at MSD with a negative family history of deafness was rather high ($\hat{x}$=0.807). However, the two earlier studies had, as noted above, removed many cases of non-genetic deafness prior to the actual analyses. The estimates of x in the H x H matings obtained by Rose in the Fay sibships (x=0.53), ODS Survey (x=0.605), and Gallaudet Survey ($\hat{x}$=0.37) were closer, though still lower, than that obtained in the MSD sibships. The large number of MSD probands with rubella deafness accounted for a large part of this difference, as evidenced by the substantial reduction in the estimate of x when the 1964-65 rubella

cohort was removed from the H x H matings. In agreement with analyses of the Clarke School and ODS Annual Survey data, the segregation of deafness in the multiplex sibships at MSD was consistent with recessive inheritance with no sporadic cases.

The maximum likelihood estimate of p ($\hat{p}$=0.287) in the overall MSD H x H matings supports the expectation that some of the deafness in the probands of these matings was the result of incompletely penetrant dominant rather than recessive alleles. An even higher estimate of p ($\hat{p}$=0.405) was obtained by Chung and Brown (1970) in the Clarke School survey. The maximum likelihood estimate of p among the MSD sibships form the D x H matings ($\hat{p}$=0.257) is similar to those obtained by Chung and Brown in the Clarke School sample ($\hat{p}$=0.350), and by Rose (1975) from the Fay data ($\hat{p}$=0.26) and from the ODS Annual Survey (+FH, $\hat{p}$=0.31; -FH, $\hat{p}$=0.21), all of which indicates that the genes causing dominant deafness in these sibships exhibited decreased and variable penetrance.

Rose demonstrated that among the H x H matings from the ODS and Gallaudet surveys, the proportions of sporadic cases were lower in the sibships with a positive family history than in those with a negative family history of deafness. Analyses of the MSD data are especially interesting in this regard, in that they extend Rose's findings by separating sibships into those with a positive family history of early versus late onset hearing loss. It is noteworthy, but not surprising, that in those sibships with a positive family history of early onset hearing loss, the hypothesis of recessive inheritance and no sporadic cases ($H_0$: p=0.25, x=0.00) was easily accepted (Table 63). This is in contrast to the results of analysis of the sibships with a positive family history of presbycusis, where the maximum likelihood estimate of

x was 0.59, with the deafness in the remaining sibships segregating as a recessive trait. This is an important observation, which implies that a positive family history of presbycusis portends some risk of childhood deafness to children of hearing couples, and which could be confirmed or refuted by continuing studies of larger populations. Admittedly, Paparella and others are, to a degree, quite justified in their criticism of the use of the term "presbycusis" and of the practice of lumping together all age-related hearing loss as a common clinical or etiologic entity. However, in counseling hearing couples with a deaf child about their recurrence risk, data that may be useful (eg hospital records) may not be available or may not include useful information on the hearing status of adult family members with age-related hearing disability. Because of such situations, which are not at all uncommon, the method used in this study, which considered sibships as having a positive family history of presbycusis if any direct blood relative of the proband reportedly had onset of hearing disability after age 40, at least approximates a "real life situation" with regard to the data analysis, and therefore makes practical sense. The results of these analyses, if confirmed, have important implications for genetic counseling, since they suggest that a positive family history of presbycusis substantially increases the recurrence risk of deafness in subsequent children born to a hearing couple with one deaf child.

This study, not unexpectedly, supports findings in previous studies of deaf populations which indicate that both genetic and non-genetic factors contribute to childhood deafness, and that the former account of a substantial proportion of the total (Stevenson and Cheeseman, 1956; Chung et al., 1959; Chung and Brown, 1970; Rose, 1975; Fraser, 1976).

A notable difference is the somewhat higher overall estimate of the proportion of sporadic deafness (66%) in the MSD population, compared to estimates of closer to 50% in Fraser's (1976) Northern Ireland study population, and Rose's (1975) studies of the Fay and ODS Annual Survey data. This observation is due in part, no doubt, to the fact that Fraser's datawere collected during 1958-67 and Rose's National Survey data during 1969-70, before the large number of children deafened as a sequella of the widespread 1964-65 rubella epidemic would have been of school age. Differences between the surveys may be more apparent than real, reflecting only expected heterogeneity of the populations sampled. On the other hand, the differences may indeed be real and thus demonstrate a natural variation in the etiological spectrum of hearing disability, both geographically and temporally (see Fraser, 1976). It may seem intuitive that poor socio-economic conditions would lead to a relative increase in the environmental factors responsible for childhood deafness. However, perhaps paradoxically, a high level of medical care and treatment may also contribute to an increase in the proportion of non-genetic deafness in individuals with otherwise lethal conditions.

It is certainly reasonable to assume that, as the proportions of genetic and non-genetic deafness vary in populations as a result of natural and extrinsic factors, the distribution of distinct alleles causing deafness might also be nonuniform. In this MSD survey, the estimated proportion of dominant deafness among all genetic deafness (39%), is only slightly higher than Chung and Brown's (1970) estimate in the Clarke School population (31%), but is considerably higher than the estimates Rose (1975) obtained in her studies. In her studies, Rose did not consider X-linked deafness, which was estimated to account for

almost 5% of genetic deafness in the MSD survey and about 3% in the Clarke School survey. Moreover, the algorithm Rose used to make the maximum likelihood estimate of y differed from the one used in the MSD survey, and her calculation resulted in a larger estimate (y=0.290 versus y=0.18) of that parameter. This difference in the estimates of y would then lead to a difference in the estimated proportion of children with recessive and dominant deafness born from D x D matings, and thus accounts for part of the difference between estimates of the proportion of dominant deafness in Rose's and in this MSD survey. Extrinsic factors might also lead to differences in proportions of dominant and recessive deafness. For example, as the economic status of the deaf improves, a concomitant increase in fertility would be expected to result in an increase in the autosomal dominant forms of deafness.

It is certainly gratifying that the estimates of the proportions of sporadic, dominant, recessive, and X-linked deafness in the questionnaire respondent and non-respondent groups were so similar, implying that use of the Hearing Loss Questionnaire did not introduce additional biases into the survey data. This observation is material in that researchers in general, and biomedical workers including human geneticists in particular, are increasingly making use of questionnaires as instruments for data collection.

It is the author's hope that additional research efforts be made in order to gain more insight into the role of inherited factors in the causation of hearing loss, allowing us to provide better services to those deaf individuals and their families who would benefit from a proper genetic evaluation and consult. It indeed behooves us to work harder at elucidating some more useful applications of basic principles, so that we might thereby disarm those who would decry the study of genetics as academic and jejune.

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# APPENDIX I

# HEARING LOSS QUESTIONNAIRE

# HEARING LOSS QUESTIONNAIRE

# *Directions*

Print the child's name in the space for Name of Child with Hearing Loss. Most of the questions ask about **this child** or the mother's pregnancy with this child. The questions in PART B ask about the relatives of the child.

Please answer each question as completely and as correctly as you can. There are no "right" or "wrong" answers. Most people do not remember all of the information asked for in the questionnaire. You may find that family scrapbooks, family Bibles, health records and other family members are helpful in answering some of the questions.

We know that the questionnaire is long and detailed. Please do not get discouraged. Just give as much information as you can. We have tried very hard to make the questionnaire easy to fill out. If you do not understand a question, read it over and try again, or leave it and go on to the next question.

You should not think that all of the diseases or conditions we ask about might be the cause of your child's hearing loss. Because there are so many possible reasons for hearing loss, we ask you to answer all of the questions — even if you know the cause of the child's hearing loss. All of your answers may give important information for our study, and will help other families with deaf children.

# PART A
# IDENTIFYING INFORMATION



Name of child with hearing loss: _____
First Middle Last

Child's home address: _____
Street

_____
City State Zip Code

Child's place of birth: _____
City State Country

Child's date of birth: _____
Month Day Year

Sex of child: ☐ Male ☐ Female

Name of Person filling out this Questionnaire

_____
First Middle Last

Address: _____
Street

_____
City State Zip Code

Telephone number: (_____) _____ ☐ TTY ☐ Voice
Area Code

Relationship to child with hearing loss: ☐ Mother ☐ Father ☐ Guardian ☐ Other (explain)

_____

Please check the ethnic or national background of the child's grandparents. You may check more than one box for each grandparent, if necessary, to show mixed background.

| ETHNIC OR NATIONAL BACKGROUND | FATHER'S PARENTS | | MOTHER'S PARENTS | |
|---|---|---|---|---|
| | CHILD'S GRANDFATHER | CHILD'S GRANDMOTHER | CHILD'S GRANDFATHER | CHILD'S GRANDMOTHER |
| American Indian | ☐ | ☐ | ☐ | ☐ |
| Black or negro | ☐ | ☐ | ☐ | ☐ |
| Chinese | ☐ | ☐ | ☐ | ☐ |
| English | ☐ | ☐ | ☐ | ☐ |
| French | ☐ | ☐ | ☐ | ☐ |
| German | ☐ | ☐ | ☐ | ☐ |
| Irish | ☐ | ☐ | ☐ | ☐ |
| Italian | ☐ | ☐ | ☐ | ☐ |
| Japanese | ☐ | ☐ | ☐ | ☐ |
| Jewish (Ashkenazi) | ☐ | ☐ | ☐ | ☐ |
| Mexican | ☐ | ☐ | ☐ | ☐ |
| Russian | ☐ | ☐ | ☐ | ☐ |
| Don't know | ☐ | ☐ | ☐ | ☐ |
| Other (specify) | _____ | _____ | _____ | _____ |

What is the highest grade or level of school or college that the child's mother and father have completed? List degrees, if any.

Child's mother _____

Child's father _____

Please write the present or most recent occupation (job) of the child's mother and father. (Be specific: for example — automobile mechanic, manager of department store, owner and pharmacist of drug store.)

Child's mother _____

Child's father _____

Please check your approximate total family income last year.

☐ None ☐ Less than $5,000 ☐ $5,000 ☐ $10,001 ☐ $15,001 ☐ $20,001 ☐ $30,001 ☐ Over $50,000

# PART B
# INFORMATION ABOUT THE FAMILY OF THE CHILD

In this part of the questionnaire you are asked to give information about all close relatives of the child with hearing loss, whether or not the relatives have a hearing loss. We would also like to have information about the child's more distant relatives who have hearing problems. For each relative with a hearing loss, write their approximate age when their hearing loss was first noticed.

## BROTHERS AND SISTERS OF THE CHILD

In the spaces below please list all of the child's brothers and sisters. Include stillbirths, miscarriages, and spontaneous abortions. Please tell if any of those you list are twins, half-brothers or half-sisters, or if they were adopted.

| | NAME | | | SEX | DATE OF BIRTH | AGE AT DEATH | PLACE OF BIRTH | HEARING STATUS | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | First | Middle Initial | Last | M or F | | | City, State (Country) | Normal | Don't Know | Mild Loss | Severe Loss | Age First Noticed |
| 1 | | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 2 | | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 3 | | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 4 | | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 5 | | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 6 | | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 7 | | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 8 | | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 9 | | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 10 | | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |

## FAMILY HISTORIES OF THE FATHER AND MOTHER OF THE CHILD

Were the parents of the child related in any way before marriage? ☐ YES ☐ NO
If YES, in what way? (e.g. first cousins) _____

In the correct spaces below, fill in as much of the requested information as you can for each person listed.

| RELATIONSHIP TO CHILD WITH HEARING LOSS | NAME | | | DATE OF BIRTH | AGE AT DEATH | PLACE OF BIRTH | HEARING STATUS | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | First | Middle Initial | Last | | | City, State (Country) | Normal | Don't Know | Mild Loss | Severe Loss | Age first Noticed |
| 1. CHILD'S FATHER | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 2. Father's father | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 3. His father | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 4. His mother | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 5. Father's mother | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 6. Her father | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 7. Her mother | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 8. CHILD'S MOTHER | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 9. Mother's father | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 10. His father | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 11. His mother | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 12. Mother's mother | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 13. Her father | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |
| 14. Her mother | | | | | | | ☐ | ☐ | ☐ | ☐ | ____ |

## AUNTS AND UNCLES OF THE CHILD

In the correct spaces below, fill in as much information as you can for each person listed (include maiden name).

| NAME: FATHER'S BROTHERS & SISTERS — First | Middle Initial | Last | SEX M or F | DATE OF BIRTH | AGE AT DEATH | PLACE OF BIRTH City, State (Country) | HEARING STATUS Normal | Don't Know | Mild Loss | Severe Loss | Age first Noticed |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ☐ | ☐ | ☐ | ☐ | |
| | | | | | | | ☐ | ☐ | ☐ | ☐ | |
| | | | | | | | ☐ | ☐ | ☐ | ☐ | |
| | | | | | | | ☐ | ☐ | ☐ | ☐ | |
| | | | | | | | ☐ | ☐ | ☐ | ☐ | |
| | | | | | | | ☐ | ☐ | ☐ | ☐ | |
| | | | | | | | ☐ | ☐ | ☐ | ☐ | |
| MOTHER'S BROTHERS & SISTERS | | | | | | | | | | | |
| | | | | | | | ☐ | ☐ | ☐ | ☐ | |
| | | | | | | | ☐ | ☐ | ☐ | ☐ | |
| | | | | | | | ☐ | ☐ | ☐ | ☐ | |
| | | | | | | | ☐ | ☐ | ☐ | ☐ | |
| 5 | | | | | | | ☐ | ☐ | ☐ | ☐ | |
| 6 | | | | | | | ☐ | ☐ | ☐ | ☐ | |
| 7 | | | | | | | ☐ | ☐ | ☐ | ☐ | |

## OTHER RELATIVES WITH HEARING LOSS

Please use the spaces below to list any other relatives with a hearing loss, and fill in as much information as you can.

| NAME — First | Middle Initial | Last | SEX M or F | DATE OF BIRTH | AGE AT DEATH | PLACE OF BIRTH City, State (Country) | HEARING STATUS Don't Know | Mild Loss | Severe Loss | Age first Noticed | RELATIONSHIP TO CHILD (e.g. COUSIN) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | | | | | | | ☐ | ☐ | ☐ | | |
| 2 | | | | | | | ☐ | ☐ | ☐ | | |
| 3 | | | | | | | ☐ | ☐ | ☐ | | |
| 4 | | | | | | | ☐ | ☐ | ☐ | | |
| 5 | | | | | | | ☐ | ☐ | ☐ | | |
| 6 | | | | | | | ☐ | ☐ | ☐ | | |
| 7 | | | | | | | ☐ | ☐ | ☐ | | |
| 8 | | | | | | | ☐ | ☐ | ☐ | | |
| 9 | | | | | | | ☐ | ☐ | ☐ | | |
| 0 | | | | | | | ☐ | ☐ | ☐ | | |

# PART C
# THE CHILD'S HEARING LOSS

. Who first thought that this child had a hearing problem?

- ☐ Mother
- ☐ Father
- ☐ Other relative
- ☐ Child
- ☐ Teacher
- ☐ Doctor
- ☐ Other (explain: _____)

. How old was the child then? _____

. Check which one of the following statements best describes the child's hearing loss?

- ☐ The hearing loss was probably present since birth or within the first few months of life.
- ☐ The hearing loss probably happened after birth or after the first few months of life.
- ☐ Don't know when the hearing loss happened.

. Check which one of the following statements best describes the child's hearing now.

- ☐ Hearing is slowing getting worse
- ☐ Hearing is quickly getting worse
- ☐ Hearing is getting better
- ☐ No change in the hearing ability
- ☐ Don't know

. Did the doctor(s) say that the child has a specific type of hearing loss or that the child has a related condition (such as Usher syndrome, Pendred syndrome, Waardenburg syndrome, or otosclerosis)?

- ☐ NO
- ☐ DON'T KNOW
- ☐ YES . . . please explain the type of hearing loss or the name of the related condition.

_____

_____

. Did the child ever use a hearing aid for one or more days?

- ☐ NO, the child never used a hearing aid
- ☐ YES, but does not use one now
- ☐ YES, the child uses one now

. Please check how well you think the child can hear now in each ear. If the child uses a hearing aid, check how he/she hears in each ear without the hearing aid.

| LEFT EAR | RIGHT EAR |
|---|---|
| ☐ Child's hearing is good in this ear | ☐ Child's hearing is good in this ear |
| ☐ A little trouble hearing with this ear | ☐ A little trouble hearing with this ear |
| ☐ A lot of trouble hearing with this ear | ☐ A lot of trouble hearing with this ear |
| ☐ Deaf in this ear | ☐ Deaf in this ear |

8. Does the child use sign language or homemade gestures and signs?

- ☐ NO
- ☐ YES . . . how old was the child when he/she began using signs? _____

). Does the child use any speech?

- ☐ NO
- ☐ DON'T KNOW
- ☐ YES . . . how old was the child when:
  - a) he/she first spoke single words? _____
  - b) he/she first spoke words together? _____

). What do you (the parent/guardian) think caused the child's hearing loss?

_____

_____

1. If you (the parents of the child) were to have another child, what do you think is the chance that the child would have a hearing problem? Check one.

- ☐ Very small chance
- ☐ About 10% (1 chance in 10)
- ☐ About 25% (1 chance in 4)
- ☐ About 50% (1 chance in 2)
- ☐ About 75% or greater
- ☐ Other (explain: _____)

2. What did the doctor say was the probable cause of the child's hearing loss?

_____

_____

_____

## PART D
## QUESTIONS ABOUT THE MOTHER WHILE PREGNANT WITH THE CHILD

Please check whether the mother had any of the illnesses listed below just before or during her pregnancy with this hild. Check the correct column for each illness listed. If you check "YES" for any illness, explain in detail below.

| ILLNESS WHEN PREGNANT | NO | DON'T KNOW | YES |
|---|---|---|---|
| 1. Rubella (German measles) | ☐ | ☐ | ☐ |
| 2. Regular measles | ☐ | ☐ | ☐ |
| 3. Flu or flu-like illness | ☐ | ☐ | ☐ |
| 4. Hepatitis | ☐ | ☐ | ☐ |
| 5. Skin rash | ☐ | ☐ | ☐ |
| 6. Chicken pox | ☐ | ☐ | ☐ |
| 7. Sugar diabetes (too much sugar in blood or urine) | ☐ | ☐ | ☐ |
| 8. Kidney or bladder infections requiring treatment | ☐ | ☐ | ☐ |
| 9. Anemia | ☐ | ☐ | ☐ |
| 0. Threatened miscarriage | ☐ | ☐ | ☐ |
| 1. Trauma or accident | ☐ | ☐ | ☐ |
| 2. Rh problem | ☐ | ☐ | ☐ |
| 3. Thyroid disease | ☐ | ☐ | ☐ |
| 4. High blood pressure or toxemia requiring treatment | ☐ | ☐ | ☐ |
| 5. Other illness (explain below) | ☐ | ☐ | ☐ |

In the space below, explain in detail any of the above illnesses which the mother had when pregnant with this child. For example, when in pregnancy, length of illness, treatment given, etc.) Also, for each illness tell if a doctor made he diagnosis.

_____

_____

_____

_____

Please check whether the mother took any of the medicines or drugs listed below just before or during her pregnancy with this child. Check the correct column for each medicine or drug. If you check "YES" for any medicine or drug, please explain in detail below.

| MEDICINE | NO | DON'T KNOW | YES |
|---|---|---|---|
| 16. Aspirin (or Excedrin, Bufferin, etc.) | ☐ | ☐ | ☐ |
| 17. Other non-Aspirin pain or fever medicine (Tylenol, Datril, etc.) | ☐ | ☐ | ☐ |
| 18. Nausea medicine | ☐ | ☐ | ☐ |
| 19. Antihistamines (Allergy medicine) | ☐ | ☐ | ☐ |
| 20. Antibiotics | ☐ | ☐ | ☐ |
| 21. Diabetes medicine | | | |
| a. Insulin shots | ☐ | ☐ | ☐ |
| b. Tablets or pills | ☐ | ☐ | ☐ |
| 22. Heart medicine | ☐ | ☐ | ☐ |
| 23. Tranquilizers or nerve pills | ☐ | ☐ | ☐ |
| 24. Epilepsy or seizure medicine | ☐ | ☐ | ☐ |
| 25. Antacids | ☐ | ☐ | ☐ |
| 26. Quinine | ☐ | ☐ | ☐ |
| 27. Hormones | ☐ | ☐ | ☐ |
| 28. Sleeping pills | ☐ | ☐ | ☐ |
| 29. Water pills or diuretics | ☐ | ☐ | ☐ |
| 30. Birth control pills | ☐ | ☐ | ☐ |
| 31. LSD | ☐ | ☐ | ☐ |
| 32. Other medicines or drugs (explain below) | ☐ | ☐ | ☐ |

In the space below, please give any details you can about the mother's use of medicines or drugs during the pregnancy with this child. (For example; month(s) in pregnancy, name and dose of medicine or drug, etc.)

_____

_____

_____

33. Did the mother smoke cigarettes during her pregnancy with this child?

☐ NO
☐ DON'T KNOW
☐ YES . . . how many cigarettes per day during pregnancy? _____

34. Did the mother drink alcoholic beverages (beer, wine, whiskey) during her pregnancy with this child?

☐ NO
☐ DON'T KNOW
☐ YES . . . how many drinks per day during pregnancy? _____
(one drink = one 12 ounce beer, or one 4 ounce glass of wine, or one ounce of whiskey)

35. Did the mother have any operations during her pregnancy with this child?

☐ NO
☐ DON'T KNOW
☐ YES . . . please explain (type of operation, when in pregnancy, etc.) _____

_____

_____

Was the mother put to sleep for the above operation(s)?

☐ NO
☐ DON'T KNOW
☐ YES

5. Did the mother of this child have any X-rays or radiation treatment during her pregnancy with this child?

- ☐ NO
- ☐ DON'T KNOW
- ☐ YES . . . what parts of body? _____
  when during the pregnancy? _____

## PART E
## QUESTIONS ABOUT THE BIRTH AND DELIVERY OF THE CHILD

Was this child born in a hospital?

- ☐ NO
- ☐ DON'T KNOW
- ☐ YES

Did the mother go into labor by herself (spontaneous) or did the doctor need to use medicines or drugs to start (induce) labor?

- ☐ No labor (Cesarean section)
- ☐ Spontaneous labor
- ☐ Induced labor
- ☐ Don't know

How long was the labor with this child? _____ hours

What kind of anesthetic was used for delivery of this child?

- ☐ General anesthesia (put to sleep)
- ☐ Spinal or epidural (needle in the back)
- ☐ Local or novocaine (numb the bottom)
- ☐ Other (explain: _____)
- ☐ Don't know

What was the type of delivery with this child?

- ☐ Vaginal delivery . . . were instruments (forceps) used to deliver baby? ☐ yes ☐ no
- ☐ Cesarean section (operation to remove baby)
- ☐ Don't know

Did the doctor think the child's birth was . . .

- ☐ Premature (early) . . . how many days? _____
- ☐ Full term (on time)
- ☐ Overdue (late) . . . how many days? _____
- ☐ Don't know

Were there any problems during the delivery (severe bleeding, injury to baby, etc.)?

- ☐ NO
- ☐ DON'T KNOW
- ☐ YES . . . please explain _____

At birth, did this child need any help to make him/her breathe or cry?

- ☐ NO
- ☐ DON'T KNOW
- ☐ YES . . . please explain _____

9. At birth, did the child need oxygen (air)?
   - ☐ NO
   - ☐ DON'T KNOW
   - ☐ YES . . . please explain _____

10. After birth, was this child put into an incubator (warmer)?
    - ☐ NO
    - ☐ DON'T KNOW
    - ☐ YES . . . how many days? _____

11. After birth, did this child need to go to a place in the hospital for special (intensive) care?
    - ☐ NO
    - ☐ DON'T KNOW
    - ☐ YES . . . how many days? _____: please explain reason _____

12. In the first few weeks after birth, did this child have yellow skin (jaundice or high bilirubin)?
    - ☐ NO
    - ☐ DON'T KNOW
    - ☐ YES . . . was the baby placed under special lights because of this problem?
      - ☐ NO
      - ☐ DON'T KNOW
      - ☐ YES . . . how many days? _____

13. Did this child have a change of blood (transfusion) in the first two months after birth?
    - ☐ NO
    - ☐ DON'T KNOW
    - ☐ YES . . . please explain reason _____

14. Was the baby on any medicines after he/she was born, when still in the hospital?
    - ☐ NO
    - ☐ DON'T KNOW
    - ☐ YES . . . please explain type of medicine, etc. _____

15. How many days did this child stay in the hospital before going home? _____ days

16. After this child was born, how many days did the mother stay in the hospital before going home? _____ days

17. How much did this child weigh at birth? _____ (lbs., ozs.)

18. How much does this child weigh now? _____ (lbs.)

19. How long was this child at birth? _____ (inches)

20. How tall is this child now? _____ (feet, inches)

21. List any medicines or drugs the mother took while breast feeding this child.

TYPE OF MEDICINE

| | |
|---|---|
| 1 _____ | 4 _____ |
| 2 _____ | 5 _____ |
| 3 _____ | 6 _____ |

# PART F
## QUESTIONS ABOUT THE HEALTH HISTORY OF THE CHILD

Please check whether this child has ever had any of the health problems listed below. Please check the correct column for each condition. When the answer is "YES", remember to write the child's age when the illness happened r began.

| HEALTH PROBLEM | NO | DON'T KNOW | YES . . . at the age of |
|---|---|---|---|
| 1. Rubella (German measles) | ☐ | ☐ | ☐ _____ |
| 2. Regular measles | ☐ | ☐ | ☐ _____ |
| 3. Mumps | ☐ | ☐ | ☐ _____ |
| 4. Chicken pox | ☐ | ☐ | ☐ _____ |
| 5. Scarlet fever | ☐ | ☐ | ☐ _____ |
| 6. Polio | ☐ | ☐ | ☐ _____ |
| 7. Whooping cough | ☐ | ☐ | ☐ _____ |
| 8. Meningitis | ☐ | ☐ | ☐ _____ |
| 9. Encephalitis (brain fever) | ☐ | ☐ | ☐ _____ |
| 0. Tuberculosis (TB) | ☐ | ☐ | ☐ _____ |
| 1. Mastoiditis | ☐ | ☐ | ☐ _____ |
| 2. Epilepsy, seizures, or convulsions | ☐ | ☐ | ☐ _____ |
| 3. Diphtheria | ☐ | ☐ | ☐ _____ |
| 4. Typhoid fever | ☐ | ☐ | ☐ _____ |
| 5. Kidney or bladder infections | ☐ | ☐ | ☐ _____ |
| 6. Thyroid disease | ☐ | ☐ | ☐ _____ |
| 7. Severe or frequent headaches | ☐ | ☐ | ☐ _____ |
| 8. Asthma, hay fever or food allergy | ☐ | ☐ | ☐ _____ |
| 9. Head or ear injuries | ☐ | ☐ | ☐ _____ |
| 0. Other (explain below) | ☐ | ☐ | ☐ _____ |

In the space below, explain in detail any of the above illnesses that the child had. (For example; length of illness, reatment given, etc.) Also, for each illness tell if a doctor made the diagnosis.

_____

_____

_____

_____

_____

_____

_____

_____

1. About how many times did this child have ear infections?

- ☐ None
- ☐ Less than 5
- ☐ 6-10
- ☐ More than 10

How were the ear infections usually treated? _____

_____

22. About how many times did the child have infections (other than ear infections) treated by antibiotics? (For example-pneumonia, bronchitis, chest infections, kidney infections, etc.)

- ☐ None
- ☐ Less than 5
- ☐ 6-10
- ☐ 11-15
- ☐ More than 15
- ☐ Don't know

Please check whether this child has had any of the operations listed below. Check the correct column for each operation. If the answer is "YES", write the child's age when the operation was done.

| OPERATION | NO | DON'T KNOW | YES . . . at the age of |
|---|---|---|---|
| 23. Tonsils taken out | ☐ | ☐ | ☐ _____ |
| 24. Adenoids taken out | ☐ | ☐ | ☐ _____ |
| 25. Sinus operation | ☐ | ☐ | ☐ _____ |
| 26. Mastoid operation | ☐ | ☐ | ☐ _____ |
| 27. Ear tube placement | ☐ | ☐ | ☐ _____ |
| 28. Eardrum lanced | ☐ | ☐ | ☐ _____ |

## PART G
## OTHER MEDICAL CONDITIONS

Check which of the following best describes the child's eye sight, without glasses or contact lenses. Check all that apply.

1. ☐ Normal vision
2. ☐ Nearsighted (trouble seeing far distances)
3. ☐ Farsighted (trouble seeing near distances)
4. ☐ Some loss of side vision (tunnel vision)
5. ☐ Some loss of night vision
6. ☐ Colorblind
7. ☐ Almost blind (explain cause, if known: _____)
8. ☐ Totally blind (explain cause, if known: _____)
9. ☐ Other (explain: _____)

0. Year of last eye examination _____

Check if this child has ever had any of the eye problems listed below. When the answer is "YES", please write the hild's age when the problem began.

| EYE PROBLEMS | NO | DON'T KNOW | YES . . . at the age of |
|---|---|---|---|
| 1. Cross-eyed (eyes point toward nose) | ☐ | ☐ | ☐ _____ |
| 2. Wall-eyed (eyes point away from nose) | ☐ | ☐ | ☐ _____ |
| 3. Nystagmus (dancing eyes) | ☐ | ☐ | ☐ _____ |
| 4. Cataract(s) | ☐ | ☐ | ☐ _____ |
| 5. Different colored eyes | ☐ | ☐ | ☐ _____ |
| 6. Glaucoma | ☐ | ☐ | ☐ _____ |

Please check whether the child ever had any of the conditions listed below. Check the correct column for each condition. If you check "YES", for any condition, explain below.

| CONDITION | NO | DON'T KNOW | YES |
|---|---|---|---|
| 17. Unusual shaped head | ☐ | ☐ | ☐ |
| 18. White patch of hair on head | ☐ | ☐ | ☐ |
| 19. Twisted brittle hair | ☐ | ☐ | ☐ |
| 20. Unusual facial appearance | ☐ | ☐ | ☐ |
| 21. Cleft lip and/or cleft palate | ☐ | ☐ | ☐ |
| 22. Unusual shaped teeth or missing teeth | ☐ | ☐ | ☐ |
| 23. Unusual shaped ear(s) | ☐ | ☐ | ☐ |
| 24. Goiter (swelling in neck) | ☐ | ☐ | ☐ |
| 25. Other thyroid problem | ☐ | ☐ | ☐ |
| 26. Heart defect or murmur | ☐ | ☐ | ☐ |
| 27. Unusual shaped fingernails or toenails | ☐ | ☐ | ☐ |
| 28. Completely or partially fused fingers or toes | ☐ | ☐ | ☐ |
| 29. Missing joint in fingers or toes | ☐ | ☐ | ☐ |
| 30. Extra fingers or toes | ☐ | ☐ | ☐ |
| 31. Clubfoot | ☐ | ☐ | ☐ |
| 32. Scoliosis (curved spine) | ☐ | ☐ | ☐ |
| 33. Frequent broken bones (more than 3) | ☐ | ☐ | ☐ |
| 34. Deformities of any bone | ☐ | ☐ | ☐ |
| 35. Albino (white skin color) | ☐ | ☐ | ☐ |
| 36. Scaly or very dry skin | ☐ | ☐ | ☐ |
| 37. Absence of sweating | ☐ | ☐ | ☐ |
| 38. Heavy freckling | ☐ | ☐ | ☐ |
| 39. Patchy skin color | ☐ | ☐ | ☐ |
| 40. Fits or fainting spells | ☐ | ☐ | ☐ |
| 41. Severe behavioral/emotional problem | ☐ | ☐ | ☐ |
| 42. Mental retardation | ☐ | ☐ | ☐ |
| 43. Diabetes (sugar) | ☐ | ☐ | ☐ |
| 44. Kidney disease | ☐ | ☐ | ☐ |
| 45. Blood in urine | ☐ | ☐ | ☐ |
| 46. Poor balance or clumsiness | ☐ | ☐ | ☐ |
| 47. Dizziness | ☐ | ☐ | ☐ |
| 48. Muscle problems | ☐ | ☐ | ☐ |
| 49. Problems with sense of smell | ☐ | ☐ | ☐ |
| 50. Very slow growth | ☐ | ☐ | ☐ |
| 51. Cancer | ☐ | ☐ | ☐ |

If you checked "YES", for any of the above conditions, please give any details you can about the problem. (For example, age of child, treatment given, etc.)

52. Has any relative of the child ever had any of the eye problems or other conditions listed in this part (PART G) of the questionnaire?

- ☐ NO
- ☐ DON'T KNOW
- ☐ YES . . . please list name of relative, relationship to child (e.g. cousin), and eye problem or other condition

| | NAME OF RELATIVE | RELATIONSHIP TO CHILD | EYE PROBLEM OR OTHER CONDITION |
|---|---|---|---|
| 1. | | | |
| 2. | | | |
| 3. | | | |
| 4. | | | |
| 5. | | | |
| 6. | | | |
| 7. | | | |
| 8. | | | |
| 9. | | | |

53. How much time did you spend filling out this questionnaire?_____

In the space below, please write any more information you can about the child or any other relatives that you think may be important. Also, please feel free to make comments about this questionnaire.

THANK YOU FOR YOUR HELP!!

# APPENDIX II

## MAILINGS TO STUDY PARTICIPANTS

# THE SIGN POST

Maryland School for the Deaf
Frederick & Columbia

VOLUME 7, NUMBER 5 JUNE, 19


## HEARING LOSS QUESTIONNAIRE

This summer parents of students at the Maryland School for the Deaf will be asked to fil out a Hearing Loss Questionnaire. The questionnaire asks for medical and family information about the students at MSD. This information will be studied by researchers at th Medical College of Virginia who are trying to learn more about the causes of hearing los

If the study is successful the Medical College of Virginia researchers hope to use their Hearing Loss Questionnaire to study hundreds of other families around the country. This research should help doctors give better information to parents about hearing loss in th children.

Watch your mail for the questionnaire. It is now at the printers and should be mailed t you in mid-summer.

★★★

## SUPERINTENDENT SPEAKS IN SOUTH AFRICA

There have been a number of exciting things happen at the School during the course of th 1978-79 school year. As always, we host an increasing number of visitors including inte national visitors. Because of the Maryland School for the Deaf's role in the implementation of Total Communication, other states and other countries look to us for help and advice. One of the highlights of the current school year, at least for me, was the rece trip to South Africa where I had a chance to share our philosophy with people from anoth nation who are caught up in a struggle to ensure that deaf children in South Africa have an opportunity to benefit from Total Communication.

In early April, a telephone call came from the city of Durban, South Africa from a membe of the Executive Committee of the South African National Council for the Deaf asking if would be willing to come to South Africa and offer the keynote address at the 50th Anniversary Congress of the South African National Council for the Deaf. The man who called was a corporate lawyer in Durban and the father of a 26 year old deaf son. This man is very active in work with the deaf in South Africa. The story does not really begin in April; however, it probably began in 1969 when a man from South Africa visited the Maryl School for the Deaf to observe our new Total Communication Program. This man, Norman Meider-Heitman, was head of a school for the deaf in the Transvaal Province of South Afr He was most impressed with our School and with the Total Communication Program and the t of us corresponded through the years following his visit here. He continued to request material and we would send him copies of speeches, copies of The Maryland Bulletin, and Proceedings of the Teachers Institutes. These materials he shared with his friends and colleagues in South Africa.

In 1973 I went to the University of Minnesota to give a talk and had a chance to visit t TVI Program in St. Paul. While visiting the program, I met the lawyer from Durban, Sout

MARYLAND SCHOOL FOR THE DEAF
Frederick, Maryland 21701

M. DENTON, Ph.D.
tendent

k Campus
62-4159

ia Campus
65-9611

July 17, 1979

Dear Parent/Guardian:

It is a pleasure to let our parents know that the Maryland School for the Deaf has been invited to participate in a research study to be conducted in cooperation with the Medical College of Virginia/ Virginia Commonwealth University. Dr. Walter E. Nance, Chairman, Department of Human Genetics, Medical College of Virginia has made several trips to Frederick over the past year to discuss this proposed project with officials of the School and with members of the Maryland School for the Deaf Board of Visitors. Dr. Nance was also guest speaker at one of the regular meetings of the Maryland School for the Deaf Parent, Teacher, Counselor Association. The parents who were present at that meeting thoroughly enjoyed Dr. Nance and found his talk to be most beneficial.

The purpose of the study is to learn more about the causes of deafness and hearing loss. As indicated above, this project has been reviewed and approved by the Maryland School for the Deaf Board of Visitors. Parents can be assured that the data provided by this study will be held in strictest confidence. We would like for you to know also that the participation of as many parents as possible will be necessary if the study is to be successful.

In a few days you will be receiving a Hearing Loss Questionnaire from Dr. Nance which we sincerely hope you will take the time to complete and return. Your help in this study is completely voluntary and all of us will be very grateful if you choose to participate. If you have any questions about the study, please don't hesitate to call Dr. Nance's office at (804) 786-9632 or the Maryland School for the Deaf at (301) 662-4159 (Voice or TTY).

Sincerely,

David M. Denton
Superintendent

DMD/cb

MEDICAL COLLEGE OF VIRGINIA
VIRGINIA COMMONWEALTH UNIVERSITY
MCV Station • Richmond, Virginia 23298 July 19, 1979

Dear Parent/Guardian:

As you recently learned from Dr. David Denton at the Maryland School for the Deaf, we have begun a study to learn more about the causes of hearing loss.

We know that there are many reasons why people lose their hearing. It could be because of birth injuries, infections, other complications of pregnancy, or because of inherited factors from the parents. However, our knowledge of the causes of hearing loss is still incomplete. To learn more about these causes we wish to collect medical and family information about present and former students at the Maryland School for the Deaf. This will allow us to give more complete information about hearing loss to families with deaf children.

For a successful study, we need information from as many families as possible. We have designed a Hearing Loss Questionnaire to collect the information we need. Please fill out the enclosed questionnaire for your child who is enrolled at the Maryland School for the Deaf and mail it back to us in the envelope we have provided. Please be sure to sign and return the Research Consent Statement as well, because we cannot include information you provide without your permission.

At the end of our study the results will be sent to you if you are interested. The information you give us will be considered confidential (private). It will be used only to learn more about the different types of hearing loss. Nobody will be identified by name in any publication resulting from this research.

Your help is entirely voluntary and you may leave the study at any time for any reason. Your decision to help or to leave the study will not affect your relationship with any doctor, medical center, or the Maryland School for the Deaf.

We hope you will agree to help us with this important research. If you have any questions about the study, or need help filling out the questionnaire, please write or call my office at (804) 786-9632 or the Maryland School for the Deaf at (301) 662-4159 (Voice or TTY).

Sincerely,

Walter E. Nance, M.D., Ph.D.
Professor and Chairman
Department of Human Genetics

WEN:clb

Enclosures

If you join our Hearing Loss Study, please read and sign the Research Consent Statement below. Please return it with the completed Hearing Loss Questionnaire. Thank you.

HEARING LOSS STUDY

RESEARCH CONSENT STATEMENT

I have read the description of the Hearing Loss Study and agree to help by filling out and returning the Hearing Loss Questionnaire.

I understand that the information I provide will be kept private and used only for the research purposes described.

I also understand that my help in the study is entirely voluntary and that I may leave the study at any time.

If you understand this form and want to help us with this study, please sign your name below.

Signed _____ Date _____ Witness _____

Signed _____ Date _____ Witness _____

I wish to receive a summary of the results of the study. ☐ Yes ☐ No

MEDICAL COLLEGE OF VIRGINIA
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Box 33

Dear Parent:

I am writing to thank you for returning your Hearing Loss Questionnaire. We had included a Research Consent Form along with the questionnaires, but must have left yours out by accident.

Would you please sign the enclosed Research Consent Statement and mail it back to us in the envelope we have provided?

Thanks again for your cooperation.

Sincerely,

Walter E. Nance, M.D., Ph.D.
Professor & Chairman
Department of Human Genetics

WEN/skf

enclosures

Dear Parent:

Several weeks ago we mailed you a research questionnaire. If yours is now in the mail to us, please accept our thanks.

If you have not yet had an opportunity to complete or return the questionnaire, we would very much appreciate your taking the time to help us with this important study. We are encouraged that almost half of the parents have already returned their questionnaires, but we need to have many more to make our study as complete and representative as possible.

If you did not receive your questionnaire or if you have any questions about the study, please call my office collect at (804) 786-9632. Thank you.

Sincerely,

Walter E. Nance, M.D., Ph.D.
Professor and Chairman
Department of Human Genetics
Medical College of Virginia
Richmond, Virginia 23298

MEDICAL COLLEGE OF VIRGINIA
VIRGINIA COMMONWEALTH UNIVERSITY
MCV Station • Richmond, Virginia 23298

Box 33

Dear Parent:

Because I was not able to contact you by telephone, I am writing to ask for your help. In late July Dr. Denton and I wrote to the parents of students attending the Maryland School for the Deaf. We explained that we are studying the causes of hearing loss and asked all of the parents to help us with our research by filling out a Hearing Loss Questionnaire and returning it to me.

We are happy that so many parents have helped us. However, some of the parents have not yet returned their questionnaires. Because people often move or are away from home during the summer and mail is sometimes delayed, I want to be sure that you received your questionnaire and have the chance to be a part of this exciting study.

If you did not receive your questionnaire, or if yours was lost or misplaced, please call my office collect at (804) 786-9532, and I will send you another one right away. If you did receive yours but have not yet returned it, I would greatly appreciate it if you would send it to me as soon as possible.

Our hearing loss study is very important and the information you can provide will allow us and other doctors to help many deaf children and their families. Thank you.

Sincerely,

Walter E. Nance M.D.

Walter E. Nance, M.D., Ph.D.
Professor & Chairman
Department of Human Genetics

WEN/skf

# THE SIGN POST

Maryland School for the Deaf
Frederick & Columbia

VOLUME 7, NUMBER 8 SEPTEMBER, 19

OOPS!

The Volume 7, Number 7 issue of The Sign Post, mailed out in the first week of August was printed as the July, 1979 issue. It should have read as August, 1979 issue. Somehow the Editor got his months mixed up. Today, you are reading the September issue and the Editor wishes you all a happy School year and regrets the error in the publication date.

HEARING LOSS QUESTIONNAIRE

In late July a Hearing Loss Questionnaire was mailed to the parents of the students at the Maryland School for the Deaf. The completed questionnaires are being studied by researchers at the Medical College of Virginia who are trying to learn more about the causes of hearing loss.

If you have not yet had an opportunity to complete or return your questionnaire, we would appreciate your taking the time to help with this important research. We are happy that many of the parents have already returned their completed questionnaires, but many more are needed to make the study as complete as possible.

If you did not receive your questionnaire or if you have any questions about the study, please call Dr. Walter E. Nance's office COLLECT at (804) 786-9632.

PTCA CALENDAR AT FREDERICK

Association Meetings: (Check your calendar and plan to attend.) October 6, 1979--HOMECOMING, 12:30 P.M. in the Ely Auditorium; brief business meeting and open house/social time. November 4, 1979--DINNER/BAZAAR. March 9, 1980--Program to be announced. April 1 1980--Election of Officers; program to be announced.

Executive Committee Meetings: October 1, 1979; October 29, 1979; March 3, 1980; and, April 7, 1980. (PTCA Executive Committee Meetings are held the Monday before the Association Meeting at 7:30 P.M. in the Ambrosen Administration Building.)

REMINDER . . . the Booster Club's 1979 Raffle will end Saturday, October 6th (Homecoming). Persons helping with ticket sales please be sure tickets are turned in by this date.

HOMECOMING 1979

This year the Homecoming Event at the Maryland School for the Deaf will be held on Saturday October 6th. A gala event is being planned for the students, parents, visiting team members, alumni, and friends. Be sure to be on the lookout for notices and circulars coming from the School through your children. For additional information regarding Homecoming activities, please contact the School at 662-4159. IMPORTANT NOTICE . . . the PTCA meeting will be held in the Ely Auditorium at 12:30 P.M. and will conclude in time for the exciting football game. COME ONE, COME ALL!!!

# APPENDIX III

## THE PHILOSOPHER AND HER FATHER

The following verses give a popular account of the mechanism of hearing. They first appeared in the Illustrated London News on January 17, 1852 (see Ellis, 1900).

## THE PHILOSOPHER AND HER FATHER

A sound came booming through the air,
"What is that sound?" quoth I.
My blue-eyed pet, with golden hair,
Made answer, presently,
"Papa, you know it very well--
That sound--it is Saint Pancras' Bell."

My own Louise, put down the cat,
And come and stand by me;
I'm sad to hear you talk like that,
Where's your philosophy?
That sound--attend to what I tell--
That sound was not Saint Pancras' Bell.

Sound is the name the sage selects
For the concluding term
Of a long series of effects
Of which the blow's the germ.
The following brief analysis
Shows the interpolations, Miss.

The blow, which when the clapper slips
Falls on your friend the Bell,
Changes its circle to ellipse
(A word you'd better spell).
And then comes elasticity,
Restoring what it used to be.

Nay, making it a little more,
The circle shifts about
As much as it shrunk in before
The Bell, you see, swells out;
And so a new ellipse is made
(You're not attending, I'm afraid).

This change of form disturbs the air,
Which in its turn behaves
In like elastic fashion there,
Creating waves on waves;
Which press each other outward, dear,
Until the outmost finds your ear.

Within that ear the surgeons find
A tympanum or drum,
Which has a little bone behind,--
Malleus, it's called by some;
But those not proud of Latin Grammar
Humbly translate it as the hammer.

The wave's vibrations this transmits
On to the incus bone
(Incus means anvil, which it hits),
And this transfers the tone
To the small os orbiculare,
The tiniest bone that people carry.

The stapes next--the name recalls
A stirrup's form, my daughter--
Joins three half-circular canals,
Each fill'd with limpid water;
Their curious lining, you'll observe,
Made of the auditory nerve.

This vibrates next--and then we find
The mystic work is crown'd;
For then my daughter's gentle Mind
First recognises sound.
See what a host of causes swell
To make up what you call "the Bell."

Awhile she paused, my bright Louise,
And pondered on the case;
Then, settling that he meant to tease,
She slapped her father's face.
"You bad old man, to sit and tell
Such gibbergosh about a Bell!"