4-18-2003

Hearing Evaluation in Infants: An Update for Pediatricians

Janet E. Sullivan
University of South Florida

Hearing Evaluation in Infants: An Update for Pediatricians

Janet E. Sullivan

A professional Research Project submitted to the Faculty of the Department of Communication Sciences and Disorders in Partial Fulfillment of the Requirements for the Degree of

Doctor of Audiology

Theresa Chisolm, Chair
Lewis Barness
Ann Barron

April 18, 2003
Tampa, FL

Key words: Auditory development, Otoacoustic emissions, Auditory brainstem response

TABLE OF CONTENTS

TABLE OF CONTENTS, continued

LIST OF TABLES AND FIGURES

Hearing Evaluation in Infants: An Update for Pediatricians

Janet E. Sullivan

(ABSTRACT)

This paper provides an overview of developmental timetables relevant to hearing and of current pediatric audiological techniques and practices. The first sections summarize structural and functional development of the auditory pathway and the development of primary auditory processing. These developmental sequences appear to follow similar paths in humans and animals. Speech and music perception involve more complex processing and are strongly influenced by experience. Hearing disorders affect the perception of complex sounds in a variety of ways, depending on the site(s) of lesions. Early onset hearing impairment, including conductive loss from chronic otitis media, can seriously impede language development.

Language cannot develop normally without adequate speech stimulation. Sensitive and inexpensive techniques are available for performing neonatal hearing screening, and early intervention has a positive effect on development of language skills in hearing-impaired children. Thus, the National Institute of Health has recommended nationwide universal newborns hearing screening. The rationale and methodology of universal screening programs is summarized in the chapter.

Advances in the field of the genetics of hearing impairment are also reviewed

Recent advances in the field of auditory physiology - coupled with longstanding concerns about delayed identification of hearing impairment - have precipitated public health initiatives (National Institute of Health, 1993) and legislation for neonatal hearing screening programs (Blake & Hall, 1990). Pediatric audiology, once more "art" than science, is now largely based on physiologic methods rather than observed behavior. With current techniques, it is not only possible to detect hearing impairment at birth but also to determine the site of the lesion and to obtain close estimates of hearing threshold at specific frequencies (Werner, Folsom, & Mancl, 1993). Habilitative measures, including amplification, can begin within weeks of birth. Protocols for the management of hearing impairment are guided not only by the site of the lesion but by the developmental sequences and interactions among all of the child's sensory modalities.

This chapter provides an overview of developmental timetables relevant to hearing and of current pediatric audiological techniques and practices.

DEVELOPMENTAL SEQUENCES

PRENATAL STRUCTURAL/PHYSIOLOGIC DEVELOPMENT OF THE AUDITORY SYSTEM

For obvious reasons, most studies of structural and physiologic development of the auditory system have been performed in animals. However, gross anatomical development of the auditory system in humans appears to follow the same sequence as that of many animal species (Pujol., Lavigne-Rebillard & Uziel, 1990). . Avian species provide particularly useful models, because their behavior, including embryonic behavior, has been studied extensively, and their hearing develops similarly to that of

humans. Comparative studies show that the relationship between the onset of hearing and time of birth varies among animal species, but the proportion of time between conception and the onset of auditory function (referred to as the *silent period*) is consistent across species. Morey and Carlile (1990) demonstrated similarity in this proportion among species by recording the time of onset of the first cochlear response (the cochlear microphonic). Although the time of appearance of the cochlear microphonic is not known in humans, other morphologic and physiologic measures indicate that the silent period in humans is remarkably similar to that of other animals (Pujol, Lavigne-Rebillard, & Uziel, 1990; Bredberg, 1968).

The otic placode can be identified around 23 days of gestation (Streeter, 1917), and differentiation of the organ of Corti begins around the tenth week of gestation. As in other mammals, structural development follows a base-to-apex gradient, corresponding to the low- and high- frequency regions of the organ of Corti (Bredberg, 1968). Differentiation of hair cells, separation of the tectorial membrane from the organ of Corti, and innervation in the human cochlea at 24 weeks gestation are similar to those of other mammals at the onset of their cochlear function. Action potentials elicited from the eighth nerve at 27 weeks gestation in preterm infants (Stockard, Stockard,& Coen, 1983) confirm that the cochlea is functional and the neural connection is present at that time.

DEVELOPMENT OF HEARING FUNCTION

Structurally, the cochlea appears capable of function around three months before birth (Lavigne-Rebillard & Pujol, 1988). However, assessing responsivity *in utero* is complicated by the attenuation of environmental sounds by the mother's abdomen and

amniotic fluid and by the high level of ambient noise *in utero.* Gross motor responses (Wedenberg, 1965). or heart rate changes (Tanaka & Arayama, 1969) can be elicited by intense sound at 26 to 28 weeks gestational age. Lower intensities are not effective. Response thresholds could be elevated by masking noise, by the lack of air conduction of sound, or by cochlear immaturity. Behavioral studies of preterm infants do not shed much light on the question. There have been no attempts to measure behavioral threshold to sound in preterm infants, because behavioral responsivity at this age is not a reliable index of hearing (Gerber, Lima & Copriviza, 1983).

Primary auditory processing refers to the extraction and coding of the physical attributes of sound, while secondary auditory processing can be thought of as the selection of combinations of both the quantitative and qualitative attributes of sound to accomplish a "perceptual goal" (Werner, 1996), tasks which might include the detection of sound, discrimination among sounds and understanding of connected speech. In children, perceptual goals would be revealed by preferential listening tasks. The following sections on the resolution of physical attributes summarize development of primary auditory processing. These fundamental abilities appear to be less influenced by experience than are secondary auditory processing tasks.

Frequency Resolution.

Frequency resolution or tuning within the auditory system refers to the specificity with which structures in the auditory system respond to sounds of a particular frequency, a primary function necessary for discrimination of frequencies. In the prenatal period, cochlear and neural maturation are the main contributors to development of frequency

resolution. Tuning within the cochlea is mature as early as it has been measured (Abdala & Sininger, 1996). , but within neural structures, it continues to develop up to six months of age (Folsom & Wynne, 1987). . After that, attention may be the primary factor for the continued improvement in frequency resolution throughout childhood (Werner & Marean, 1996).

Temporal Resolution.

Temporal resolution refers to abilities to detect changes in the timing of sound such as detection of brief gaps in sound, discrimination of sounds of varying duration, and improvement of performance with increasing duration of sound. It has a longer developmental course than intensity or frequency resolution, possibly because it is more dependent upon attention and memory (Werner & Marean, 1996). Early in development, factors such as myelination, fiber diameter, and synaptic efficiency are significant contributors to development of temporal resolution.

Intensity resolution

The dynamic range of auditory neurons is restricted in developing mammals. This might be expected to influence an infant's ability to detect small changes in stimulus intensity or to perceive loudness in a mature fashion. The amplitude of the auditory brainstem response would be a reasonable approach to measuring this ability in infants, but its variability is too large. Thus, the few studies performed to date have relied primarily on behavioral methods, and little is known about the time course of the development of intensity resolution.

Hearing Sensitivity.

Developmental studies using physiologic estimates of hearing threshold reveal that there is a period of rapid improvement from birth to six months, followed by a slower phase of development until around ten years of age (Werner & Marean, 1996). Several mechanisms could explain the improvement in hearing threshold with age.

Maturation of external and middle ear structures is an important contributor. Studies of energy reflectance have shown that energy transfer through the external and middle ear continues to mature beyond 24 months of age (Keefe, Ling & Bulen, 1992). A caudal to rostral progression of maturation occurs within the auditory pathway: two months for the eighth nerve, two to three years for the auditory brainstem pathway, and the teen-years for cortical pathways (Ponton et al, 1996). .

In children mature enough to understand and cooperate, behavioral measures are used for threshold assessment. These tests are highly dependent upon listening strategies, motivation and attention, which also change with age.

Prenatal factors other than auditory experience may also influence the course of auditory development. Newborns of mothers who smoke are less readily aroused by auditory stimuli than those of non-smokers (Franco et al, 1999). Not surprisingly, maternal undernutrition can result in delayed development of the auditory brainstem pathway. One study suggested more rapid development of brainstem auditory conduction time in breastfed vs formula-fed newborns (Amin et al, 2000).

Complex Sound Perception

The preceding sections have dealt with the most fundamental abilities to distinguish quantitative features of simple sounds. But, the most important properties of hearing-function involve the analysis of complex environmental sounds varying in frequency and amplitude over time. Our ability to perceive the qualitative attributes of sound, such as loudness, pitch and timbre, are more difficult to measure but are essential to the understanding of speech and perception of music.

The pitch of tones in sequence gives rise to melody, while timbre evokes a quality of sharpness or brightness. The vowels in speech can be described as harmonic complexes of different timbres (Werner & Marean, 1996). While adults can be asked to rate various attributes of complex sound, we can only infer infants' abilities and preferences from discrimination studies based on behavior. From such studies, it appears that infants are particularly responsive to speech stimuli (Hutt et al, 1968) and that newborns prefer their mother's voice over that of another female (DeCasper & Fifer, 1980).. Furthermore, infants are more responsive to "baby talk" or *infant directed speech*, characterized by high fundamental frequency and unique patterns of intonation (Fernald, 1985). When presented with tonal, non-speech stimuli mimicking the intonation-contour of infant-directed speech, infants prefer these stimuli over tonal stimuli without the unique contour (Fernald & Kuhl, 1987). Some investigators hypothesize that infant directed speech facilitates language acquisition either by providing cues to syntactic structure and by segmenting ongoing speech to separate individual words (Morgan, Meier & Newport, 1987) or simply by promoting social interaction (Snow, 1993). Infants have poor low-

frequency discrimination (Olsho, 1984; Olsho, Koch & Halpin, 1982) and this ability continues to develop well into childhood (Maxon & Hochberg, 1982). Whether this contributes to their preference for the large intonation contours of infant-directed speech is not known. In contrast, high frequency discrimination, an important ability for the perception of subtle differences among the consonants of speech, develops quickly during infancy.

Three month old infants appear to have an adult-like perception of pitch as it relates to octaves (Demany & Armand, 1984), in that, as one tone approaches an octave above a second tone, the two tones are perceived as similar. When multiple tones are harmonically related, we perceive them as one pitch, which is related to the fundamental or lowest frequency. If the fundamental frequency is removed from the complex, leaving only the harmonics, the perception of pitch is unchanged. This *virtual pitch* perception appears to be present in infants at least by 7 months of age (Clarkson & Clifton, 1985). but It is not known whether learning and experience play a role. Very little is known about the development of musical pattern perception prior to six months of age. It appears that infants are able to process different aspects of music simultaneously. For example, 6 month olds are sensitive to changes in rhythm even when melody and tempo are changed simultaneously (Trehub & Thorpe, 1989).

Speech Perception.

The smallest segments of speech, which assign or change meaning in words, can be identified by adults regardless of the voice-variations among speakers. Therefore, invariant acoustic cues exist, which label these segments or *phonemes*. All of the

specific abilities relating to intensity, frequency and timing discussed in previous sections are recruited in the development of detection of these cues for speech perception. For example, the phonemes /b/ and /p/ differ in *voice onset time* by a matter of milliseconds, but the small timing difference allows us to distinguish the two sounds in words. This example of *categorical perception* is present in early infancy, but the boundaries between categories in the native language sharpen with development (Aslin, 1981).

Young infants demonstrate the ability to distinguish phonemes, which do not exist in their native language (Aslin, 1981; Lasky, Syrdal-Lasky & Klein. 1975). They become less sensitive to non-phonemic differences among consonants between 6 and 12 months of age, apparently as a result of lingusitic experience (Werker & Lalone, 1988). . The loss of this ability is permanent. American adults can discriminate the English phonemes /r/ and /l/, but the acoustic difference between these sounds in Japanese does not signal a change in meaning and is not discriminated by mature native Japanese (Miyakawa et al, 1975).

Similarly, vowels vary greatly in spectral characteristics among speakers, yet adults are able to sort them into equivalent classes based upon a general spectral contour, where relative pitch is attended to over absolute pitch. Two-month-old infants are apparently able to categorize at least some vowels (Marean, Werner & Kuhl, 1992).

NORMAL SEQUENCE OF DEVELOPMENT OF SENSORY SYSTEMS

Sensory systems in all animals develop in a predictable order: somatosensory, vestibular, olfactory, auditory, and visual (Gottleib, 1971). Animal studies indicate that interactions between auditory structures and the environment are critical to normal development. Knowledge of the effects of abnormal sequencing of sensory events is derived from animal data, but human preterm birth or the absence of auditory stimulation

in the deaf infant can approximate those experimental conditions.

It has been proposed that sensory stimulation, which occurs earlier in development than usual, can interfere with learning from other sensory modalities in immature animals (Turkewitz & Kenny, 1982). For example, visual structures mature in early intrauterine life, but patterned visual stimuli are not available in that environment. In contrast, auditory structures, which are nearly mature in late intrauterine life, **do** receive patterned stimulation, primarily from biologic noise and the voice of the mother. Early auditory perception is normally free to develop in the absence of competition from the developing visual system. In the preterm infant, however, patterned visual stimuli are experienced much earlier than usual. Animal studies have clearly demonstrated deficits in auditory learning as a result of improper sequencing of sensory stimulation. Gottlieb et al demonstrated that ducklings hatched at a normal time and exposed to mother's vocalizations recognized and "preferred" her vocalizations over other sounds. However, ducklings exposed to light prior to normal hatching did not learn to recognize the mother's call (Gottleib, 1980; Gottleib, Tomlinson & Radell, 1989; Radell & Gottleib, 1992). Unnatural stimulation of an *earlier* developing system, in this case the vestibular system, interferes with auditory learning in duck embryos. When embryos and hatchlings were exposed to rapid oscillations of a waterbed, those exposed prior to hatching were unable to recognize or learn the mother's call, whereas hatchlings exposed to the same stimulation recognized the call (Radell & Gottleib, 1992). It is not known whether these differences result from changes in neural organization (Trukewitz & Kenny, 1982) or from altered attention Gottleib, Tomlinson & Radell, 1989) . The normal sequence of patterned stimulation in various modalities is certainly interrupted in

infants born prematurely, but the consequences are not known at this time.

The organization of neurons in the auditory areas of the cerebral cortex into clusters occurs in response to stimulation. The period during which the development of sensory areas of the cortex can be compromised by stimulus-conditions is referred to as the *sensitive period*. Premature infants at 23 weeks gestation through the early months of life in the neonatal intensive care unit are in the sensitive period for cochlear development. The*critical* period for language development spans the first 2-3 years of life during which adequate speech stimulation is required. Congenitally deaf children who are not provided early amplification should be considered at risk for permanent structural and functional changes in development.

Neuropathologic studies of seven profoundly deaf humans revealed that cell size in the cochlear nucleus was inversely correlated with the duration of deafness. Similarly, auditory deprivation in animals has been shown to alter functional and structural development in the peripheral and central auditory pathways (Batkin, Groth & Watson, 1970; Webster & Webster, 1977; Moore, 1990; Tierney, Russell & Moore, 1997). Deprivation of "meaningful" or patterned sounds results in Impaired auditory discrimination and processing in animals. Structural changes in the central auditory pathway can also result from unilateral deafness. All of these findings have implications for global developmental processes in children with hearing impairment.

AUDITORY EXPERIENCE AND LEARNING IN THE FETUS

Although data are limited, it appears that prenatal experience influences auditory development in humans as well as in animals. Although sounds are attenuated by the

abdomen and fluid, normal conversation near the pregnant abdomen is probably recognizable in pitch and rhythm and can be appreciated by the term infant (Stein, Spieker & MacKain, 1982). Newborns prefer their mother's voice over other voices. They can be conditioned to suck on a pacifier at a particular rate in order to initiate the sound of mother's voice (DeCasper & Fifer, 1980) . However, they show no preference for their father's voice - with which they had little or no prenatal experience – over another male voice (DeCasper & Prescott, 1984). Infants exposed for the last six weeks *in utero* to mothers' reading a story with a distinctive cadence preferred hearing it over another story shortly after birth. Newborns who did not have that prenatal experience showed no preference (DeCasper & Spence, 1986).

HEARING IMPAIRMENT AND DIAGNOSTIC TECHNIQUES

EPIDEMIOLOGY OF HEARING IMPAIRMENT

As estimated by the most recent survey of the prevalence of "serious" hearing impairment in children in this country (CDC, 1997), the average annual prevalence rate is 1.1 per thousand children (aged 3-10 years). Two-thirds of the children with impairment had a sensorineural loss that did not result from a postnatal cause. Half of those with prenatal/neonatal onset were diagnosed after the age of three. The survey included only those children with hearing loss >40dBHL. However, a loss of 30-40 dBHL in the speech frequencies would render most consonants in conversational level speech inaudible to prelingual children. Thus, the reported prevalence from this study is probably not an accurate indication of *significant* childhood hearing impairment.

Niskar and associates (1998) tested a sample of 342 children, and found that 17% had

a hearing loss of at least 25 dB HL at 1, 2, 4, and/or 6k in one or both ears. Other prevalence studies including bilateral hearing impairment of this magnitude have revealed rates of 3-5 per thousand (Sorri & Rantakllio, 1985; Watkin, Baldwin & Laoide, 1990).

Data from groups of hospitals with universal hearing screening programs have provided specific information on the prevalence of hearing impairment among newborns. In Colorado, over 41,000 infants were tested and bilateral congenital hearing loss requiring amplification was found to occur in 2 per thousand infants (Mehl & Thompson, 1998). The Rhode Island study of over 53,000 infants also yielded a rate of 2 per thousand (Vohr, Carty & Moore, 1998). A study of 54,228 newborns in Texas yielded a rate for bilateral sensorineural hearing loss of 3.14 per thousand (Finitzo, Albright & O'Neal, 1998).

In Hawaii, 10,372 newborns were screened, and the incidence of bilateral hearing impairment was 1 per thousand and 5 per thousand in the well-baby and the intensive care unit populations, respectively (Mason & Herrman, 1998). Van Naarden and Decoufle (1999) used the CDC surveillance data to estimate that 19% of cases of presumed congenital hearing impairment in the sample were associated with low birth weight. Black infants, particularly males, had a higher prevalence rate than other races, even when birth weight was normal.

EARLY IDENTIFICATION OF DEAFNESS

Language cannot develop normally without adequate exposure to speech-stimuli during the first three years of life. This underscores the urgency of early identification of hearing impairment in children. The prevalence of hearing impairment in infancy

exceeds that of all other handicapping conditions for which mandated neonatal screening programs exist (Johnson, Mauk & Takakawa, 1993). Yet despite the relative frequency of its occurrence, there remains an average delay of two to three years in the identification of neonatal-onset deafness (Harrison & Roush, 1996), because most infants with severe hearing impairment will startle to loud sounds, will laugh and learn to babble at appropriate ages. Less than 10% of parents of infants with moderate-to-severe hearing loss were concerned about the child's hearing at the time of diagnosis (Garganta & Seashore, 2000). Delayed habilitation throughout the critical period for language development virtually ensures a language deficit in children with early-onset deafness, and that language delay can result in severe learning deficits, including reading problems which are resistant to remediation.

Historical Perspective

The release of the position statement of the Joint Committee on Infant Hearing (1982) served as the impetus for the development of a number of hearing screening programs for "high-risk" neonates in this country. Methodology for achieving the recommended timetable for identification was not specified, because technology had not yet provided a sensitive, reliable and efficient tool for identifying infants with hearing impairment. Since the publication of that position statement, the milieu in which screening programs were evolving was altered by the introduction of two new techniques: auditory brainstem responses (ABR) and evoked otoacoustic emissions (OAE). The latter offered a rapid, inexpensive screen for hearing impairment (Kemp & Ryan, 1993), while the former provided an estimate of hearing threshold in neonates (Picton, Oulette & Hamel, 1979).

With these developments, cost-effective identification *and* diagnosis became attainable goals.

Once the financial hurdle was lowered, interest shifted toward universal screening rather than screening limited to high-risk neonates. Over half of deaf neonates have no identifiable risk factor for hearing loss, thus would not be detected by a risk-based screening program (ASHA, 1989). This, along with the advent of otoacoustic emissions, prompted the National Institute of Health to recommend universal neonatal hearing screening using otoacoustic emissions as the first-level screen with confirmation by auditory brainstem responses (NIH, 1993).

The wisdom of universal hearing screening was challenged by Bess and Paradise (!994) who argued that empirical evidence supporting more favorable outcomes in deaf children identified earlier as compared with those identified later was lacking. However, Yoshinaga-Itano and her associates (1998) have since demonstrated a clear association between age of identification and outcome in hearing impaired children. Children identified before 6 months of age have expressive and receptive language quotients significantly higher than those of children identified after 6 months. The impact of early identification is present regardless of gender, presence of secondary disability, socioeconomic status or age at testing. The same group has calculated the actual cost of public services to affected children, the average cost to affected families, and the estimated cost of a screening program in Colorado, thus laying the groundwork for a cost-benefit analysis of universal hearing screening. It was estimated that the direct costs of a screening program in Colorado would be recovered within ten years of implementation (Mehl & Thompson, 1998). False-negative rates are negligible, and

false-positive rates in long-standing programs range from 0.3%% to 7%.

Methodology

Equipment with automated "pass/refer" decision-making capability is now commercially available for neonatal screening by otoacoustic emissions and by auditory brainstem responses. In selecting equipment, consideration should be given only to those systems employing a statistically-proven algorithm for pass/refer decisions.

Because Eustachian tube function is inefficient, reabsorption of middle ear fluid and mesenchymal tissue is incomplete in newborns. Ear canals are typically full of debris in the first day(s) of life. Most "false-positive" hearing screens in newborns can be attributed to altered middle ear function or obstruction (Stockard & Curran, 1990).

Either OAE or ABR can be used successfully in universal screening programs. OAE equipment is less expensive, easier to operate, and faster. It is unaffected by electrical noise. On the negative side, refer rates are higher because of OAE's sensitivity to middle ear dysfunction. High levels of ambient noise (as in the NICU) can interfere with testing.

Infants in the NICU are at increased risk of eighth nerve and/or brainstem dysfunction, which would not alter OAEs. ABR can detect such lesions. This test is also less affected by transient middle ear dysfunction and ambient noise, so refer rates are lower than those of OAE-based programs. But, start-up costs are higher, screening requires more time, and electrical noise can interfere with the test. When the nursing staff is responsible for screening, the time factor becomes critical.

The ideal model is a two-level inpatient screen with an OAE-screen followed by ABR in those infants failing the OAE. Babies who fail the second level screen are referred to a

physician for medical management, an audiologist for diagnosis and aural rehabilitation and an early intervention program, if available in the community.

Training

Reimbursement rates for screening are low (or non-existent in some states). For that reason, existing hospital staff, low pay-scale employees or volunteers usually serve as screeners. Nurses may be resentful of additional responsibilities, turn-over rates are high for poorly paid employees, and volunteers may not be sufficiently committed to the screening program. Efficient and effective training programs are therefore essential to a national implementation plan.

Data Management

Tracking of children who were discharged without a screen or who failed the screen is a critical component of an effective program. It is not sufficient to inform a parent of the possibility of deafness. In mass screening programs, data management must be computer-based. Software packages designed specifically for universal hearing screening are available, the most commonly used being *Oz Screening Information Management Solution (SIMS)* and *HI*TRACK*. Most automated OAE or ABR systems are compatible with one or both of these database programs.

TYPES OF HEARING IMPAIRMENT

Encoding of acoustic information occurs at multiple levels of the auditory pathway, and lesions from the end organ upward can disrupt the processing of auditory

information. Consequently, the nature of and severity of symptoms vary widely as a function of the site of the lesion in the auditory pathway.

Conductive hearing impairment

Normally, low to moderate intensity sound reaches the cochlea via air conduction through the external auditory canal, where it impinges sequentially on the tympanic membrane, the ossicular chain, and the oval window of the cochlea. The middle ear normally serves as a mechanical amplifier. Any condition, which impedes the flow of air in the canal or the movement of the structures of the middle ear will reduce the efficiency of this amplifier and result in attenuation of sound intensity with less distortion of quality than other types of hearing impairment. Higher intensity sounds (>60 dB) will still reach the cochlea via vibration of the bones of the skull, bypassing the middle ear system. Mild, transient conductive hearing impairment is relatively inconsequential in an older child or adult. In a young child, mild to moderate conductive loss may render imperceptible many of the consonants in conversational-level speech thus interfering with speech and language development. If the loss persists over long periods during the critical period for language acquisition, it can have serious structural and functional consequences for language development. For example, 4 to 5 year old children with histories of chronic otitis media are less able to distinguish words signaled by different voice onset times, regardless of intelligence or hearing sensitivity on the day of testing (Clarkson, Eimas & Marean, 1989).

Hearing loss associated with chronic otitis media is usually fluctuating in nature, interfering with normal binaural hearing experience. This could result in impaired sound

localization ability and speech processing in noisy environments. Binaural function has been shown to be abnormal in 5 to 7 year old children with past histories of chronic otitis media (Gunnaron & Finitzo, 1991). Brier and Gray (1993) were not able to demonstrate any improvement in sound localization or speech processing abilities following surgical correction of unilateral atresia in children, suggesting that the effects were permanent.

Sensory (cochlear) hearing impairment

The fluid within the cochlea can be set into motion either by vibration of the skull (bone conduction) or by movement of the stapes in the oval window of the cochlea (air conduction via the middle ear). The fluid motion results in shearing of the stereocilia of the sensory cells (hair cells), which, in turn, initiates the firing of single nerve fibers terminating in the eighth nerve (Figure 1). Coding of frequency-information begins in the cochlea. Injuries at this level are irreversible and can have devastating effects on both the loudness and quality of sound. Even unilateral hearing loss in children affects speech perception, learning, self-image and social skills.

Hearing aids are usually effective in cases of pure cochlear hearing loss if there is residual hearing in the speech frequencies. Unfortunately, in many cases, neurons within the cochlea begin to deteriorate, and eighth nerve dysfunction complicates rehabilitation.

Neural Hearing Impairment

Axons of the single nerve fibers of the cochlea assemble to form the auditory portion of the eighth cranial nerve. Their concentric organization by frequency provides evidence of the nerve's function as a second-level coding device for acoustic information. Complex analyses of the intensity, frequency and temporal information in speech are

based in part on firing patterns of the eighth nerve. Auditory nerve pathology can lead to total deafness or to such severe distortion that speech sounds cannot be discriminated. Extraction of meaningful sounds from background noise becomes extremely difficult. Hearing aids are less effective or ineffective.

Sensory hearing loss may progress to *sensorineural* hearing loss, when neurons within the cochlea begin to degenerate. This progression helps to explain the variability in reported efficacy of hearing aids among individuals with similar audiograms. In fact, hearing thresholds to pure tones are extremely poor predictors of the success of amplification-devices.

Until recently, sensory and neural hearing impairments were not distinguishable by objective testing techniques, thus the term sensorineural hearing impairment was applied to virtually all permanent hearing disorders. Since the development of techniques for separate assessment of the eighth nerve and the hair cells of the cochlea, *auditory neuropathy* has been recognized as a distinct auditory disorder. It is characterized by poor speech discrimination out of proportion to the pure tone hearing thresholds (Starr, Picton & Sininger, 1996), which may be within normal limits. Binaural processing of sound, frequency discrimination and intensity discrimination are impaired. Ambient noise severely alters speech intelligibility. Temporal aspects of auditory perception are compromised in these patients (Sininger, Doyle & Moore, 1999). They are unable to detect brief gaps in sounds normally. The symptoms are attributed to abnormal *neural synchrony*, which is important for the perception of acoustic cues in speech. They may act behaviorally deaf as infants and then demonstrate responsivity at later ages, despite the fact that responses cannot be recorded from the eighth nerve or auditory brainstem

pathway. Cochlear responses (otoacoustic emissions and cochlear microphonics) are present but may deteriorate with age, possibly as a result of retrograde degeneration of the cochlea. Auditory neuropathy is frequently associated with severe neonatal hyperbilirubinemia, which tends to affect structures above the level of the cochlea. Hearing aids are not helpful in these patients.

GENETICS OF DEAFNESS.

Inherited syndromic deafness does not present the same identification-dilemma as that of non-syndromic deafness, because related anomalies usually lead to early testing. New techniques in molecular genetics have greatly increased our understanding of monogenic inherited disorders. Linking to a single gene requires analysis in large affected families, and long-term studies of several families are currently underway. Based on the symptoms of a disorder in a family and existing knowledge about the function of specific genes, a *candidate gene* is first analyzed in the family for abnormal sequencing. Genes serve as templates for the creation and regulation of proteins, guiding development, providing for renewal of tissues and regulating the function of organs at the biochemical level. Fifteen genes with various mutations responsible for non-syndromic hearing loss have been identified. The inheritance of monogenic congenital hearing loss is autosomal recessive in 75%, autosomal dominant in 20%, x-linked in 5% and mitochondrial in less than 1% (Willems, 2000).

The *POU* family of genes is responsible for encoding transcription factors. Mutations on chromosome xq21 in or around the nuclear gene POU3F4 are responsible for x-linked deafness type 3 (DFN3), with progressive hearing loss and fixation of the stapes.

DFN15, an autosomal dominant form of progressive hearing loss, is related to POU4F3 gene on chromosome 5q which is responsible for transcription of target genes important for the survival of cells in the organ of Corti. Table 1 lists the all of the known loci for non-syndromic hearing loss.

Figure 2 shows a cross-section of the cochlea and sites where genetic defects can occur. The two ducts flanking the cochlear duct are filled with perilymph. Potassium-rich endolymph fills the cochlear duct housing the organ of Corti between the basilar and the tectorial membranes, which serve as resonators. The relative movement of these membranes leads to the influx of potassium ions through channels on the myosin-controlled filaments linking the tips of the stereocilia of the hair cells. Depolarization of the hair cells results in an electrical signal, which is transmitted to the eighth nerve. Potassium ions probably then flow out through potassium channels in the lateral wall of the hair cells to surrounding support cells, to cochlear fibrocytes and the stria vascularis via connexin channels where they are secreted back into endolymph through another potassium channel.

Mutations have been identified in genes affecting middle ear and cochlear bone development, structural characteristics of the tectorial membrane, myosin (present in the stereocilia), diaphanous (involved in maintenance of the actin-filled stereocilia of the hair cells), fibrocytes (associated with ion channels), and connexin (Willems, 2000). Connexins are channel-forming proteins in membranes, fibrocytes and supporting cells of the cochlea. Mutations in the gene for connexin-26 accounts for as much as 50% of autosomal recessive hearing loss (Willems, 2000).

The mechanism by which the mutation results in a disorder may be investigated by developing a mutant strain of animal (Anderson, Herrup & Breakfield, 1996). Several animal models of genetic deafness have been developed, contributing greatly to our understanding of variability in the type, severity and time-course of inherited hearing disorders. For example, one x-linked mouse model produced profoundly deaf mice with no gross cochlear anatomical defects but with a marked reduction in the endocochlear potential. Fibrocytes, which play a role in the regulation of cochlear potassium homeostasis, are severely affected by the mutation. Another mutant strain has been developed which blocks the normal development of the bony labyrinth and the ossicles.

Data from both humans and animals may lead to gene therapies for preventing or reversing hearing loss.

Contributions of Genetic Studies to Rehabilitation.

Studies in families with progressive hearing loss have been particularly useful in revealing patterns of destruction of the cochlea and neurons within the cochlea and their relationship to speech intelligibility, effects of noise and efficacy of hearing aids and cochlear implants. Temporal bone studies have been performed in many cases (Halpin, Herrmann & Wheaty, 1996). As mentioned earlier, pure tone thresholds do not correlate well with hearing aid efficacy, probably because the detection of simple sounds do not require as many functional *channels* of intact hair cells, single nerve cells and functional connections among auditory structures as are required for speech perception and extraction of signals from noise. When speech intelligibility deteriorates following depopulaton of neurons within the cochlea, hearing aids become less effective, and

cochlear implants or sign language must be considered.

Disorders of Central Auditory Processing

Structural organization by frequency or *tonotopic organization* is characteristic of every level of the auditory pathway. Functionally diverse eighth nerve fibers branch to the separate frequency-regions of the cochlear nuclei of the brainstem. These structures - the first way- stations in the brainstem auditory pathway - demonstrate selective vulnerability to bilirubin toxicity (Gerrard, 1952) and perinatal hypoxic/ischemic injury (Hall, 1964), thus represent a common site of lesion in perinatally acquired auditory dysfunction. In many cases, children with lesions of the brainstem auditory pathway will demonstrate deficiencies in the processing of auditory stimuli rather than reduced sensitivity to sound in a quiet environment, and learning disabilities are common in these children.

Cortical deafness is a clinical rarity not readily diagnosed, because patients tend to show inconsistent responsivity to sound with poor speech production and understanding, in spite of normal physiologic responses from the peripheral and brainstem auditory pathways. In behavioral audiometric testing with pure tones in a sound room, they may exhibit normal "hearing" thresholds. Bilateral temporal lesions and cortical deafness have been described secondary to fever (Hood, Berlin & Allen), congenital malformation (Landau, Goldstein & Kleffner, 1957), meningitis (Lechevalier, Rosa & Estache, 1984), or cerebral infarcts (Jerger, Weilers & Sharbrough, 1969). Amplification in such patients is ineffective and inappropriate. Rather, training in sign language should begin immediately upon diagnosis.

HEARING SCREENING AND DIAGNOSTIC METHODS

Assessment of Middle ear Status

Tympanometry and acoustic reflex (stapedius muscle) testing are collectively known as immittance audiometry. The probe of the tympanogram contains a miniature microphone to measure the intensity of a tone which, when introduced into the ear canal, reflects off the tympanic membrane (TM) and travels back to the probe. The air pressure in the ear canal is systematically changed from positive to negative in order to alter the compliance of the TM which, in part, determines the amount of sound energy that will be reflected versus absorbed (Figure 3).

Tympanometry is a sensitive test for the presence of fluid in the middle ear, retraction of the TM (negative pressure), disarticulation of the ossicles or perforation of the TM in children 7 months of age or older. Before that age, the walls of the ear canal are cartilaginous and may expand when air pressure is increased in the canal, resulting in a falsely normal reading.

Acoustic reflexes are absent or elevated in threshold when there is a sensorineural hearing loss or middle ear dysfunction. The acoustic reflex was at one time used to assess brainstem integrity, but more sensitive tests have since replaced it.

Tests of Cochlear Integrity

Before the discovery of evoked otoacoustic emissions, no direct physiologic test of cochlear integrity existed. Clinical application of this hair cell response, in combination with the auditory brainstem response, now permits the separate assessment of cochlear-

and the eighth nerve-function. The OAE is rapid (4-5 minutes), inexpensive, reliable, and objective. It can be recorded in the preterm / term newborn (awake or asleep) and is highly sensitive to moderate hearing impairment of either conductive or sensory (cochlear) origin. Evoked otoacoustic emissions are thought to be generated by the elongation and contraction of the outer hair cells of the cochlea in response to either repetitive clicks (transient evoked otoacoustic emissions or TEOAEs) or to two-tone stimulation (distortion product otoacoustic emissions or DPOAEs). DPOAEs can be elicited at specific frequencies to assess cochlear function at specific locations along the basilar membrane on which the hair cells are situated. A small probe placed at the entrance to the ear canal presents the tones and delivers the response to a microphone (Figure 4). Computer software generates either a series of clicks or a "sweep" of two tones across a wide range of frequencies. The same software generates a graph of the spectrum of the emissions recorded in response to the stimuli. These tests do not provide an estimate of hearing threshold.

Tests of Neural Function

The eighth nerve action potential can be recorded non-invasively from the early preterm period onward. It is usually recorded in combination with the auditory brainstem response, using the same electrode configuration and signal averaging equipment.

Tests of central auditory function

Auditory brainstem responses (ABRs) are used both for the objective assessment of the brainstem auditory pathway (Figure 5) and for the estimation of hearing threshold.

The latter permits the selection of appropriate amplification at an early age. Electrodes are taped to the scalp, and repetitive clicks or brief tones are presented through an earphone. Brief samples of the electroencephalogram are collected following the presentation of each stimulus, stored in a computer, and then summated by a signal averaging system. Noise is nulled through averaging, leaving only the response, which is time-locked to the stimulus. The patient must be sleeping during threshold estimation.

Sensitive, objective and simple tests of function of higher levels of the auditory pathway have not been developed at this time. Behavioral batteries of tests of central auditory processing have not proven to be sensitive or specific (Singer, Hurley & Preece, 1998).

SUMMARY

Hearing impairment of any type in early childhood can have serious permanent effects on development. It can be detected and diagnosed in the newborn period, and early intervention significantly improves language development and reading abilities. Chronic otitis media during the critical period for language development may result in altered production and perception of consonants of speech. An aggressive approach to identification, diagnosis and prompt treatment of all types of auditory disorders is recommended.

REFERENCES

Abdala, C, & Sininger, Y. (1996). The development of cochlear frequency resolution in the human auditory system. *Ear Hear*, *17*(5), 374-385.

American Speech and Hearing Association Committee on Infant Hearing. (1989). Audiologic screening of infants who are at risk for hearing impairment. *ASHA*, *31*(3), 61-64.

Amin, S.B., Merle, K.S., Orlando, M.S.& Dalzell, L.E. (2000) Brainstem maturation in premature infants as a function of enteral feeding type. *Pediatrics, 106*(2), 318-322.

Anderson, J., Herrup, K. & Breakfield, X. (1992). Creation of transgenic mice that over-express MAO-B neuronally. *Ann Am Acad Sci* , *648,* 178-188.

Aslin, R.N.. (1981). Experiential influences and sensitive periods in perceptual development: A unified model. In RN Aslin, JR Alberts, MR Petersen (Eds): *Development of Perception: Psychological Perspectives*. Academic Press, New York, pp 45-94.

Batkin, S., Groth, H., Watson, J.R., & Ansberry, M, (1970). Effects of auditory deprivation on the development of auditory sensitivity in albino rats. *Electroencephalogr Clin Neurophsiol* , *28*(4), 351-359.

Bess, F.H. & Paradise, J.L. (1994). Universal screening for infant hearing impairment: not simple, not risk-free, not necessarily beneficial, and not presently justified. *Pediatrics,* 93, 330-334.

Blake, P.E. & Hall, J.W. (1990). The status of statewide policies for neonatal hearing screening. *J Am Acad Audiol*, *1*: 67-74.

Bredberg, G. (1968). Cellular pattern and nerve supply of the human organ of Corti. *Acta Otolaryngolica, (Suppl)*, *236*.

Breier, J.I. & Gray, L.. (1993). Pre- and postnatal postoperative source localization in patients with unilateral atresia. *Assoc for Res in Otolaryngol Abstracts*, *16,* 40.

CDC (1997). Serious hearing impairment among children aged 3-10 years – Atlanta, Georgia, 1991-1993. *MMWR,; 46*(45), 1073-1076.

Clarkson, M.G. & Clifton, R.K (1985). Infant pitch perception: Evidence for responding to pitch categories and the missing fundamental.. *J Acoust Soc Am*, *7,* 1521-1528.

Clarkson, R.L., Eimas, P.D. & Marean, G.C..(1989) Speech perception in children with histories of recurrent otitis media. *J Acoust Soc Am 85.* 926-933.

DeCasper, A.J., Fifer, W.P. (1980). Of human bonding: newborns prefer their mothers' voices. *Science, 208*, 1174-1176.

DeCasper, A.J. & Prescott, P.A. (1984). Human newborns' perception of male voices: Preference, dsicrimination, and reinforcing value. *Developmental Psychobiology 17*, 481-491.

DeCasper, A.J. & Spence, M.J. (1986) Prenatal maternal speech influences newborns' perception of speech sounds. *Infant Behavior and Development , 6*: 19-25.

Demany, L. & Armand, F. (1984). The perceptual reality of tone chroma in early infancy. *J Acoust Soc Am*, *76*: 57-66.

Fernald, A. (1985). Four-month-old infants prefer to listen to motherese. *Infant Beh Devel 8,* 181-195.

Fernald, A. & Kuhl, P. (1987). Acoustic determinants of infant perception for motherese speech. *Infant Beh Devel* , *10*: 279-293.

Finitzo, T., Albright, K. & O'Neal, J. (1998). The newborn with hearing loss: Detection in the nursery. *Pediatrics*, *102*, 1452-1460.

Folsom, R.C. & Wynne, M.K. (1987). Auditory brainstem responses from human adults and infants: wave V tuning curves. *J Acoust Soc Am* , 81 412-417.

Franco, P, Groswasser, J., Hassid, S., & Lanquart, J.P. (1999) Prenatal exposure to cigarette smoking is associated with a decrease in arousal in infants. *J Pediatr*, *135*(1), 34- 38.

Garganta, C. & Seashore, M.R. (2000). Universal hearing screening for hearing loss. *Pediatr Ann, 29*(5)*,* 302-308.

Gerber, S.E., Lima, C.G. & Copriviza, K.L. (1983). Auditory arousal in peterm infants. *Scand Audiol (Suppl), 17*: 88-93.

Gerrard, J. (1952). Nuclear jaundice and deafness. *J Laryngol* , *66*: 387-397.

Gottleib, G. (1971). Otogenesis of sensory function in birds and mammals. In: *The Biopsychology of Development,* (Eds: Tobach E, Aronson LR, Shaw E). Academic Press, NY, 67-128.

Gottleib, G. (1980). Development of species identification in duckings: VII. Highly Specific early experience fosters species-specific perception in wood ducklings. *J Comp Physiol*, *94*(6): 1019-1027.

Gottleib, G., Tomlinson, T.W., Radell, P.L. (1989). Developmental intersensory interference: premature visual experience suppresses auditory learning in ducklings. *Infant Behav Dev, 12*(1), 1-12.

Gunnarson, A.D. & Finitzo, T. (1991). Conductive hearing loss during infancy: Effects on later auditory brainstem eletrophysiology. *J Sp Hear Res* , *34*, 1207-1215.

Hall, J.G. (1964). On the neuropathological changes in the central nervous system following neonatal asphyxia. *Acta Otolaryngol*, *Suppl 188*: 331-338.

Halpin, C., Herrmann, B. & Wheaty, M. (1996). A family with autosomal dominant progressive sensorineural hearing loss: Rehabilitation and counseling. *Am J Audiol,* 5:23-32.

Harrison, M. & Roush, J. (1996). Age of suspicion, identification, and intervention for Infants and young children with hearing loss: a national study. Ear Hear, *17*(1), 55-62.

Hood, L.J., Berlin, C.I. & Allen, P. Cortical deafness: A longitudinal study. *J Am Acad Audiol*, *5*, 330-342.

Hutt, S.J., Hutt, C., Lenard, H.G., VonBernuth, H. & Muntjewerff, W.J. (1968). Auditory responsivity in the human neonate. *Nature* , *218*: 888-890.

Jerger, J., Weikers, N., Sharbrough, F.W., Jerger, S. Bilateral lesions of the temporal lobe. *Acta Otolaryngol, 258*:5-51.

Johnson, J.L., Mauk, G.W., Takakawa, K.M., Simon, P.R., & Sia, C.C. (1993). Implementing a statewide system of services for infants and toddlers with hearing disabilities. *Seminars in Hearing*, *14*: 105-119.

Joint Committee on Infant Hearing. (1994). Joint Committee on Infant Hearing Position Statement. *Pediatrics*, *95*(1): 152-156.

Keefe, D.H., Ling, R. & Bulen, J.C. (1992). Method to measure acoustic imedance and reflection coefficient. *J Acous Soc Am*, *91*: 470-485.

Kemp, D.T. & Ryan, S. (1993). The use of transient evoked otoacoustic emissions in neonatal hearing screening programs. *Seminars in Hearing*, *14*(1), 30-45.

Landau, W.M., Goldstein, R. & Kleffner, F.R. Congenital aphasia: a clinicopathologic study. *Neurology*, *7*: 915-921.

Lasky, R., Syrdal-Lasky, A. & Klein, R.E. (1975). VOT discrimination by four to six and a half month olds from Spanish environments. *J Exper Child Psychol* 1975; 20: 215-225.

Lavigne-Rebillard, M. & Pujol, R. (1988). Hair cell innervation in the fetal human cochlea. *Acta Otolaryngologica*, *105,* 398-402.

Lechevalier, B., Rosa, Y., Eustache, F. & Schupp, C. (1984) Case of cortical deafness sparing the music area. *Rev Neurol* (Paris), *140*: 190-201.

Marean, G.C., Werner, L.A. & Kuhl, P.K. (1992). Vowel categorization by very young infants. *Devel Psychol*, *28*, 396-405.

Mason, J.A. & Herrman, K.R. (1998). Universal hearing screening by automated auditory brainstem response measurement. *Pediatrics, 101*(2), 221-228.

Maxon, A.B. & Hochberg, I. (1982). Development of psychoacoustic behavior: sensitivity and discrimination. *Ear Hear, 3*: 301-308.

Mehl, A.L. & Thompson, V. (1998). Newborn hearing screening: The great omission. *Pediatrics, 101*(1), 4-14.

Miyakawa, K., Strange, W., Verbrugge, R. & Lieberman, A.M. (1975). An effect of linguistic experience: the discrimination of /r/ and /l/ by native speakers of Japanese

and English. *Perception and Psychophysics, 18*: 331-340.

Moore, D.R. (1990). Auditory brainstem of the ferret: Early cessation of developmental sensitivity of neurons in the cochlear nucleus to removal of the cochlea. *J Comp Neurol, 302*(4), 810-823.

Morey, A.L. & Carlile, S. (1990). Auditory brainstem of the ferret: Maturation of the brainstem auditory evoked response. *Developmental Brain Research, 52*: 279-288.

Morgan, J.L., Meier, R.P. & Newport, E.L. (1987). Structural packaging in the input to language learning: Contributions of prosodic and morphological marking of phrases to the acquisition of language. *Cognitive Psychology, 19,* 498-550.

National Institute of Health (1993). Early identification of hearing impairment in infants and young children. *NIH Consensus Statement*, *11*(1): 1-24.

Niskar, A.S., Kieszak, S.M., Holmes, A., & Esteban, E. Prevalence of hearing loss among children 6 to 19 years of age: The Third National Health and Nutrition examination survey, *JAMA*, *279*(14): 1071-1075.

Olsho, L.W. (1984). Infant frequency discrimination. *Infant Behav Devel, 7*: 27-35.

Olsho, L.W., Koch, E.G. & Halpin, C.F. (1982). Level and age effects in infant frequency discriimination. *J Acoust Soc Am*, *82*, 454-464.

Picton, T.W., Ouellette, J., Hamel, G., & Durieux-Smith, A. (1979). Brainstem evoked potentials to tonepips in notched noise. *J Otolaryngol*, *8,* 289-314.

Ponton, C.W., Don, M., Eggermont, J.J. & Waring, M. Maturation of human cortical auditory function: differences between normal-hearing children and children with cochlear implants. *Ear Hear*, 17(5): 430-437.

Pujol, R., Lavigne-Rebillard, M. & Uziel, A. (1990). Physiological correlates of development in the human cochlea. *Seminars in Perinatology*, *14*, 275-280.

Radell, P.L., Gottleib, G. (1992). Developmental intersensory interference: Augmented prenatal sensory experience interferes with auditory learning in duck embryos. *Dev Psychol, 28*(5): 795-803.

Singer, J., Hurley, R.M., Preece, J.P. (1998). Effectiveness of central auditory processing tests with children. Am J Audiol, 7: 1-11.l

Sininger, Y.S., Doyle, K.J., Moore, J.K. (1999). The case for early identification of hearing loss in children: auditory system development, experimental auditory deprivation and development of speech and hearing. *Pediatr Clin N Am* 1999; 46, 1-14.

Snow, C.E. (1993). Understanding social interaction and language development: sentences are not enough. In M Bornstein and J Bruner (Eds). *Interaction in Human Development*, Hillsdale, NJ: Erlbaum.27.

Sorri, M. & Rantakallio, P. Prevalence of hearing loss at the age of 15 in a birth cohort of 12,000 children from northern Finland. *Scand Audiol, 14*:203-207.

Starr, A., Picton, T.W., Sininger, Y., Hood ,L.J. & Berlin, C.I. Auditory neuropathy. *Brain, 11*, 741-753.

Stern, D.N., Spieker, S., MacKain, K. Intonation contours as signals in maternal speech to prelinguistic infants. *Dev Psychol 18*(5): 727-735.

Stockard, J.E., Stockard, J.J., Coen, R.W. Auditory brain stem response variability in infants. *Ear Hear*, 4(1): 11-23.

Stockard, J.E. & Curran, J.S. Transient elevation of threshold of the neonatal auditory brain stem response. *Ear Hear, 11*(1): 21-28.

Streeter, L. (1917). The development of the scala tymapni, scala tymapni and perioticular cistern in the human embryo. *Am J Anat*, 21, 299-320.

Tanaka, Y. & Arayama, T. (1969). Fetal responses to acoustic stimuli. *Practica in Oto-Rhino- Laryngol, 31*: 269-273.

Tierney, T.S., Russell, F.A. & Moore, D.R. (1997). Susceptibility of developing cochlear nucleus neurons to deafferentation-induced death abruptly ends just before the onset of hearing. *J Comp Neurol, 378*: 295-306.

Trehub, S.E. & Thorpe, L.A. (1989). Infants' perception of rhythm. Categorization of auditory sequences by temporal structure. *Canadian J Psychol*, *43,* 217-229.

Turkewitz, .G.,& Kenny, P.A. (1982). Limitations on input as a basis for neural organization and perceptual development: A preliminary theoretical statement. *Dev Psychobiol, 15*(4): 357-368.

Van Naarden, K. & Decoufle, P. (1999). Relative and attributable risks for moderate to profound bilateral sensorineural hearing impairment associated with lower birth weight in children 3 to 10 years old. *Pediatrics*, *104*: 905-910.

Vohr,, B..R.., Carty, L..M., Moore, P..E..,& Letourneau, K. (1998). The Rhode Island assessment program: Experience with statewide hearing screening (1993-1996*). J Pediatr, 133*(3): 353-358.

Watkin, P.M., Baldwin, M. & Laoide, S. (1990) Parental suspicion and identification of hearing impairment. *Arch Dis Child*, 65: 846-850.

Webster, D.B. & Webster, M. (1977). Neonatal sound deprivation affects brain stem auditory nuclei. *Arch Otolaryngol*, *103*(7), 392-396.

Wedenberg, E. (1965). Prenatal tests of hearing. *Acta Otolaryngolgica* , 206, 27-31.

Werker, J.F. & Lalone, C.E. (1988). Cross-language speech perception: initial capabilities and developmental change. *Devel Psychol*, 24: 672-683.

Werner, L.A. (1996). The development of auditory behavior (or what the anatomists and physiologists have to explain, *Ear Hear* 17(5): 438-446.

Werner,, L.A., Folsom, R.C. & Mancl, L.R.. (1993). The relationship between auditory Brainstem response and behavioral thresholds in normal hearing infants and adults. *Hear Res*, *68*(1): 131-141.

Werner, L..A. & Marean, G..C. (1996). *Human Auditory Development*, Westview Press, Boulder, CO.

Willems, P.J. (2000). Genetic causes of hearing loss. *NEJM*, *342*(15), 1101-1108.

Yoshiniga-Itano, C., Sedey, A.L., Coulter, D.K &, Mehl AL. (1998). language of early- and later-identified cildren with hearing loss. *Pediatrics*, *102*: 1161-1171.

Table 1. Nuclear Gene Loci for Non-Syndromic Hearing Loss

Locus	**Gene**	**Chromosomal Location**
Autosomal dominant (DFNA)		
DFNA1	Diaphanous	5q31
DFNA2	Connexin 31 And KCNQ4	1p34
DFNA3	Connexin 26	13q12
DFNA4		19q13
DFNA5	ICERE-1	7p15
DFNA6		4p16
DFNA7		1q21-23
DFNA8	a-Tectorin	11q22-24
DFNA9	COCH	14q11-13
DFNA10		6q22-23
DFNA11	Myosin 7A	11q12-21
DFNA12	a-Tectorin	11q22-24
DFNA13		6p21
DFNA14		4p16
DFNA15	POU4F3	5q31
DFNA16		2q24
DFNA17		22q
DFNA18		3q22
DFNA19		10
Autosomal recessive (DFNB)		
DFNB1	Connexin 26	13q12
DFNB2	Myosin 7A	11q13
DFNB3	Myosin 15	17p11
DFNB4	Pendrin	7q31
DFNB5		14q12
DFNB6		3p14-21
DFNB7		9q13-21
DFNB8		21q22
DFNB9	Otoferlin	2p22-23
DFNB10		21q22
DFNB11		9q13-21
DFNB12		10q21-22
DFNB13		7q34-36
DFNB14		7q31 and 19p13
DFNB15		3q21-25
DFNB16		15q21-22
DFNB17		7q31
DFNB18		11p14-15
DFNB19		18p11
DFNB20		11q25-ter

Table 1 continued

DFNB21	a-Tectorin	11q
X-linked recessive (DFN)		
DFN 1*	DDP	xq22
DFN 2		xq22
DFN 3	POU3F4	xq21
DFN 4		xp21
DFN 5		Withdrawn
DFN6		xp22

Figure 1: Schematic representation of the inner and outer hair cells of the organ of Corti

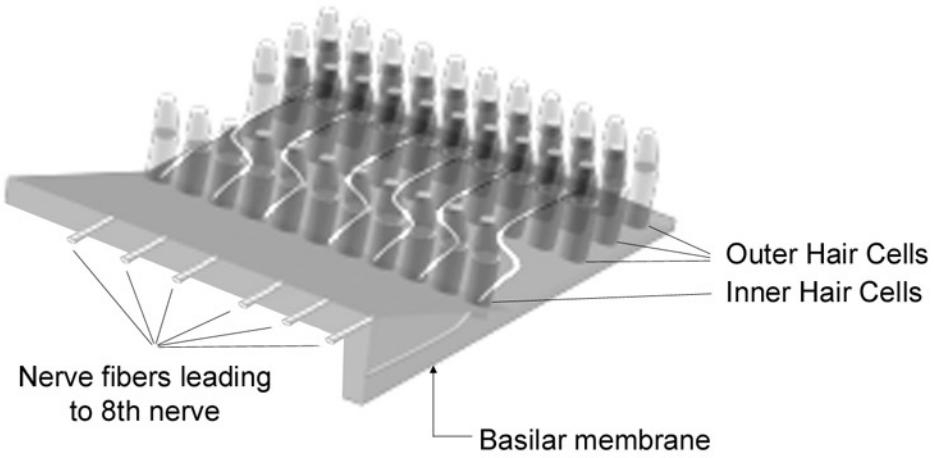


Figure 2: Cross-section of the cochlea showing the position of the organ of Corti between the basilar membrane and the tectorial membrane.

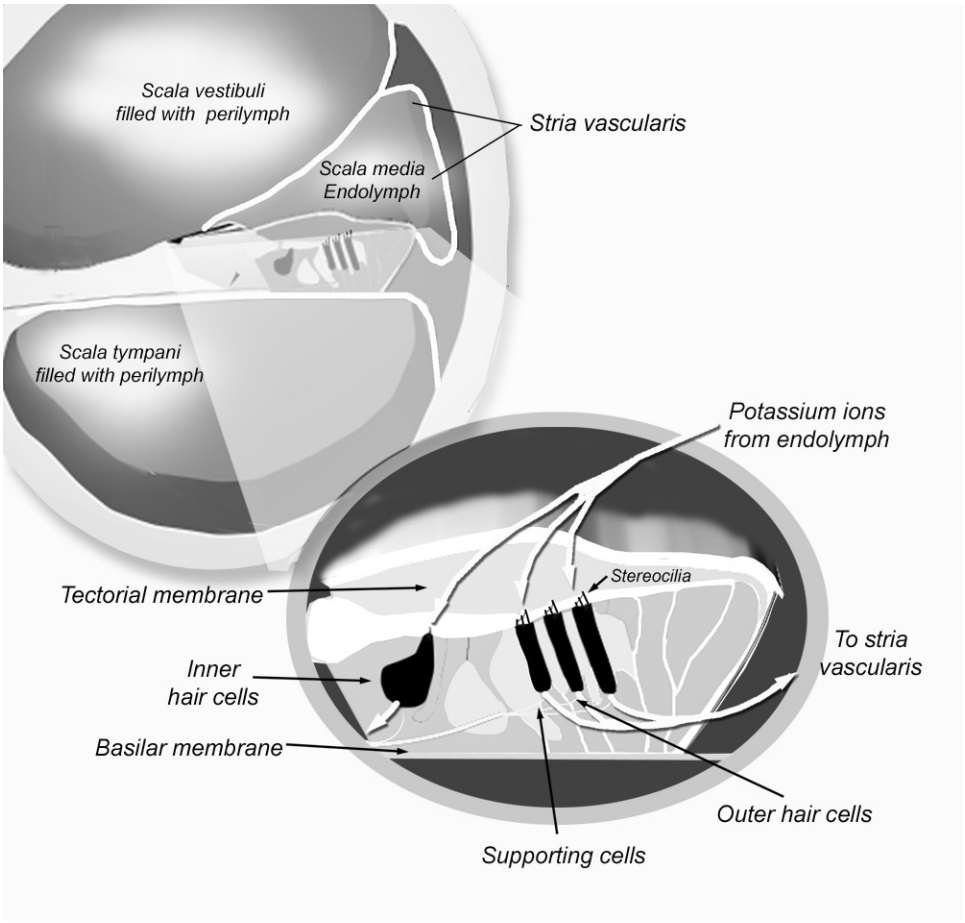


Figure 3: Schematic representation of tympanometry

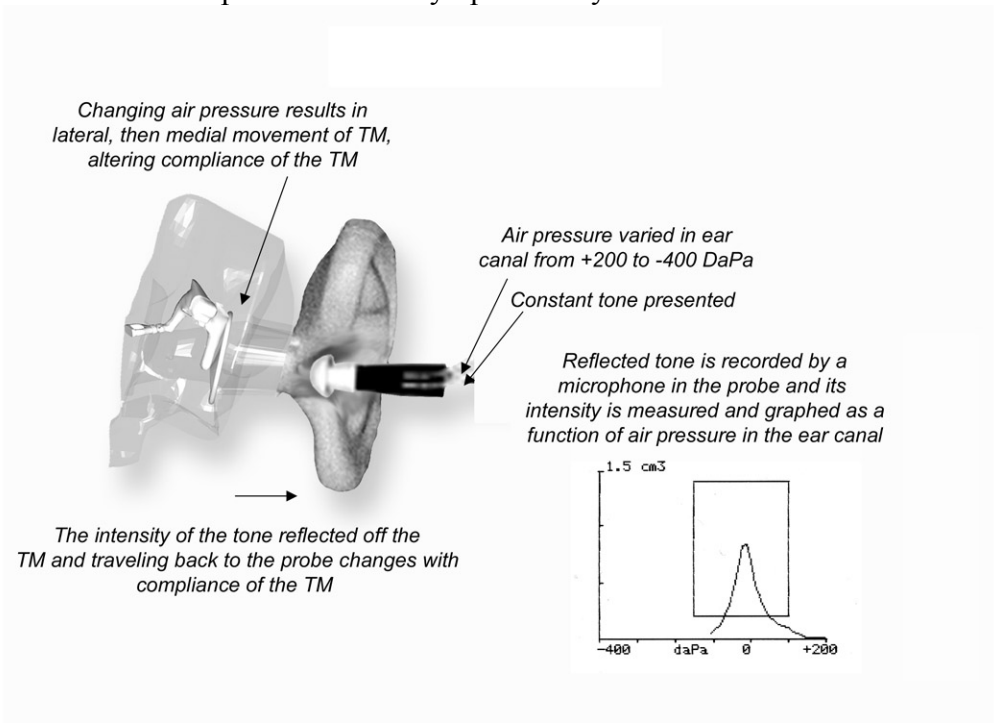


Figure 4: Schematic representation of the measurement of distortion product otoacoustic emissions

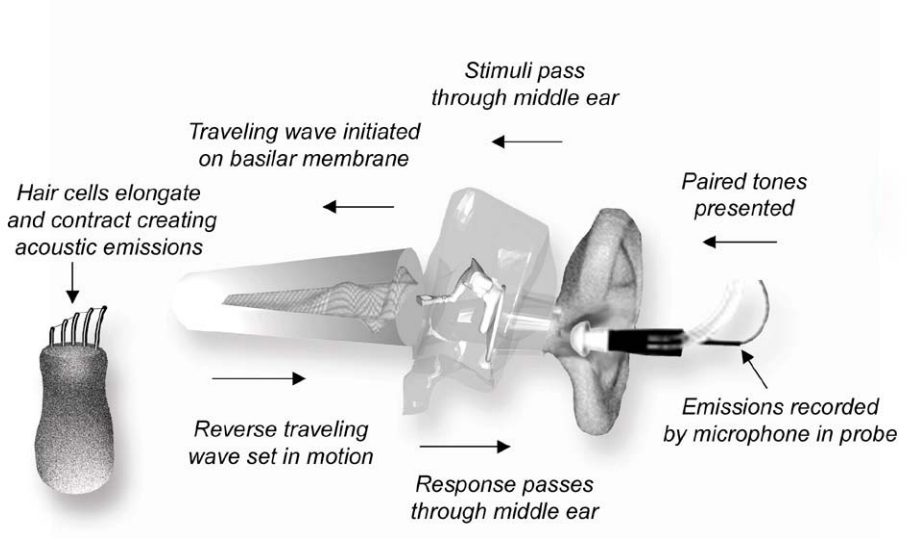
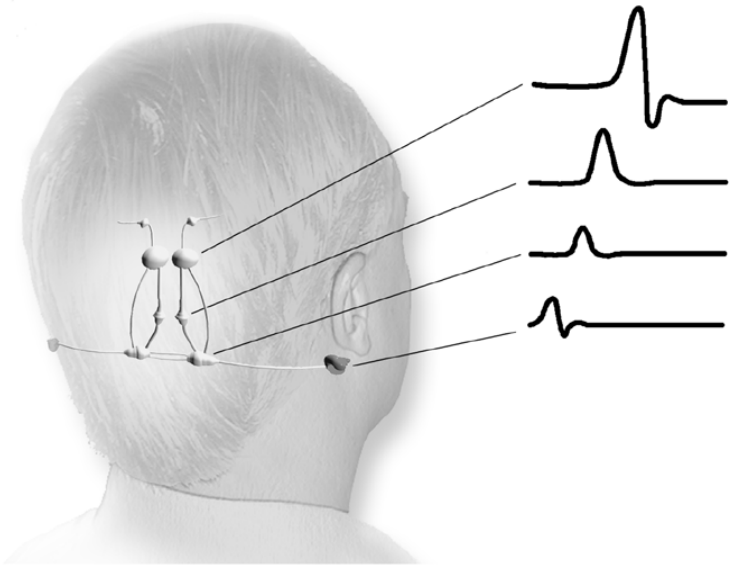


Figure 5: Schematic representation of the origin of the auditory brainstem response.



Filename: ThesisManuscript.WPD1.doc
Directory: C:\Documents and Settings\jvanoss\Local Settings\Temporary Internet Files\OLK21
Template: C:\Documents and Settings\jvanoss\Application Data\Microsoft\Templates\Normal.dot
Title: Recent advances in the field of auditory physiology - coupled with longstanding concerns about delayed identification of heari
Subject:
Author: Infectious Disease
Keywords:
Comments:
Creation Date: 4/7/2003 10:21 AM
Change Number: 15
Last Saved On: 4/8/2003 10:45 AM
Last Saved By: janet E Sullivan
Total Editing Time: 319 Minutes
Last Printed On: 4/8/2003 10:57 AM
As of Last Complete Printing
Number of Pages: 47
Number of Words: 9,301 (approx.)
Number of Characters: 53,016 (approx.)