REVIEW ARTICLE

Risk Factors for Sensorineural Hearing Loss in Children

Faustino Núñez-Batalla,* Germán Trinidad-Ramos, José Miguel Sequí-Canet, Valentín Alzina De Aguilar, Carmen Jáudenes-Casaubón

Comisión para la Detección Precoz de la Hipoacusia Infantil (CODEPEH), Madrid, Spain

Received 23 February 2011; accepted 27 February 2011

KEYWORDS
Hearing screening; Sensorineural hearing loss; Risk factors

Abstract In the last decade, tremendous progress has been made very rapidly in the development of Early Hearing Detection and Intervention (EHDI) systems as a major public health initiative. The percentage of infants screened annually in Spain has increased significantly since the EHDI systems have expanded to all autonomic regions. Historically, high risk indicators have been used for the identification of infants who should receive audiological evaluation but who live in geographic locations where universal hearing screening is not yet available, to help identify infants who pass neonatal screening but are at risk of developing delayed-onset hearing loss and to identify infants who may have passed neonatal screening but have mild forms of permanent hearing loss. In this review, the standard risk factors for hearing loss are analysed and the risk factors known to be associated with late onset or progressive hearing loss are identified. The recommendation for infants with a risk factor that may be considered as low risk is to perform at least one audiology assessment in 24–30 months. In contrast, for an infant with risk factors known to be associated with late onset or progressive hearing loss (such as cytomegalovirus infection or family history), early and more frequent assessment is appropriate. All infants should have an objective standardised screening of global development with a validated assessment tool at 9, 18 and 24–30 months of age or at any time if the health care professional or the family is concerned.
© 2011 Elsevier España, S.L. All rights reserved.

PALABRAS CLAVE
Cribado auditivo; Hipoacusia neurosensorial; Factores de riesgo

Indicadores de riesgo de hipoacusia neurosensorial infantil

Resumen En la última década hemos asistido a un rápido y tremendo progreso en el desarrollo de los sistemas de diagnóstico y tratamiento precoz de la hipoacusia infantil dentro de programas de salud pública. El porcentaje de niños cribados anualmente en España se ha incrementado significativamente al haberse extendido los programas de atención al déficit auditivo infantil a todas las autonomías. Históricamente, los indicadores de alto riesgo han sido empleados para la identificación de los niños que debían ser evaluados auditológicamente por vivir en

* Corresponding author.
E-mail address: fnunezb@telefonica.net (F. Núñez-Batalla).

2173-5735/$ - see front matter © 2011 Elsevier España, S.L. All rights reserved.
areas remotas donde los programas de cribado no existían, para ayudar a identificar aquellos niños que, aunque hayan pasado el cribado, siguen presentando riesgo de desarrollar una hipoacusia diferida y para identificar los niños que presentan hipoacusias permanentes leves no detectadas en el cribado. En esta revisión se analizan los indicadores de riesgo de hipoacusia y se identifican los factores que se asocian a sus formas de presentación diferida. La recomendación establecida es que se lleve a cabo al menos una revisión audiológica entre los 24 y los 30 meses de edad en los niños con un indicador de bajo riesgo. Sin embargo, para aquellos que presenten factores de alto riesgo como la infección por citomegalovirus o antecedentes familiares de hipoacusia es apropiado realizar un seguimiento más frecuente y temprano. Para todos los niños, incluidos los que carecen de indicadores de riesgo, se debería comprobar su desarrollo global con una herramienta validada a los 8, 18, 24 y 30 meses de edad o antes si existe preocupación de los padres o cuidadores.

© 2011 Elsevier España, S.L. Todos los derechos reservados.

Introduction

In 1999, the Spanish Commission for Early Detection of Hearing Loss (CODEPEH), proposed the development of a Programme for Early Detection, Treatment and Prevention of Childhood Hearing Loss,1,2 based on the recommendations established in the Position Statement of the Joint Committee on Infant Hearing Screening (JCJHS) from 1994.3 Since 1972, the JCJHS had identified specific risk indicators that are often associated with hearing loss in children. These indicators have been used around the world with 2 purposes: first, to help identify children who should undergo audiological studies living in geographic locations where there is no universal neonatal screening for hearing loss (for example, developing countries or remote areas). Although screening programmes for children at high risk area no longer recommended because they fail to detect approximately 50% of hearing loss cases, this approach can be still be used in places where limited resources prevent universal screening. Second, to help identify those children who should be monitored and supervised medically and audiolologically, because normal hearing at the time of birth does not guarantee that hearing loss may not have a deferred development or late onset.4 More recently, a third necessity has appeared in programmes for early detection of hearing loss: identification of children with increased risk of auditory neuropathy.5

After considering the recommendations for early detection of hearing loss from the year 2010,6 CODEPEH considered it necessary to analyse the risk indicators of childhood hearing loss, as this subject is under constant update and also considered as an important tool for the development of Childhood Auditory Deficit Care Programs.

Evolution of Risk Indicators for Childhood Hearing Loss

The first risk indicators were established in 1972,7 in order to identify infants with a considerable probability of suffering from hearing loss. At that time it was known that it was necessary to identify hearing loss early in order to avoid its consequences, but the technology required to conduct population screening was not available. A total of 5 indicators were established: family history of deafness, congenital infection of the TORCH group (toxoplasmosis, rubella, cytomegalovirus, herpes), hyperbilirubinemia, craniofacial malformation and birth weight below 1500 g. In 1982, 2 new risk indicators were added: bacterial meningitis and severe asphyxia. In addition, the need to follow or monitor certain children due to their increased probability of developing late-onset hearing loss was also recognised, although no specific periodicity of reviews was recommended. In order to help identify these children, 3 indicators were defined: family history of hearing loss, neurodegenerative diseases and intrauterine infection. There were subsequent modifications and additions to the list of risk indicators in 1990 and 1994,3 which took into account new knowledge derived from multicentre studies of large populations of infants. It was then recognised that the risk indicators could be divided into 2 categories: those present during the neonatal period and those which appeared later as a result of certain diseases or were iatrogenic during childhood treatment. Thus, indicators were classified into 3 groups by age of onset: the first group, to be used in infants up to 28 days of age, to identify those who should be screened as being at greater risk in areas where there was no universal screening. The second group, was to be used in children aged between 29 days and 2 years, to conduct a re-screening when certain risk indicators were identified. Finally, the third group, was to be used in children aged between 29 days and 3 years, to identify those with an increased risk of suffering progressive or late-onset hearing loss (Table 1).

In 2000,4 a list was published which continued to group factors both by age at which they should be observed and by the purpose for which they should be used. However, this list introduced changes, eliminating some indicators with respect to the list from 1994. The indicators which should be taken into account from birth until 28 days of age were: admission at a neonatal intensive care unit (NICU) for 48 h or more, stigmata or findings associated with a syndrome including hearing loss, family history of permanent childhood sensorineural hearing loss, craniofacial malformations including those affecting the ear and ear canal, and intrauterine infections (cytomegalovirus, herpes, toxoplasmosis and rubella).

The indicators to be considered in infants aged between 29 days and 2 years were: suspicion by parents or caregivers, family history of hearing loss, stigmata or findings associated with syndromes including deafness, postnatal infections associated with sensorineural hearing loss, such as...
meningitis, intratereineinfections (TORCH), neonatal indicators (hyperbilirubinemia requiring exchange transfusion, persistent pulmonary hypertension of the newborn with mechanical ventilation and use of extracorporeal membrane oxygenation), head trauma and recurrent or persistent oitis media with serous content for 3 months or more.

Following the identification of 1 or more of these indicators, the recommendation was to audiology monitor the case every 6 months until the age of 3 years.

In 2007, JCIIHS further amended the list of indicators and proposed a single list, since the indicators associated with congenital/neonatal hearing loss and those associated with progressive/late onset hearing loss overlapped significantly. This publication updated the definition of hearing loss target, expanding it to include neural hearing loss or auditory neuropathy (AN) in children admitted to a neonatal intensive care unit. Concern that auditory neuropathy was not overlooked in screening programmes led to separate protocols being recommended for children admitted to NICUs: in programmes based on otoacoustic emissions this population should be screened by automated brainstem auditory evoked potentials (aABEP). A major change was introduced in risk factor number 3, which now considered an admission of over 5 days at a NICU instead of 48h. This was done because it was observed that stays under 5 days were not associated with increased risk of hearing loss. This modification was established because it was considered easier to implement a time criterion (>5 days) than for personnel conducting the screening to identify specific risk indicators by only studying medical records of children admitted to a NICU. Following that from 2000, the Position Statement of 2007 continued to recommend 3 applications for the list of risk indicators: historically, the first use was to identify children who should be studied audiologically but who lived in geographic locations which hindered it or where there was no universal screening. The second purpose of the indicators was the identification of children who, having passed the initial screening, were at risk of developing late-onset deafness, so they should be under medical, audiological and speech and language acquisition surveillance. The third purpose was to identify those children who, having passed the neonatal screening, presented mild or moderate permanent hearing loss.

Of the 11 risk indicators included in this single recommended list (Table 2), those marked with an asterisk are those with a higher probability of being associated with hearing loss: earlier and more frequent monitoring should be implemented for children in whom these increased risk indicators were identified.

An important recommendation was to carry out monitoring of developmental milestones and listening skills in paediatric primary care. This was done in order to

### Table 1 Risk Indicators Recommended in the 1994 Position Statement.

**Indicators for use in places where there is no universal screening from the time of birth until 28 days of age:**

1. Family history of hereditary childhood deafness
2. Intrauterine infection (TORCH)
3. Intracranial malformations including the ear and auditory canal
4. Birth weight under 1500 g
5. Hyperbilirubinemia with levels requiring exchange transfusion
6. Ototoxic drugs, including but not limited to aminoglycosides, used in various rounds or in combination with loop diuretics
7. Bacterial meningitis
8. Apgar score of 0–4 at 1 min or 0–6 at 5 min
9. Mechanical ventilation during 5 or more days
10. Stigmas or findings associated to syndromes including conductive or sensorineural hearing loss

**Indicators for use between 29 days and 2 years of age, when certain medical conditions developed make re-screening necessary:**

1. Concern by parents or caregivers for a delay in hearing or development of speech and language
2. Bacterial meningitis or other infections associated with sensorineural hearing loss
3. Head trauma with loss of consciousness or fracture
4. Stigmas or findings associated to syndromes which include conductive or sensorineural hearing loss
5. Ototoxic drugs including, but not limited to, aminoglycosides, used in multiple rounds or in combination with loop diuretics
6. Recurrent or persistent oitis media with serous content for over 3 months

**Indicators for use between 29 days and 2 years of age, when periodic monitoring of hearing is indicated. Some children develop late-onset hearing loss after being screened. These children require their hearing to be monitored every 6 months until 3 years of age and upon demand thereafter.** The indicators of late-onset sensorineural hearing loss are:

1. Family history of hereditary infant deafness
2. Intrauterine infection (TORCH)
3. Type II neurofibromatosis and neurodegenerative diseases

The indicators of deferred conductive hearing loss are:

1. Recurrent or persistent serous oitis media
2. Anatomical malformations or other anomalies affecting the Eustachian tube
3. Neurodegenerative diseases
Some risk indicators deserve to be analysed separately, either because they have been removed from the list or because their identification poses other problems.

**Acute Perinatal Hypoxia–Ischaemia**

Subsequent amendments to the list of hearing loss risk indicators featured the removal of the acute perinatal hypoxia–ischaemia indicator, which was defined with the Apgar score. This was motivated by the findings of numerous studies on the subject. Mencher and Mencher studied 16 factors which had been associated with perinatal hypoxia–ischaemia and found that 5 of them were related to the presence of hearing loss. The most interesting result was the Apgar score at 1 min, which was supposed to be a critical factor for hearing loss. It was the only factor to present statistical significance, but paradoxically in the opposite direction: an abnormal Apgar score at 1 min was more commonly associated with the normal hearing group than with the group affected by hearing loss. This result had already been reported by Sykes et al. and Sankaran and Vivek, so it could not be considered as unexpected nor lacking in credibility. In their study of 760 children with hypoxia–ischaemia, Brown et al. concluded that the Apgar score should be analysed in association with other neurological and behavioural signs, since the test is based on subjective interpretation and, therefore, may not reflect the assumptions correctly. In summary, medical literature initially questions the Apgar score at 1 min due to its inconsistency and, therefore, lack of reliability as an indicator of neonatal asphyxia and hearing loss. Thus, its inclusion in the high-risk registry is considered inappropriate. Successive recommendations were sent, from including this risk indicator to its definitive exclusion in the Year 2000 Position Statement of the JCIH.

**Hyperbilirubinemia**

Hyperbilirubinemia is one of the main problems encountered in the neonatal period, especially in children with other risk factors. Its sequelae include neurological deficits, such as kernicterus, generalised encephalopathy and sensorineural deafness. At present, early treatment of hyperbilirubinemia by phototherapy and exchange transfusion avoids severe neurological sequelae, but associated hearing loss is still relatively frequent. Sensorineural involvement occurs as a result of increased indirect bilirubin in the blood, but has no proportional relationship with the levels reached, so it is possible to find cases with involvement and 8 mg/dl of bilirubin and normal cases with 25 mg/dl. This effect may be due to the interaction with other risk factors present in the patient which may enhance the effect of hyperbilirubinemia (prematurity, low birth weight, hypoxia, metabolic acidosis or perinatal infections). In these patients, bilirubin levels above 14 mg/dl represent a risk for hearing loss in 30% of cases. The mechanism of bilirubin neurotoxicity and its risk levels are not known at present, but it is thought to require prior crossing of the blood brain barrier in order to exert a neurotoxic effect potentiated by other metabolic disorders, such as acidosis, hypoxia, hypercapnia or hyperosmolarity. Cochlear function is intact due to the presence of

<table>
<thead>
<tr>
<th>Table 2 Risk Indicators Recommended in the 2007 Position Statement and Currently Recommended by CODEPEH.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Suspicion of hearing loss or delay in the development or acquisition of speech</td>
</tr>
<tr>
<td>2. Family history of permanent infant hearing lossa</td>
</tr>
<tr>
<td>3. All children, with or without risk indicators, admitted at a NICU for over 5 days, for any of the following: extracorporeal oxygenation, assisted ventilation, ototoxic antibiotics (gentamicin, tobramycin) and loop diuretics (furosemide). Moreover, hyperbilirubinemia requiring exchange transfusion, regardless of length of stay</td>
</tr>
<tr>
<td>4. Intracranial infections, such as cytomegalovirus, herpes, rubella, syphilis and toxoplasmosis (TORCH)</td>
</tr>
<tr>
<td>5. Craniofacial anomalies, including those affecting the ear, ear canal and temporal bone malformations</td>
</tr>
<tr>
<td>6. Physical findings such as a white forelock, which are associated with a syndrome including permanent sensorineural or transmissive hearing loss</td>
</tr>
<tr>
<td>7. Syndromes associated with progressive or late onset hearing loss or deafness, such as neurofibromatosis, osteopetrosis and Usher syndrome. Other syndromes frequently identified include Waardenburg, Alport, Pendred and Jervell and Lange-Nielsen</td>
</tr>
<tr>
<td>8. Neurodegenerative diseases like Hunter syndrome, sensorimotor neuropathies, such as Friederichax ataxia and Charcot-Marie-Tooth syndrome</td>
</tr>
<tr>
<td>9. Postnatal infections associated with sensorineural hearing loss, including confirmed cases of bacterial and viral meningitis (especially herpes virus and varicella)</td>
</tr>
<tr>
<td>10. Head trauma, especially at the skull base or temporal fracture, requiring hospitalisation</td>
</tr>
<tr>
<td>11. Chemotherapy</td>
</tr>
</tbody>
</table>

a Risk indicators marked are associated with a considerable probability of late-onset hearing loss.
otoacoustic emissions in affected patients, but involvement of the auditory pathway is demonstrated through the BAEP test. This is currently the most used test in children, both to identify this involvement and to demonstrate its reversibility after the fall of bilirubin levels following treatment. Hearing loss varies depending on nerve involvement and can range from mild to profound, with a fall at high tones which may be reversible or remain stable over time. Other cases may develop late-onset, progressive hearing loss.\(^\text{18}\) Neonatal hearing loss screening using only otoacoustic emissions (OAE) has the risk of not identifying hearing losses caused by hyperbilirubinemia. On the other hand, using only aBAEP for screening would leave important information concerning the presence of auditory neuropathy in the hearing loss cases detected. Therefore, the recommended method is the use of a screening protocol which adequately combines otoacoustic emissions and aBAEP.\(^\text{19,20}\) Regular hearing checks are recommended, since there is a possibility that children may suffer developmental changes in their hearing, as well as fitting of prosthetics when required.

### Birth Weight Under 1500 g

This indicator was included in the lists until the Position Statement of 2000, when it was excluded. Therefore, it is no longer considered as a risk indicator of congenital hearing loss or late-onset hearing loss. Considering this indicator alone, studies with populations of children with low birth weight have shown rates of prevalence and relative risk of developing hearing loss which were inversely proportional to the weight quantified at birth. This indicator increases in importance when associated with other common disorders in the population of infants requiring admissions over 5 days at a NICU.\(^\text{21}\)

### Stay at NICU Over 5 Days

This factor refers to all children, with or without risk indicators, admitted to a NICU for over 5 days, for any of the following reasons: extracorporeal oxygenation, assisted ventilation, ototoxic antibiotics (gentamicin, tobramycin) and loop diuretics (furosemide). Moreover, it also includes hyperbilirubinemia requiring exchange transfusion, regardless of length of stay. This risk indicator was introduced in the Position Statement of 2007 by modifying the previous recommendation of 48 h admission at a NICU, which served as the basis for the new recommendation of conducting separate screening protocols for populations of infants admitted or not at a NICU. Although this risk indicator is not specific and no pathophysiological basis is suggested for its association with hearing loss, it responds to the fact that there is a clear association between sensorineural hearing loss and problems occurring at the time of birth.\(^\text{22}\) This risk indicator simplifies the task of reviewing the medical history of infants, thus reducing the likelihood of errors. It is supported by the observation that 52% of newborns admitted to a NICU are discharged within 5 days and have very small probability of a showing an identifiable risk indicator.\(^\text{5}\)

Mencher and Mencher\(^\text{9}\) found that a combination of hypoxic–ischaemic encephalopathy, seizures, associated organ damage and delayed intrauterine growth represented a solid indicator of probable hearing loss. Observations such as these do not go unnoticed, since newborns with this type of disease far surpass 5 days admission at a NICU.

This new indicator represents significant organisational changes and equipment requirements for screening programmes based on otoacoustic emissions, but also simplifies the process of reviewing medical records for staff who are conducting the screening process. Indeed, in order to avoid auditory neuropathy going unnoticed, staff were faced with the overhead of having to carefully analyse the medical history of each infant so as to determine whether there were risk factors which indicated a BAEP test in addition to otoacoustic emissions, even if these were normal. Thus, directly testing the population admitted for over 5 days at a NICU with automated BAEP as a screening method minimises the possibility of auditory neuropathy going undetected, and also simplifies the process. Other advantages of this risk indicator are that it also includes other adverse factors which are unique to NICU admission, such as ambient noise at those units. Children may be exposed to noise levels between 45 and 135 dB, thus exceeding the maximum recommended level of 58 dB,\(^\text{23}\) for extended periods of time.\(^\text{24}\) This has a synergistic action with the administration of aminoglycosides in producing auditory damage.\(^\text{25}\)

### Extracorporeal Membrane Oxygenation Therapy

Treatment with extracorporeal membrane oxygenation (ECMO) consists of a prolonged, life support bypass for patients with acute and reversible respiratory or cardiopulmonary failure. It allows the lungs to recover whilst also avoiding barotrauma and oxygen toxicity. ECMO enables life preservation for critical newborns with a success rate of 78%. However, there are high rates of neurodevelopmental disorders among children who have survived with this technique, including cerebral palsy, mental retardation and hearing loss.

This population has to be monitored closely, since immediate or late-onset hearing loss is detected in 26% of cases. Out of these cases, hearing loss is progressive in 72%. Receiving aminoglycoside therapy also increases the probability of hearing loss, with a direct relationship with the duration of both factors. Hearing loss is usually bilateral and symmetrical, with a severity ranging from mild forms at high tones to profound deafness. Half of the children with a normal initial audiological assessment develop late-onset hearing loss. Given these presentation forms, it is recommended to monitor these children audiologically by BAEP at discharge and then at 12, 18, 30 and 42 months with appropriate audiometric tools. Moreover, the use of aminoglycosides warrants closer monitoring at shorter time intervals.\(^\text{26}\)

### Family History of Hereditary Childhood Deafness and Auditory Neuropathy

By aetiology, congenital sensorineural hearing loss is inherited in over half of the newborns. In general (75%–80% of cases), both parents present normal hearing and their children suffer non-syndromic sensorineural hearing loss due to an autosomal recessive mechanism. Other inheritance possibilities are autosomal dominant (20%), X-linked (2%–5%)
and mitochondrial (1%). Sensorineural hearing loss due to GJB2 allelic variants can be explained by an altered function of the protein which they encode, connexin 26. The Q829K mutation in the otoferlin gene (OTOF) is the third most common mutation responsible for prelingual deafness in the Spanish population. The most prevalent mutations are 35delG in the connexin 26 gene and the deletion which truncates the connexin 30 gene. This genetic defect causes non-syndromic auditory neuropathy with recessive inheritance, so in affected cases it is possible to verify the functional integrity of external ciliated cells in the context of sensorineural hearing loss. This makes it possible to find newborn patients with normal otoacoustic emissions who also present a more or less significant hearing loss, consistent with auditory dis-synchrony/auditory neuropathy. The most common form of syndromic hereditary sensorineural hearing loss is Pendred syndrome. In most cases it is characterised by congenital sensorineural hearing loss, generally significant, a dilated vestibular aqueduct with or without cochlear hypoplasia (Mondini malformation) and a pathological perchlorate test or goitre. This syndrome is rarely diagnosed in the neonatal period, since goitre has not yet appeared, and also because imaging tests are not usually performed so early. Most affected children have mutations in the SLC26A4 gene on chromosome 7q31.

**Intrauterine Infection**

The term TORCH refers to the following infections: toxoplasmosis, rubella, cytomegalovirus, herpes and, additionally, syphilis. They cause prenatal, acquired, sensorineural hearing loss through transplacental transmission from mother to foetus, leading to cases of deafness which are present at birth or with a progressive or belated onset. The incidence of congenital rubella has decreased dramatically in developed countries due to the introduction of rubella vaccine in the late 1960s. However, the global importance of rubella as a cause of acquired sensorineural hearing loss is still considerable, even representing the leading cause in various developing countries. In developed countries, congenital infection by cytomegalovirus (CMV) is the most common cause of acquired sensorineural hearing loss in newborns, although its exact incidence is still unknown. Half of these children with clinical signs have sensorineural hearing loss and in many other cases it is progressive. Infants with silent infections do not usually present neurodevelopmental sequelae, but 8%-10% develop sensorineural hearing loss belatedly.

**Syndromes Including Hypoacusis or Physical Exploration Findings Which Orient Towards Them**

Approximately 30% of patients with childhood deafness present clinical findings which define a particular syndrome. Over 400 syndromic forms of deafness have been characterised. Table 3 summarises some syndromes, along with their phenotype, responsible gene and inheritance pattern. In many cases, this risk indicator overlaps with the craniofacial malformations risk indicator.

**Chemotherapy**

Treatment with chemotherapeutic agents is considered as an important risk factor for hearing loss in children. Cisplatin is the most commonly used agent, since it exhibits the most potent ototoxic action. Cisplatin (cis-diaminedichloroplatinum II) is a platinum divalent compound with a potent, non-specific action on the cell cycle which can lead to an irreversible, sensorineural hearing loss at high frequencies. In addition, it can be associated with renal failure by tubular necrosis and interstitial nephritis and peripheral neuropathy. There is considerable variability in the individual presentation and susceptibility to cisplatin ototoxicity, manifested by the appearance of transient tinnitus in 7% of cases, accompanying hearing loss. Individual susceptibility to the ototoxicity of this agent can even lead to hearing loss from a single, high dose. In general, hearing loss occurs in 62% of treated patients and is usually bilateral, affecting frequencies from 4000 to 8000 Hz. The first signs appear 3 or 4 days after administration and become clinically apparent in 7% of individuals. This ototoxicity is more important in children, due to its widespread use for the treatment of solid tumours in this population (osteosarcoma, germ cell tumours, neuroblastoma) and its higher severity (range between 84% and 100%), probably enhanced by concurrent cranial irradiation. In the case of children, acute hearing loss induced by cisplatin (defined by thresholds higher than 40 dB at 1000 Hz or more) occurs in half of the children with a standard dose (60–100 mg/m² per course). Of these, one third will require hearing aids to compensate for hearing loss.

**Continued Monitoring of Auditory Health in the Infant Population**

There are 2 problems which require a search for specific risk indicators in every newborn: auditory neuropathy in programmes based on otoacoustic emissions and the identification of children with probability of late-onset hearing loss, both in programmes based on otoacoustic emissions and in those based on automated BAEP.

Auditory neuropathy (AN) is a hearing disorder affecting newborns with a history of acute perinatal hypoxia–ischaemia, family history of hearing loss and hyperbilirubinemia. Methods of neonatal screening for hearing loss based on otoacoustic emissions are not able to detect this disorder, so it is important to identify children at risk for auditory neuropathy in order to test them with BAEP, even if they present normal otoacoustic emissions. Their identification is linked to specific screening and audiological diagnostic tests and can go undetected depending on the screening strategy employed. Diagnosis may be delayed after discharge from the Neonatal Unit. The JCIH comments on this issue in its Year 2000 Position Statement, recommending an assessment of the prevalence of the problem and its natural history, in order to treat the disorder with better knowledge.

The need to review screening protocols is becoming clear as knowledge of auditory neuropathy increases. In fact, the Position Statement from 2007 has expanded the definition of the hearing loss screening target to include...
AN, and also recommended profound changes in screening strategies in the newborn population admitted at a NICU for over 5 days. The term auditory neuropathy was first used by Starr et al. in 1996 to describe 10 patients who had developed hearing loss in the presence of normal, external, cochlear ciliated cells. In 2001, Berlin et al. recommended using the term auditory neuropathy/auditory dis-synchrony due to the presence of poor synchrony of the auditory nerve. This suggests a more logical relationship with viable treatment options. The pattern of auditory neuropathy has been observed in various presentations from infants to adults with acquired hearing loss. Therefore, auditory neuropathy/auditory dis-synchrony is not a diagnosis but a presentation form of hearing loss, currently identifiable by screening with otoacoustic emissions and BAEP. It is not a new disease, but rather an entity which is currently recognised through advances in audiology. Since auditory neuropathy is still a relatively unknown disorder due to the lack of long-term prospective studies, we cannot determine a prognosis about the auditory potential and speech and language development in these children. In some children, it is important to establish close monitoring during the early development of speech and language, due to a lack of data on the long-term evolution and variability of auditory neuropathy. This monitoring should be coordinated with primary healthcare services from neonatology. Furthermore, it should be made clear to parents that successfully passing a newborn hearing loss screening does not rule out the possibility of a child suffering mild-moderate or belated hearing loss. These facts make it imperative to identify children with a probability of late-onset hearing loss.

Some hearing disorders in childhood are not detectable in neonatal screening, as they are not present at that time. This includes late-onset and acquired hearing loss, as well as congenital hearing loss which is not sufficiently severe to be detected at the time of screening. The overall prevalence of late-onset hearing loss is about 10% of all childhood hearing losses, but it is suspected to be higher. This fact does not affect the intrinsic relevance of universal neonatal screening for hearing loss. Instead, it means that additional actions should be conducted and that screening programmes should be designed to ensure that all children with significant hearing loss are detected early. Many programmes include some type of re-screening aimed at children who present certain risk factors for late-onset or progressive hearing loss. However, early identification of these deferred disorders requires a level of attention and knowledge by the medical establishment which must be developed through training programmes and information strategies.

One of the most important changes in the JCIH recommendations is monitoring the hearing health of children. The recommendation is to establish a monitoring and screening programme in primary care which, ideally, would be responsible for the following activities:

- Each regular visit in the programme of a healthy child should include an evaluation of auditory skills, middle ear status and developmental milestones. The use of a validated tool to implement comprehensive screening at 9, 18, 24, and 30 months of age, or earlier if there are concerns by parents or caregivers, is also recommended.
- If a child does not pass the speech and language evaluation within the overall screening, or if the paediatrician or parents suspect hearing loss, the case must be immediately referred to a hearing unit for study.

### Table 3 Syndromes Associated With Hearing Loss.

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Physical Signs (in Addition to Deafness)</th>
<th>Inheritance Pattern</th>
<th>Gene Responsible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alport</td>
<td>Nephritis, ocular anomalies</td>
<td>80% linked to X chromosome, 15% AR, 5% AD</td>
<td>XLAS: COL4A5</td>
</tr>
<tr>
<td>Branchio-oto-renal</td>
<td>Branchial remains, renal anomalies</td>
<td>AD</td>
<td>ARAS: COL4A3</td>
</tr>
<tr>
<td>CHARGE</td>
<td>Alterations in eyes, ears, heart, delay in growth, genitalia</td>
<td>Sporadic or AD</td>
<td>ADAS: COL4A3</td>
</tr>
<tr>
<td>Jervell and Lange-Nielsen</td>
<td>Alterations in cardiac electric conduction</td>
<td>AR</td>
<td>JLN1: KCNQ1</td>
</tr>
<tr>
<td>Type II neurofibromatosis</td>
<td>Acoustic nerve neurinomas Goitre Retinitis pigmentosa, vestibulopathy</td>
<td>Sporadic or AD</td>
<td>JLN2: KNE1</td>
</tr>
<tr>
<td>Pendred Usher</td>
<td></td>
<td>AR</td>
<td>NF2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AR</td>
<td>SLC26A4 (PD5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AR</td>
<td>USH1B: MYO7A, USH1C:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>USH1C, USH1D: CDH23,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>USH1E: unknown, USH1F:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PCDH15, USH1G: USH1G,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>USH2A: USH2A, USH2C:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>GPR98, USH3: CLRN1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>WS1: PX3, WS2: ATIF,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SNAI2, WS3: PX3, WS4:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>END3, ENDRB, SHOX10</td>
</tr>
</tbody>
</table>

AD, autosomal dominant; AR, autosomal recessive.
After confirming hearing loss in a child, his siblings are considered at high risk of deafness and must undergo an audiological evaluation.

Regardless of the findings in monitoring, all children with a risk indicator for hearing loss (Table 2) should be referred for audiological assessment at least once between the ages of 24 and 30 months. Children presenting risk indicators which are strongly associated with late-onset hearing loss, such as extracorporeal oxygenation or cytomegalovirus infection, should be audiollogically assessed more frequently.

All children in whose family there is significant concern about their hearing or communication should undergo relevant audiological and speech and language evaluations without delay.

A careful examination of middle ear status during each review is recommended for healthy children. Children in whom serous otitis is found for at least 3 months should undergo an otological evaluation.

References


