A Tutorial on Auditory Neuropathy/ Dyssynchrony for the Speech-Language Pathologist and Audiologist

Kristin Uhler, Ph.D., CCC-A, FAAA,[1] Amanda Heringer, B.A. (Au.D. candidate),[2] Nanette Thompson, M.A., CCC-SLP,[3] and Christine Yoshinaga-Itano, Ph.D.[2]

ABSTRACT

This article presents information about developmental outcomes of children with auditory neuropathy/auditory dyssynchrony (AN). Colorado data on the number of children screened and the number of children identified with unilateral and bilateral AN will be described. Descriptive information about the percent of children with AN with cognitive disability and disabilities other than hearing loss will be presented. Language outcomes of children with normal cognitive development will be presented. This article will also provide information about etiologies and audiological information of children with AN. It includes assessment tools that have been useful in decision making for children with AN.

KEYWORDS: Auditory neuropathy, auditory dyssynchrony, auditory neural hearing loss, auditory neuropathy spectrum disorder, language development

Learning Outcomes: As a result of this activity, the reader will be able to (1) describe the anticipated number of children with auditory neuropathy/auditory dyssynchrony (AN) with cognitive disability and the percentage of children anticipated with any disability other than hearing loss, (2) describe the etiologies associated with AN, (3) describe the considerations for cochlear implant candidacy of children with AN, (4) describe an assessment procedure that can be used in the first year of life to examine the child's vocal development and the contribution of auditory skill to that development, (5) discuss issues related to choices of communication approaches and AN.

[1]University of Colorado, Denver—Medical Campus, Denver, Colorado; [2]University of Colorado, Boulder, Boulder, Colorado; [3]University Hospital, Aurora, Colorado.

Address for correspondence and reprint requests: Christine Yoshinaga-Itano, Ph.D., Department of Speech, Language, and Hearing Sciences, University of Colorado, CB 409, Boulder, CO 80309-0409 (e-mail: Christie.yoshi@colorado.edu).

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Auditory neuropathy (AN) is a disorder that was first identified in 1996; however, it is not as rare as once thought.[1,2] Hinchcliffe and colleagues[3] were the first to report the characteristics of AN in a Nigerian sample. In 1996, Starr et al[4] assessed individuals with similar characteristics and developed the term *auditory neuropathy*. Researchers have long disagreed over the term *auditory neuropathy*. Opponents argued that AN implied a known pathology of the eighth nerve limited to the spiral ganglion cells and their axons; and, as research has expanded our knowledge regarding AN, we know that AN is much more complex. There may be many etiologies and multiple locations affected such as the inner hair cells, the spiral ganglion fibers, the myelinated fibers of the eighth cranial nerve, and the brain stem. Therefore, in 2008, experts at the International Newborn Hearing Screening Conference coined the term *auditory neuropathy spectrum disorder* (ANSD) because the issues regarding the disorder lie on a continuum. They stated that AN should be restricted to cases where the locus of the pathology is identified as the spiral ganglion cells or the eighth cranial nerve.[5–8] The interested reader is referred to Rapin and Gravel[9] for an in-depth discussion regarding the anatomical structures of the auditory system and what sites of pathology constitute the definition of a neuropathy. Rapin and Gravel argue that the site of pathology is rarely attributed to the spiral ganglion cells, but rather to the central auditory pathway, leading them to conclude that the term AN is a misnomer. Although it is true that there is a complex spectrum of children with auditory neural hearing loss (HL), the use of the term that includes "spectrum disorder" has been very confusing for parents who have greater familiarity with "autism spectrum disorder" and we are therefore, in this article, referring to the disorder as AN, though we acknowledge that there is a significant number of children with auditory dyssynchrony and that there is great variety or a "spectrum" of characteristics. The use of AN in this article is meant to encompass the heterogeneity of the disorder. Terminology aside, the transient behavior of the disorder and the multiple theories surrounding its epidemiology, etiology, and prognosis leave researchers, health care professionals, and families with an abundance of unanswered questions.[10]

AN is characterized by abnormal temporal encoding and neural asynchrony. It leads to delayed speech acquisition, verbal learning disability, and HL. The consequences of these factors can negatively affect a child's social, emotional, physical, and educational development.[11–13]

Audiological Characteristics of AN. Audiologically, AN is characterized by present transient otoacoustic emissions (OAEs); the presence of the cochlear microphonic (CM); the absence or abnormality (prolonged latency or poor morphology) of an automated brain stem response (ABR); elevated or absent middle ear muscle reflexes (MEMR), also known as *acoustic reflexes*; normal tympanometry; and no evidence of a space occupying lesion upon neurological examination. Individuals with AN display normal to profound HL that may fluctuate, be characterized with poor speech perception ability (particularly in the presence of noise) that may not correlate to the audiogram, and a flat or reverse slope audiogram configuration is common. These individuals may vary significantly from one another in their ability to use temporal cues because AN results in degraded processing of temporal cues in speech.[2,6,7,9,11,12,14–17] Sininger and Starr[18] state that AN is typically bilateral and shows no gender preference. Prevalence of AN has been found to be ~10% of the children identified with HL from the universal newborn hearing screening (UNHS) programs.[11,17,19]

Sites of Lesion and AN. The specific sites and mechanisms of AN are not yet known and the variable behavior of the disorder means that the disorder can improve, remain stable, or worsen over time. The inconsistency in the clinical course and the prognosis often makes management of the disorder difficult. Individuals with AN are often misdiagnosed as having central auditory processing disorder or attention deficit disorder due to their inability to attend to a signal in noise.[2,6,10] Research has shown evidence that AN is a hearing disorder where sound enters the ear normally but the transmission of signals from the inner ear to the brain is impaired.

Research by Akman et al[2] and Foerst et al[7] concludes that possible sites of lesion include

the inner hair cells, the tectorial membrane, the synaptic junctions between the inner hair cells, the auditory neurons in the spiral ganglion, the eighth nerve fibers, or a combination of the above. In addition, they state that neural problems may be axonal or demyelinating, may affect the afferent and efferent pathways, and may possibly relate to the biochemical abnormalities that involve the release of neurotransmitters.

AN and Comorbidities. Previous research has shown that AN may coexist or be associated with a multitude of other disorders, but may be diagnosed in individuals with no risk factors or associated disorders. Some of the associated disorders include Friedreich's ataxia, hydrocephalus, ischemic-hypoxic neuropathy, spinocerebellar degeneration, Charcot-Marie-Tooth neuropathy syndrome, hereditary sensory motor neuropathies, perinatal intracranial hemorrhage, low birth weight, poor Apgar scores, hyperbilirubinemia, prematurity, ototoxic drug exposure, mechanical ventilation, cerebral palsy, anoxia, other peripheral neuropathies, or an underlying genetic cause.[11,15,17]

Risk Factors and AN. Dowley et al[14] conducted a study in the United Kingdom that examined the audiological data from the local newborn hearing screening program. Out of the 45,050 infants screened, 30 were diagnosed with hearing impairment, and 12 of those 30 babies were also diagnosed with AN, making the annual incidence of AN 0.27/1000. The authors concluded that all infants diagnosed with AN were treated in the neonatal intensive care unit (NICU) with the most significant risk factors being hyperbilirubinemia, sepsis, and gentamicin exposure. These risk factors agree with other published research indicating the presence of hyperbilirubinemia to be 50 to 73%, prematurity to be 30 to 46%, ototoxic drug exposure to be 41 to 80%, family history of HL to be 36 to 38%, mechanical ventilation to be 36%, and cerebral palsy to be 9 to 15%. In addition, two (~10%) of the infants with AN showed improvement in their auditory brain stem response thresholds at 10 months and 7 months.

Hyperbilirubinemia causes degeneration of the spiral ganglion fibers and is one of the most common conditions observed in newborn infants. Recently, emerging bodies of evidence have surfaced suggesting that the auditory nervous system is the most sensitive nervous system to the effects of bilirubin toxicity, leading to the conclusion that severe hyperbilirubinemia often results in a sensorineural hearing loss (SNHL). Akman et al[2] sought to evaluate if a correlation existed between increased serum bilirubin and neuron-specific enolase (NSE) assays and AN. They examined 19 infants who were treated for hyperbilirubinemia. None of these infants had a 5-minute Apgar score of less than 7, and infants with bilirubin levels above 20 mg/dL were given a full assessment, screened for glucose-6-phosphate dehydrogenase deficiency, and treated with phototherapy and/or exchange transfusion. All infants returned to normal after therapy, which eliminated the possibility of Crigler-Najjar syndrome. The 19 infants were split into two groups: group A had total bilirubin equal 20 to 25 mg/dL and group B had total bilirubin over 25 mg/dL. These infants were compared with a control group; seven of these infants were diagnosed with AN by utilization of ABR, transient evoked OAE, and presence of a CM, six being within group B and one infant within group A. Repeatable ABRs at 3 to 4 months and again at age 1 year showed no improvement for five of the seven infants. One infant was lost to follow-up and one infant was deceased at 2 months of age. The authors were not able to find a statistically significant difference in serum NSE levels between the groups; however, infants with AN had higher NSE levels than those who passed the ABR, indicating a possible relationship between serum NSE levels and ABR results. Although they were not able to perform further tests in their patients, an animal model of bilirubin toxicity in rats demonstrated that high bilirubin concentrations can result in abnormal ABRs in the presence of normal CMs supporting the notion that AN may be a sequela of hyperbilirubinemia. Xoinis et al[13] concluded that infants with AN were more premature and had lower birth weights (<1000 g), and they experienced longer ventilation periods and chronic lung disease than those infants with SNHL.

Madden et al[15] conducted a retrospective medical chart review of 428 children with HL

from the Children's Hospital Medical Center in Cincinnati, Ohio. Of the 428 children diagnosed with HL, 22 children were given a diagnosis of AN. This indicates the prevalence of AN is 5.1% of their population with known SNHL. In 1996, they implemented the routine utilization of OAE's. Since then, their incidence of AN is 10% per year in their population with SNHL. Of the 22 children diagnosed with AN, nine were male, 13 were female, 18 were white, and four were African-American. Fifteen children had a complicated perinatal course, with 11 being diagnosed with hyperbilirubinemia, 10 were premature, nine had ototoxic exposure, eight were subjected to mechanical ventilation, and two were diagnosed with cerebral palsy. Eighteen of the 22 children diagnosed with AN had complete audiological data, of these 18, nine (50%) showed evidence of spontaneous improvement in the hearing thresholds that tended to stabilize by a mean of 5.8 months. They compared the spontaneous improvement to children with and without hyperbilirubinemia and found that children with jaundice were more likely to display a profound HL but spontaneously improve. The improvement was noted to be statistically significant at 500 Hz, 1 kHz, and 2 kHz with the children having a stable audiogram by a mean of 18 months. Interestingly, in eight of their patients they noted a recessive inheritance pattern indicating a possible genetic factor. These children did not display improvements in hearing thresholds.

Rance et al[19] conducted a retrospective study of 20 infants and young children who were assessed as part of a HL identification program because the children displayed risk factors for HL and required testing regarding their hearing status and/or speech and language development. The authors concluded the prevalence of AN within the at-risk population was 1 in 433, or 0.23%. Within the group of children with permanent HL, the prevalence of AN was 1 in 9, or 11.11%.

Genetic Basis of AN. Recently, research has been conducted that has focused on the genetic basis of AN. Manchaiah et al[8] published a report that served to provide an overview of the genetic conditions associated with AN. AN is a heterogenous disorder that can have either acquired or congenital causes and it is estimated that roughly 40% of individuals with AN display an underlying genetic basis. The largest proportion of AN with genetic cause is syndromic, nonsyndromic, or mitochondrial related. In addition, all four inheritance patterns can be included. Marlin et al[20] stated that in developed counties, there is a genetic origin in 60 to 80% of congenital deafness cases. Nonsyndromic HL accounts for 90% of these individuals where mutations lie in the otoferlin (OTOF) and pejvakin genes, whereas 10% are syndromic. OTOF presents itself in the inner hair cells and leads to synaptopathy and peripheral auditory dysfunction and is often defective in DFNB9 deafness, which is associated with AN. If OTOF is not present in the cochlea, adequate performance of the inner hair cells will not occur, leading to a mismatch in neural firing and asynchrony of the auditory pathway. The OTOF gene contains 48 exons, and 41 OTOF mutations have been described worldwide.[21]

Temperature-Dependent Deafness. Manchaiah et al[8] ascertain that different gene mutations may trigger different pathological changes in each individual with AN. One pathological change that occurs in some individuals with AN is temperature-dependent deafness. Berlin et al[6] suggests that the fluctuating listening abilities in some individuals with AN may be due to changes in their core body temperature. Marlin et al[20] studied a consanguineous family with one son and two daughters. The parents were first cousins who were not afflicted with any auditory impairments nor did they display a family history of auditory impairments. The children were assessed utilizing tympanometry, MEMR, ABRs, transient evoked OAEs, distortion product OAEs, and brain imaging. The children were diagnosed with AN based upon abnormal or absent ABRs, normal transient evoked OAEs, and no lesions or malformations of the auditory pathways observed on the brain images. When the children's temperature was 38°C or lower, they displayed normal to mild hearing impairment. However, when their body temperatures rose above 38°C, the son displayed a profound hearing impairment and the daughters displayed severe hearing impairments. Genetic screening was conducted and the

researchers concluded that the hearing impairments were due to OTOF mutations. Wang et al[22] found a similar case of temperature-sensitive AN when the authors were attempting to identify OTOF mutations in Chinese Han patients with nonsyndromic AN.

Relationship of Ethnicity and AN. Research has also been conducted to identify the locus of pathology relating to other ethnicities with AN. Rodríquez-Ballesteros et al[23] concluded that in a Spanish cohort of 15 individuals, 13 (87%) carried two mutations of OTOF. In their cohort of non-Spanish countries, they found two mutations of OTOF in 11 out of 20 individuals. They reported that the large difference between the cohorts is due to the high frequency of p.GIn829X in Spain. Romanos et al[24] reported a 64% prevalence (7 of 11) of individuals carrying a mutation in the OTOF gene among a Brazilian population.

We know of four loci that are responsible for gene mutation leading to AN: DFNB9 (OTOF gene) and DFNB59 (pejvakin gene) that are responsible for autosomal-recessive AN, AUNA1 for autosomal-dominant AN, and AUNX1 for X-linked ANSD. We also know that mitochondrial mutations may be related to AN.

CT and MRI Scans. In a 2012 research presentation, Gardner-Barry[25] reported that in a population of 142 children younger than 10 years seen at the Sydney Cochlear Implant Center, 16% had abnormalities on their CT scans, which included Mondini deformities, wide internal auditory meatus, dysplastic apical turn, and abnormal vestibule and lateral semicircular canals. In this population of 142 children, 20% of the children with bilateral AN (B-AN) and 6% of the children with unilateral AN (U-AN) had compromised auditory nerves. A total of 43% of the children had disabilities in addition to HL. Children with AN and associated cochlear nerve deficiency have worse speech perception 1 year post–cochlear implantation than children with AN and normal cochlear nerves.[26]

Teagle et al reported the preimplant imaging results of 48 children that found that 18 (38%) children had 23 different abnormalities.[27] Abnormalities included periventricular leukomalacia (15%, $n = 7$), cochlear nerve deficiency in at least one ear (19%, $n = 9$), Dandy-Walker malformation (4%, $n = 2$), severe inner ear malformation including cochlear hypoplasia (6%, $n = 3$), Arnold Chiari type II malformation (2%, $n = 1$) and optoinfundibular dysplasia (2%, $n = 1$). No child with cochlear nerve deficiency achieved open set discrimination post–cochlear implantation.

CHARACTERISTICS OF AN IN A COLORADO STATE POPULATION

Prevalence of the Disorder. The state of Colorado instituted UNHS in two hospitals in 1992. Legislation for UNHS was passed in the late 1990s, and by 2000 the birth population of the state was being screened universally. The number of babies born from 2002 to 2010 was 626,701. The number of babies screened from 2002 to 2010 was 610,829. Of newborns, 97.5% were screened from 2002 to 2010. The overall percentage of babies screened is well above the 95% recommended benchmark established by the Joint Committee on Infant Hearing 2007 Position Statement on Principles and Guidelines for Early Hearing Detection and Intervention Programs.[28] The follow-through rate from referral to diagnostic audiology ranged from 80 to 87%, one of the highest follow-through rates of all states in America. The state of Colorado has a relatively small number of audiologic diagnostic evaluation sites and by 2002, they were routinely conducting evaluations of AN. Children in the NICU were screened with automated ABR (AABR), whereas ~50% of the children in well-baby nurseries were screened with AABR and 50% with OAE screening. More infants in the well-baby nursery were screened with AABR in 2002 than in 2010.

U-AN versus B-AN. From 2002 to 2009, 873 Colorado infants were diagnosed with SNHL from the UNHS program. The overall incidence of SNHL within the UNHS population from 2002 to 2009 is 0.16%.

From 2002 to 2012, 67 infants were diagnosed with AN. Of the 67 infants with AN, 14 were unilateral and 53 were bilateral. The prevalence of ANSD in the total population of babies screened in Colorado from 2002 to 2010 is 0.01%. The prevalence of B-AN in the total population of babies screened in Colorado

from 2002 to 2010 is 0.0087%. The prevalence of unilateral ANSD in the total population of babies screened in Colorado from 2002 to 2010 is 0.0023%.

Proportion of Children with of AN in the NICU and Well-Baby Nurseries. Of the 67 babies, 14 (21%) were unilateral, and 53 (79%) were bilateral. Of the 67 babies, 60 (90%) were in the NICU, and seven (10%) were in the well-baby nursery. Of the seven babies from the well-baby nursery, three (43%) were unilateral, and four (57%) were bilateral. Of the 60 babies in the NICU, 11 (18%) were unilateral, and 49 (82%) were bilateral.

Developmental Characteristics of Colorado Children with B-AN. Developmental data on AN children was available for 40 of the 67 (60%) children. Thirty-seven of the 53 (72%) children with B-AN in this birth cohort had some developmental information. Of the 11 children with U-AN from the NICU, there was information on two of the children, or 18%.

Proportion of Children with B-AN with Additional Disabilities. In the state of Colorado, children with U-AN qualify for developmental progress monitoring but not for early intervention services. Of the 37 children with B-AN who have developmental information, 12 of the 37 have significant cognitive delays/disorders. This number represents 32%—or one in three children. Among children with sensory HL, ~10% of the population has an additional cognitive delay. The prevalence of cognitive disorder and AN is ~3 times more than that found among children with sensory HL. Nine or 75% (three-fourths) of the children with significant cognitive delays had complex significant additional cognitive and neurological, sensory, and motor disabilities, developmental quotients ranging from developmental quotients (DQs) of 12 to 52. This represents one in every four of the children with AN (9/37).

The other 5 of 12 children had DQs ranging from 65 to 79. Less than half of the children with cognitive disabilities and AN had cognitive quotients (CQs) within what is typically considered the educable range. A total of 21 of 37 children had additional disabilities in addition to the HL for a prevalence of 57% with additional disabilities. Of the children with additional disabilities, about half of them had a significant cognitive delay. Thus, only 4 of 10 children with AN did not present with additional disabilities.

Sixty-eight percent or 25 of 37 children with B-AN had CQs within the normal range. A remarkable 84% or 21 of these 25 children had normal cognitive levels and normal language levels. This statistic is remarkable because it represents 57% of the total 37 children with B-AN despite the fact that 62% of the total population had HL with additional disabilities.

Nine of these 24 children (37.5%) with normal cognitive levels had significant additional disabilities. These nine children are 24% of the 37 children with B-AN. However, it is significant to note that of the children with nonverbal CQs within the normal range, there were a significant number of children with additional disabilities (e.g., motor/orthopedic or sensory) that impact learning but not language potential.

In summary, 32% of the Colorado children with B-AN had significant cognitive disabilities in addition to AN, 57% of the Colorado children with B-AN had normal CQs and normal language levels, 24% of the Colorado children with B-AN had normal CQs and additional disabilities. A total of 57% of the children with bilateral AN had additional disabilities.

Language in the Home. Twelve of the 37 (32%) Colorado children with B-AN were Hispanic/Latino. Of the Hispanic/Latino families with children who had B-AN, 83% were from Spanish-speaking homes. Ten of the 37 were first language Spanish in the home; in other words, 27% of the 37 families were from non-English-speaking homes. Although almost one in three of these children with B-AN were not native English speakers, it is critical to have clear understandable information for parents in Spanish.

Gender. Thirty-five percent of the Colorado children with B-AN were female and 65% of the Colorado children with B-AN were male. The incidence in males is almost twice the incidence of females for B-AN.

Children with U-AN and Developmental Data. Only two of the U-AN children had developmental data. Both the children with U-AN had significant additional cognitive and neurological disabilities. The reason that

there were not more children with U-AN with developmental data in this age group is because children with U-AN are not eligible for early intervention services in the state of Colorado unless they have significant developmental delay.

There are three distinctive groups: (1) children with no additional disabilities, normal cognition, and normal language; (2) children with normal cognition additional disabilities, some of whom have normal language development; and (3) children with cognitive disability and AN.

Amplification Options. Four of the 37 children (10.5%) got a cochlear implant (CI). Five of 37 (13.5%) children did not use amplification. Twenty-eight of 37 (76%) used hearing aids. It is generally accepted that the earlier that children with B-AN are amplified, the better the longitudinal results. Unfortunately, it is often difficult to amplify children early when there are no behavioral thresholds and no responses on the ABR testing. It is hoped that cortical auditory evoked potentials (CAEPs) might provide some information about audibility especially in the absence of ABR thresholds and behavioral responses.

Communication Approach Selection. Thirty-one of 37 of the families chose to learn sign language from a deaf or hard of hearing fluent or native signer. This represented 82% of the population of Colorado children with AN. The use of sign language in communication with their children was variable and dependent upon the child's receptive and expressive spoken language. Many parents learned sign language in the event that their children were unable to learn to listen and speak or had significant difficulties that compromised their language development.

CANDIDACY FOR COCHLEAR IMPLANTATION

Children with AN can present with a variety of audiograms, ranging from normal thresholds, mild to profound HL improving behavioral thresholds, fluctuating behavioral thresholds, and stable behavioral thresholds. They can be congenital or acquired HLs. Rance et al[19] reported that ~50% of the children with AN who they studied benefited from conventional amplification. However, often these children did not perform as well with their amplification as one would anticipate based on their behavioral thresholds. Some of the children are excellent candidates for cochlear implantation, whereas others do not appear to benefit from the CI. Some of the children, particularly children with unilateral profound AN, have aplastic or absent auditory nerves, thus an indicator that cochlear implantation would not be a good habilitative choice.

For children with congenital AN, cochlear implantation is often attempted in the first year of life. In the past, there were few assessment options to assist in this decision making. Little was known about the auditory development of children.

Audiological Assessments. Children with AN should have regular assessments within the first year of life, at least three to four times. Madden[15] reported nine children from the NICU who were diagnosed as AN but whose thresholds resolved to normal levels within the first year of life and whose audiological data stabilized by 18 months of age. It is not clear from this report whether or not the ABR as well as the behavioral thresholds also resolved to normal. Berlin et al[6] reported that 7% of the population had resolved behavioral thresholds. The primary question, therefore, must focus on the behavioral development of the children.

It is important to determine whether the children have audibility to the range of sounds across the speech spectrum for spoken English or spoken Spanish, for those children in Spanish-speaking homes. Many of these infants are being diagnosed within the first few months of life and there are no behavioral tests that are accepted as standard clinical audiologic diagnostic practice until the age of ~6 months.

Speech-language pathologists (SLPs)/early interventionists (EIs) can help the parents observe responses in the home and determine whether those responses to specific sounds are consistent or variable. With early intervention services, the parents can learn to stimulate the child on a regular basis with a variety of stimuli to get a better idea about the auditory behavior and development of the child. In cases where no ABR thresholds are

available and no behavioral responses have been obtained to sound in the sound suite, it may be possible to investigate whether sounds are reaching the auditory cortex through cortical evoked auditory potentials, but there are a limited number of research laboratories that are doing this testing. Therefore, the SLP/EIs are a critical component in teaching the parents to observe and report responses in the daily environment to sound. Daily checks with the Ling 6 sound test (/a/, /u/, /i/, /s/, /sh/, /m/) can help determine the child's auditory behavior with and without amplification and where the behavior is consistent or fluctuating.

Infant Monitor of Vocal Production.[29] The Infant Monitor of vocal Production (IMP) assesses the nature, pace, and integrity of an infant's auditory-vocal progress toward speech and first words following neonatal diagnosis of HL (i.e., birth to 12 months postamplification). The instrument takes the form of a short parent interview about the child's current vocal behavior. The IMP is presented at regular 3-month intervals. Online training enables professionals to become reliable with the coding. The training is free of charge; however, participants are required to register before they can access the training modules. They are also asked to consider sharing data collected using the IMP via the online database form on the training Web site. (Go to http://www.ridbcrenwickcentre.com/imp to register. Once registered, you will receive an email containing your login credentials.)

Sixteen probe questions elicit parents' observations of hierarchical changes characterizing phonation and primitive articulation—such as question 3 ("What sounds do you hear Tommy make with his voice?")—through to canonical and prelinguistic babble—such as question 13 ("Do you hear Tommy 'talk' to himself when he is playing alone? What does he do?"). Parent observations are recorded both in quantity, as a relative frequency of behavior using a Likert scale, and in quality, variety, and complexity. The baseline IMP interview should be conducted at 4 to 5 months of age (16 to 23 weeks chronological or corrected age) to ensure evaluation of innate vocal competence prior to the infant's anticipated transition from reflexive phonation to vocalizations influenced by auditory access to spoken language. The second interview should occur at 7 to 8 months of age when the typically developing infant makes the transition to an active Audition-Production Loop and has the physical ability to produce vocal patterns imitating speech. The third interview should occur at10 to11 months of age to monitor the timely emergence of vocal productions reflecting the integrity of the infant's auditory processing of sound variety and suprasegmental aspects of native language prior to the use of first words. The manner and rate of an infant's progress through these three major vocalization periods can assist the CI candidacy team in evaluating the benefit of any amplification being worn by the child.

Auditory Skills Checklist from the Children's Hospital in Cincinnati. This instrument can be found in the published article, which also includes data on the average gain in auditory skill post–cochlear implantation.[30] To date, there are no data on children with normal hearing or children using hearing aids on this instrument.

Visual Reinforcement Infant Speech Discrimination. Once audibility across the speech spectrum has been assured, it is then possible to measure the child's ability to detect differences in phonemes and consonant-vowel syllables, words, or even babbling streams. Using a traditional visual reinforcement audiometry paradigm for response, a conditioned head turn, it is possible to determine whether the child is able to discriminate the difference between two stimuli pairs at a criterion level indicating the probability of skill mastery and replicability. Any phoneme pair can be used as the stimulus. We initially select the three vowel sounds in English at the boundaries of the vowel triangle, /a/, /u/, /i/, /s/, /sh/, place discrimination (e.g., pa/ka, or ba/ga) and voicing /ta/-/da/, /ka/-/ga/. Any phoneme combination can be used in any prerecorded language in the world. The assessment is, itself, a training, and children are often observed to master a discrimination paradigm within the half-hour session and often begin to vocalize either a phoneme or consonant-vowel syllable not previously used. Identified early, children implanted with CIs demonstrate mastery of the vowel discrimination at 1 month, place discrimination at 2 months, and voicing at 3 months post–cochlear implantation.[31]

Language Development. Parent questionnaires are a useful, reliable, and quick way of documenting developmental progress. The MacArthur-Bates Communicative Development Inventories, Words and Gestures, and Words and Sentences[32] can be administered and information about the development of spoken words and signed words, or words in other languages, can be observed and documented. The Child Development Inventory[33] is a useful tool to investigate overall development and includes general development, expressive language, language comprehension, self-help, social, gross motor, fine motor, letters, and numbers. We typically also administer the Situation Comprehension subscale from the 1972 edition as an additional index of development. As stated previously, because of the 61% of the population of children with AN who have additional disabilities, it is crucial to have an instrument that charts developmental progress across a broad range of development. Only with this information, will it be possible to interpret the language development outcomes for children with AN.

First Contact. After diagnosis of the HL, families receive contact from a Colorado Hearing Coordinator within 48 hours, and attempts for a first home visit are made within a week after the diagnosis. There are 11 Colorado Hearing Coordinators throughout the state of Colorado. They provide parents with information about the diagnostic audiologic evaluation and the characteristics of AN. They discuss early intervention options and help the families coordinate services. Because the vast proportion of these infants were in the NICU, there are often many medical professionals involved in the care and treatment for these children.

Sessions per Week. Families have access to an early intervention specialist with specific training in early childhood deafness and HL and family centered early intervention services. The EI provider makes a home visit weekly for 1.5 hours a visit.

Sign Language Instruction. The Colorado Home Intervention Program offers all families with newly identified children with HL weekly sign language instruction from deaf and hard of hearing sign language instructors who are native or fluent in American Sign Language.

Early Intervention in Spanish. Eighty percent of the children in Spanish-speaking homes in the Colorado Home Intervention Program receive early intervention services from a primary provider who conducts the training in Spanish without an interpreter. When the early intervention provider does not have adequate Spanish skills, the parents have the option of an interpreter who can accompany the early intervention provider for home visits and who has been trained on the early intervention curriculum.

Counseling Parents about AN. Parents in the United Kingdom have reported that they do not find it helpful to have their children compared with children with SNHL because they have no experience with SNHL. They suggest that talking about "auditory dyslexia" is helpful. They also found explaining AN as listening to static or a broken radio, or listening between frequencies helps them understand why their children appear to hear but not understand.[27] Some families refer to "fuzzy" hearing days and "clear" hearing days. Some parents describe their children as having hearing days or moments and nonhearing days or times.

CASE STUDIES

Eddie

Eddie moved in from another state, so we do not have access to his UNHS results. Eddie was diagnosed at 18 months of age. He received his first CI at 20 months of age and the second at 23 months of age. Eddie's nonverbal cognitive potential was assessed on several instruments at the low average level. However, his personal social development was 6 months above age level indicating that his motor challenges could be impacting his developmental scores. He received parent-infant intervention, preschool services through a center-based program, a 6-week oral preschool experience, and was mainstreamed into kindergarten with overall developmental functioning at age level and commensurate with his hearing peers. At the age of 33 months, Eddie's articulation included most of the vowels and consonants of spoken English. His vowels were 61% correct but his consonants were only 32% correct. His early

interventionist and parents rated him considerably more intelligible than the linguistic coder who was not familiar with his speech. At almost 3 years of age, his parents knew 213 of 400 signs. Eddie used up to three-word sentences in sign language. He used up to four-word sentences using spoken English. It is significant to note that initially within the first year and a half to 2 years postimplantation, the quality of his articulation was variable. Eddie is currently mainstreamed into a typical classroom with no special education services. By 5 years of age, Eddie had developed language within the range of his typically developing peers and increased his intelligibility. Eddie is characteristic of a child with auditory dyssynchrony. Child-centered auditory spoken language habilitation began after the cochlear implantation. Eddie transitioned from heavy reliance upon visual communication for instruction to a dominant auditory/spoken language communication for learning.

Carlos

Carlos was born in Colorado. He initially referred on AABR screening in the left ear only. Upon rescreening, he did not pass transient evoked otoacoustic emissions (TEOAE) or AABR bilaterally and had normal neonatal tympanometry. He was diagnosed at 2 months of age with AN, TEOAEs were absent bilaterally; distortion product otoacoustic emissions were partially present in the right ear and absent in the left ear. There were no repeatable neurologic responses to click stimuli, there were robust, reversing polarity CMs bilaterally, and MEMR were absent bilaterally. His first behavioral assessment at 6 months of age revealed pure tones in the profound rising to moderate HL range. By his first birthday, he had no spoken words and limited vocalizations. He was fit bilaterally with hearing aids, and at 18 months of age he demonstrated significant functional gain with the hearing aids. He appeared to benefit from the hearing aids, but was not making speech and spoken language progress. Additionally, communication concerns were noted such as limited eye contact, preference for playing with cars above anything else, not responsive to sign or spoken language, and limited vocalization. However, he was quite social. A comprehensive developmental assessment with a psychologist with training and skills in deafness and HL ruled out autism spectrum disorder. He continued to receive weekly home intervention services with a skilled interventionist who used sign and spoken language and a SLP who worked on listening and spoken language. Vestibular testing revealed normal vestibular evoked myogenic potentials bilaterally, MRI was normal, and there were absent CAEP P1 potentials. He received his first CI at 18 months of age. At the time of surgery, there were no electrical compound action potentials (ECAP) with normal impedances, an indicator that is associated with atypical, poor, or absent speech perception.[28,34] When his CI was activated, he continued to have absent ECAP, with slow progress in spoken and visual language system, and P1s were then present with the first CI. One year later, due to poor progress, a third P1 testing was repeated and at that time the P1s were absent. He continued weekly intervention services as well as working with a therapist skilled in listening and spoken language intervention two times each month, alternating with an early interventionist who used simultaneous communication. The family as well as the interventionists reported good and bad hearing days. He continued to be unable to discriminate speech but demonstrated the ability to detect speech. At 26 months of age the parents started to inquire about a second CI. The Language ENvironment Analysis (LENA) digital language processor was used to assess his daily auditory language learning environment to aid in determining if he had adequate access to spoken language at home. LENA recorded that his parents used ~23,990 adult. He used 675 conversational turns, which was at the 72nd percentile of children with normal hearing and typical development and he made 2312 vocalizations at the 57th percentile. However, his Automatic Vocalization Analysis standard score was 73.9 at the 4th percentile, indicating that his vocalizations were not developing toward intelligible speech. For more information about LENA, please see the article in this issue by Aragon and Yoshinaga-Itano.[35]

Carlos received a second CI at 35 months of age. At the time of surgery, his impedances were

within normal limits, and ECAP was absent. Two weeks later when the CI was activated, he was observed responding to sound, and ECAP responses were measured on some channels but not all. He responded consistently to the Ling 6 sound test. With bilateral CIs, he responded to speech and tones in the mild HL range. Spoken language continues to be significantly delayed. However, he is using more signs and can communicate his needs fairly well. His communication with sign language consists more of pantomime than verbal language. He does not appear to be able to functionally use sound/speech. It seems the electrical stimulation using current processing strategies may not be sufficient to overcome underlying processing effects of AN. P1s were repeated 4 months after the activation of his second CI and 17 months following the activation of the first CI. At that time, the P1 was present, but delayed for the first ear and absent for the second ear alone. But the P1s fluctuated from present to absent during the CAEP evaluation.

Carlos' nonverbal cognitive potential was assessed on several instruments and on all instruments he was within the normal range, as was his personal social developmental quotient. Currently he has discontinued auditory-spoken language therapy, works weekly with a speech therapist using simultaneous communication, and prefers sign language He began preschool in a total communication classroom when he turned 3 years of age. At the age of 33 months, the number of vowels and consonants in his spontaneous vocalization were insufficient for intelligible speech and oral language. His early interventionist and parents rated him slightly better than the linguistic coder who was not familiar with his speech, but his speech is largely unintelligible. At almost 3 years of age, his parents knew 400 of the 400 signs assessed. Carlos used primarily one-word sentences in sign language. Although delayed in language expression, Carlos is increasing the rate of his language learning. However, he remains a puzzle and his teachers and therapists use differential diagnostic teaching to determine the most appropriate and successful teaching strategies.

SUMMARY

AN/dyssynchrony is very heterogeneous in site of lesion, abnormality of brain scans, and presence of HL and comorbidities. Parent exposure and knowledge of visual communication in addition to listening and spoken language therapies can result in age level language development even in the presence of multiple comorbidities when parents make educated decisions about the use, combination, and flexibility of communication approaches.

Two in every three children with B-AN have cognitive development in the normal range. Two in every three children with B-AN have HL and an additional disability. Half of these children have a cognitive disability. One in every three children with B-AN has a significant cognitive disorder. Additionally, data from Australia indicates that one in five of the children with B-AN had compromised auditory nerves and one in every six had abnormal CT scans. Because of the high percentage of the children with B-AN from the NICU, there is also a high proportion of children with histories of hyperbilirubinemia, prematurity, low birth weight, otologic drug history, and mechanical ventilation. An estimated four of 10 children with B-AN are believed to have a genetic cause. HL can be normal to profound, can fluctuate, and in a few cases can improve over time, but typically within the first year of life.

It is possible for two out of every three children with B-AN to develop language skills, birth to 36 months, within the normal range of development despite the high proportion of children with additional disabilities, albeit often at low average and borderline normal range.

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