1 Epidemiology of permanent childhood hearing impairment

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INTRODUCTION

Hearing impairment is the most frequent sensory impairment in humans, with significant social and psychological implications. The effect of the impairment will vary from individual to individual due to factors such as severity, age of onset, treatment / management options and the hearing status of their parents. It is likely that the greatest impact of hearing impairment upon a child is on the acquisition of language and development of communication, which in turn can lead to poor literacy skills\(^1\,^2\) and altered long-term employment opportunities.\(^3\,^4\) It is likely that other areas of development will also be affected, for example, mental health,\(^5\,^6\) with one study finding 50% of a sample of hearing-impaired 11- to 16-year-olds met diagnostic criteria for a mental illness.\(^7\)

Despite these difficulties, it is possible that, given adequate support, their impact may be reduced. For example, language development may be enhanced through the use of language support programmes, and residual hearing may be used effectively through adequate amplification from hearing aids or cochlear implants.\(^4\,^8\) It has long been suspected that earlier diagnosis leads to better adjustment,\(^9\) and evidence increasingly shows that a support programme starting in the first few months of life, used in tandem with early identification procedures, is beneficial for hearing-impaired children and their families (see Davis et al.\(^10\) for an overview or Barton et al.\(^11\) for an example). Support may be available through educational services, audiology services, social services and mental health services – and this support should be individualised, family-friendly and culturally sensitive.\(^10\,^12\,^13\)

In the light of the impact that permanent childhood hearing impairment (PCHI) can have on children and their families, the importance of epidemiological studies cannot be underestimated. Epidemiological studies can provide information concerning the aetiology of hearing impairment and the groups within a population who are most at risk, which can be used to plan primary prevention by modifying relevant risk factors; it can be used to target those most likely to become hearing impaired and help detect them. They can also provide information on the overall prevalence of hearing impairment that can help estimate how many children have PCHI in different areas, helping plan secondary prevention of complications. Demographic and follow-up data can be used to make sure the services on offer are appropriate for users. For meaningful epidemiological studies, hearing impairment needs to be classified. Definitions may take into account not only the severity of the hearing impairment, but also the pathology and ontogenesis of the impairment, hence these factors are a major focus of this chapter.
DEFINITIONS USED IN EPIDEMIOLOGICAL STUDIES

Epidemiology is the study of how often diseases occur in different groups of people and why. When talking about research into hearing impairment, Sancho et al.\textsuperscript{14} use the term ‘epidemiology’ to refer to ‘the study of the distribution and determinants of hearing disorders in a population, and the application of the knowledge obtained to the prevention and amelioration of hearing problems’. A population study is the primary methodology for gathering information. The word ‘population’ in this case refers to the whole collection of units from which a sample may be drawn, but not necessarily to a population of people. For example, it may be a collection of hearing aid clinics or schools for the deaf. The sample is intended to give results that are representative of the population as a whole. A cohort is that component of a population born during a particular period and identified by period of birth, so that its characteristics (such as prevalence of childhood hearing impairment or age at first hearing aid fitting) can be ascertained as it enters successive time and age periods. If an epidemiological study follows a cohort and studies the group at several different intervals, the project is called a cohort study. A cohort study can be a follow-up study, a prospective study or a longitudinal study. It is essential for understanding change over time and the impact of services.

Another key term associated with epidemiology is incidence. This refers to the number of new instances of a specific condition (such as hearing impairment from meningitis) occurring during a certain period in a specified population. The incidence rate is the rate at which this occurs per standard population, for example 10 new cases per year per 100,000 children. The term prevalence is often confused with incidence. However, these are not the same thing. Prevalence is the total number of instances within a given population at a specific time in which a specific condition (for example, Pendred syndrome) is present. In the case of hearing impairment, prevalence may be described as ‘the proportion of individuals with a defined type of hearing impairment in a specified population cohort’.\textsuperscript{14} Accordingly, the prevalence rate is the number of individuals who have the condition or attribute divided by the population at risk at a point in time.

When attempting a prevalence study, if there are $n$ children with hearing impairment in the study and the whole population is $N$, then the prevalence rate is $\left(\frac{n \times 100}{N}\right)\%$. In this case we must be sure that the $n$ hearing-impaired children really come from all the birth cohorts of children represented by the population of $N$ and that there is a coterminosity of $n$ and $N$ in terms of geographical boundaries. It is quite common to either underestimate $n$ (because not all children with a given condition have been found) or to confuse populations (often because of migration of children into or out of particular districts).

THE DIFFICULTIES IN ESTIMATING PREVALENCE

Accurate estimations for the prevalence of childhood hearing impairment worldwide are hindered by the great difficulty in interpreting the data; perhaps leading to the variability in prevalence rates seen from study to study. These variations may be thought of as arising from three factors: how cases of hearing impairment are defined; how cases of hearing impairment are found; and the population from which the cases come. The importance of having agreed definitions for epidemiological studies, such as the ones outlined in the previous section, can be seen to be of paramount importance. The lack of agreed prevalence rates hinders investigation of possible risk factors and aetiologies, in turn, having implications for the planning of
service provision. Boxes 1.1 and 1.2 present the commonly used definitions for the various types of hearing impairment.

The term ‘deaf’ is generally associated with the most extreme form of hearing impairment, in which there is no response to auditory stimuli in excess of 120–125 dB at any frequency. This condition is practically never seen and is considered very rare. Hearing impairment, on the other hand, primarily refers to a series of descriptive terms that define the decibel level at which an individual responds to sound (see Box 1.2). Hearing impairment is also defined by the frequency range the person can hear. That is, a low-frequency range is <500 kHz; a mid-frequency range is 500 to 2,000 kHz; a high-frequency range is 2,000 to 8,000 kHz; and an extended high-frequency range is >8,000 kHz. The pattern of the frequencies is also important with some fairly self-explanatory terms, such as u-shaped, low-frequency ascending, flat and high-frequency sloping, used as descriptors of the responses plotted on an audiogram.

### Box 1.1 Definitions of the various types of hearing impairment.

<table>
<thead>
<tr>
<th>Type of impairment</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensorineural</td>
<td>Related to disease/deformity of the inner ear/cochlear nerve with an air–bone gap less than 15 dB averaged over 0.5, 1 and 2 kHz</td>
</tr>
<tr>
<td>Conductive</td>
<td>Related to disease or deformity of the outer/middle ears. Audiometrically there are normal bone conduction thresholds (less than 20 dB) and an air–bone gap greater than 15 dB averaged over 0.5, 1 and 2 kHz</td>
</tr>
<tr>
<td>Mixed</td>
<td>Related to combined involvement of the outer/middle ears and the inner ear/cochlear nerve. Audiometrically greater than 20 dB HL in the bone conduction threshold together with greater than or equal to 15 dB air–bone gap averaged over 0.5, 1 and 2 kHz</td>
</tr>
<tr>
<td>Sensory</td>
<td>A subdivision of sensorineural related to disease or deformity in the cochlea</td>
</tr>
<tr>
<td>Neural</td>
<td>A subdivision of sensorineural related to a disease or deformity in the cochlear nerve</td>
</tr>
<tr>
<td>Central</td>
<td>Sensorineural hearing loss related to a disease or deformity of the central nervous system rostral to the cochlear nerve</td>
</tr>
</tbody>
</table>

### Box 1.2 Definitions of hearing impairment in dB levels.

<table>
<thead>
<tr>
<th>Type of impairment</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average hearing level</td>
<td>The level of the thresholds (in dB HL) measured in the better hearing ear at 0.5, 1, 2, 4 kHz</td>
</tr>
<tr>
<td>Mild</td>
<td>Average hearing level 20–39 dB HL</td>
</tr>
<tr>
<td>Moderate</td>
<td>Average hearing level 40–69 dB HL</td>
</tr>
<tr>
<td>Severe</td>
<td>Average hearing level 70–94 dB HL</td>
</tr>
<tr>
<td>Profound</td>
<td>Average hearing level +95 dB HL</td>
</tr>
</tbody>
</table>
Given the variety of types of hearing impairments presented in Box 1.1, it can easily be understood why there may be some confusion when attempting to define prevalence and/or incidence. However, the problem is compounded even further when various generalised categories for the course of the hearing impairment and the pattern of the hearing impairment are taken into consideration. Hearing impairment can be *congenital*, meaning to be present and detectable using appropriate tests at or very soon after birth, or *acquired*. However, there can be a difference in the meanings of these terms when considering aetiology as well as prevalence – as the cause of hearing impairment may be present at birth, but problems in hearing appear later in life. *Temporary* hearing impairment (usually, but not always, a conductive hearing impairment) can be treated and corrected by medical or surgical intervention. Such an impairment is often short-lived and of a mild nature. On the other hand, *permanent* hearing impairment cannot be readily treated by surgical or medical intervention. Both temporary and permanent hearing impairments can be *unilateral* (one ear only has either a greater than 20 dB hearing impairment through 500, 1,000 and 2,000 kHz or one frequency exceeding 50 dB, with the other ear normal) or *bilateral* (a greater than 20 dB hearing impairment through 500, 1,000 and 2,000 kHz or one frequency exceeding 50 dB in both ears). A unilateral situation is, of course, asymmetrical. However, in studies of hearing, the term *asymmetrical* hearing impairment specifically refers to a greater than 10 dB difference between the ears in at least two frequencies, with the pure-tone average in the better ear exceeding 20 dB HL. Finally, both temporary and permanent hearing impairments can be *progressive* – that is, there is a deterioration greater than or equal to 15 dB in the pure-tone average within a 10-year period.

Traditionally, studies have tended to be cross-sectional and based on retrospective ascertainment. A selection of these studies is shown in Table 1.1. It can be seen that estimates for prevalence of PCHI vary up to 10-fold (0.58 per 1,000, Baille et al.,\textsuperscript{15} to 6.59 per 1,000, Parving and Hauch\textsuperscript{16}) depending on definition, but most found levels of between 1.1 per 1,000 and 1.7 per 1,000 for their broadest definition.

Another method of cross-sectional study uses results from screening. This has the advantage of including cases that have not yet been diagnosed and works best for generating epidemiological data when the impairment is mild (and common) or where the whole population is screened. There are three common types of screen for hearing impairment: newborn; infant distraction test; sweep test.\textsuperscript{23} A ‘sweep’ test asks a child to respond to low-intensity pure tones at three or four set frequencies, and has been done by school nurses and others. It has been used routinely on school entry in the UK since 1955, but protocol and implementation vary around the country, and there have been few attempts at measuring outcomes until recently. The infant distraction test assesses children as young as seven months by testing their behavioural response to noise, but it has the potential to miss serious cases, and refer many infants with no hearing problem. Again, despite being routine in the UK, sensitivity, specificity and outcome were not monitored. In the 1990s, technology became available to provide proxy measures of hearing in even newborn babies. Transient evoked otoacoustic emissions identify the presence or absence of outer hair cell activity from the inner ear, and auditory brainstem response (ABR) identifies the presence or absence of electrophysiological activity from the early auditory pathway. Automated equipment is now available for each of these tests, which can be used by trained screeners in the NICU, at the mother’s bedside or in the community soon after birth. This has led to programmes of screening either high-risk babies or offering the test universally to every newborn baby. Universal newborn hearing screening (UNHS) has been has been recommended by the Joint Committee on Infant Hearing since 2000,\textsuperscript{24} and by
Table 1.1 Selection of studies showing how population, definition of case and method of ascertainment can affect prevalence.

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Definition of case</th>
<th>Method of detection</th>
<th>Prevalence per 1,000 children</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Congenital or acquired</td>
<td></td>
<td>2.09</td>
</tr>
<tr>
<td></td>
<td>All racial origins</td>
<td>Both</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Asian origin</td>
<td>All</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parving and Hauch 2001[^16^]</td>
<td>Aged &lt;1–10 living in Copenhagen, Denmark born 1990–1999</td>
<td>&gt;20 dB either ear at any frequency</td>
<td>Surveillance programme of all hearing impaired</td>
<td>2.91</td>
</tr>
<tr>
<td></td>
<td>Aged 11–20 living in Copenhagen, Denmark born 1980–1989</td>
<td></td>
<td></td>
<td>6.59</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>All</td>
<td></td>
<td>1.09</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>Sensorineural</td>
<td></td>
<td>1.11</td>
</tr>
</tbody>
</table>

Threshold: Pure tone thresholds measured in dB HL (hearing level). Most studies averaged across thresholds at 0.5, 1, 2 and 4 kHz. Better ear unless stated.
2005, approximately 95% of newborn infants in the United States were screened for hearing loss before they were 1 month old.\textsuperscript{12} UNHS has been piloted in the UK since 2001 and became standard in England in 2006. Unlike its predecessors, it was accompanied by an IT system and rigorous quality control (see Bamford et al.\textsuperscript{23} and the programme website http://hearing.screening.nhs.uk).

With the implementation of UNHS in some areas, more data are becoming available for estimating prevalence. Results from studies of UNHS express a ‘rate’ of hearing impairment detected per baby screened. Depending on the coverage the sensitivity of the test and the confidence of the diagnosis, prevalence of congenital hearing impairment can be made with increasing confidence. Uus and Bamford\textsuperscript{25} gave the rates for the newborn hearing screening programme (NHSP) in England based on the 21 pilot sites around the UK between February 2002 and June 2004. A total of 169,487 babies were screened and amongst the children referred from the screen, a confirmed permanent bilateral hearing loss of moderate or greater severity was found in 169. This leads to a rate of 1.00 (95% confidence interval 0.78–1.22) per 1,000 babies screened. The programme achieved 96% coverage, and 90% of those babies who needed further tests were followed up. Yields of PCHI outside the UK have ranged from 0.68 per 1,000 in Western Australia\textsuperscript{26} to 4.4 per 1,000 in Jackson, Mississippi, USA.\textsuperscript{27} Trying to look for true geographical differences is once again difficult due to definition of a case, which sometimes includes unilateral and mild impairments, and other differences between studies. Some hospitals excluded results from NICU babies when reporting and other hospitals were tertiary referral centres handling very ill babies. Some programmes / studies found that effectiveness was limited by poor rates of screening or attending for follow-up. Vohr et al.\textsuperscript{28} in Rhode Island, US, found that those with traditional Medicaid insurance were less likely to be screened or re-screened, whilst Prince et al.\textsuperscript{29} in Hawaii found that low birth weight babies and those born to women who had not completed high school were twice as likely not to complete follow-up.

**Prevalence of hearing impairment in the UK**

Various studies have been carried out in the UK to ascertain accurate prevalence rates; however, there has been considerable disagreement between the rates established. Variation in sample populations, hearing levels included in the study, the fluctuating numbers of children with hearing impairment, and no easy way of ensuring complete ascertainment of cases were all factors that led to such variation in prevalence figures. With no agreement on numbers, there was uncertainty about the extent of the problem that extended into the 1990s. For example, in Nottingham, prevalence of PCHI was estimated at 0.55/1,000 by Pabla et al.\textsuperscript{30} but 1.2/1,000 by Davis and Wood.\textsuperscript{31}

An extensive study of epidemiology of PCHI was carried out for the Trent Regional Health Authority by Fortnum and Davis.\textsuperscript{19} The aim was to include all children with a permanent hearing impairment of 40 dB HL average or greater in their better ear, who had been born between 1 January 1985 and 31 December 1993 and were living within the boundary of Trent Regional Health Authority at the time of data collection (June–September 1995). Sources of information included the Education Database, the Community Audiology and Child Health Database, the Neonatal Screening Database, audiology, medical records and hearing aid records. The data collected were divided into two main groups: congenital hearing impairment and acquired hearing impairment. The congenital group consisted of those children presumed to have had a prenatal or perinatal hearing impairment. The acquired
group included those whose hearing impairment came later in life due to disease, progressive hearing impairment or late-onset hearing impairment where there was evidence that the child may have been able to hear at an earlier stage. Prevalence rates of 1.3/1,000 for both acquired and congenital permanent hearing impairment were reported. For congenital hearing impairment alone, the prevalence rate was 1.1/1,000. Taking the prevalence estimates derived from the Trent region, it was possible to estimate that there would be approximately 1,000 children with a hearing impairment of at least moderate severity in the UK per annual birth cohort, around 84% having a congenital hearing impairment. These numbers undoubtedly contributed to a decision by the government of the UK to develop a newborn hearing screening programme.

For a more accurate calculation of prevalence across the whole of the United Kingdom, Fortnum et al.\textsuperscript{20} approached the health professionals and the education professionals responsible for hearing-impaired children around the country, requesting details on every child with PCHI under their care. A total of 486 professionals replied, with over 26,000 sets of details. Many of these overlapped if the child was known to education and health services and the child’s details were provided by both. The fact that there was no total overlap implies that there was some under-ascertainment. This can be adjusted for with a capture–recapture method – thus records for 17,160 children suggested there were around 21,500 children aged 3 to 18 in the UK with a permanent bilateral hearing impairment more than 40 dB. The inclusion of such a large number in the study allowed a more accurate breakdown into subgroups. It was shown that the observed prevalence increased with age until reaching a plateau at age 9, and that this was present at all three severities studied (41–70, 71–95, >95 dB HL). The adjusted prevalence at age 3 was around 1.1 per 1,000, rising to 2.1 per thousand at ages 9–16, a rise of 92%. This significant rise in prevalence during early childhood could be highly relevant for the planning of audiology and support services for secondary prevention of complications of hearing impairment, but this cross-sectional study is not ideal to confirm changes over time – because the change could arise either from the age of the cohort or the year in which the cohort was born.

Better ideas of change over time come from longitudinal studies, such as those carried out in the East London borough of Waltham Forest.\textsuperscript{32} The relevant cohorts were born between 1992 and 2000 and numbered around 33,000. The numbers of children with PCHI, the method of identification and audiological data were collected from educational and audiology services. These children had UNHS, some had the infant distraction test, and they all had a school-entry ‘sweep’ screen. Newborn screening identified 1.58 per 1,000 children as having PCHI. More babies with PCHI were later identified due to concerns raised by parents or health visitors before the children were 12 months old in a further 0.24 cases per 1,000. A further 1.30 per 1,000 children were identified as having permanent hearing loss before they entered school at age 5, mainly due to parental concern. Finally, 0.34 per 1,000 were identified by the school-entry screen. This gives a combined total prevalence of 3.47 per 1,000 children by primary school age identified as having PCHI – of which 43% were of a moderate or greater severity bilateral hearing impairment, 35% mild bilateral and 22% unilateral (mild or above). This increase came partly from people moving into the area, but also from children who had not been offered, who had declined or who had failed to complete the screening process. Around 10% of the later identified children had a history of meningitis, 15% a family history of hearing impairment, and 30% had some other developmental abnormality (especially craniofacial). Thus, it seems there is a real increase in prevalence of PCHI as a cohort ages, and therefore a need for services to identify and manage this impairment.
Prevalence of hearing impairment in the United States

Early detection and hearing intervention (EDHI) programmes were legally required in 41 states by 2007 to help improve outcomes for children with hearing impairments. In order to design these programmes and their predecessors, an estimate of prevalence is essential. The Metropolitan Atlanta Developmental Disabilities study was partly set up to help develop methods of surveillance of children with special needs such as hearing impairment. The study collected data on the prevalence of mental retardation, cerebral palsy, hearing loss, vision impairment and epilepsy in children aged 10 years living in five counties in metropolitan Atlanta. Cases were actively sought from records at a number of sources, educational and medical, public and private, to maximise ascertainment. A hearing loss was defined as a permanent impairment of 40 dB HL averaged across thresholds at 0.5, 1 and 2 kHz in the better ear. Drews et al. report on the prevalence of hearing loss in the cohort born during 1975, 1976 and 1977; who were age 10 in 1985–87. One hundred of the 10-year-old children had been identified and confirmed with PCHI out of a population of 89,534. This gives a prevalence of 1.1 (CI 0.9–1.4) per 1,000. Van Naarden et al. looked at children aged 3 to 10 in 1991–1993, finding 411 cases, giving a prevalence of 1.10 (CI 1.00–1.20) per 1,000 children aged 3 to 10. The prevalence varied with age, being lowest at 0.67 per 1,000 3-year-olds and rising steadily to 1.38 per 1,000 10-year-olds. The latter number shows an apparent increase in prevalence from the previous study of 10-year-olds. Both studies found that about 30% of the children had another disability, the most common being mental retardation. They also found that the prevalence was around 20% higher amongst black residents than white. An accompanying paper gives evidence for much of this difference being due to differing birth-weights: more babies with low birth weight are born to black mothers, and their outcome is less favourable than babies of low birth weight born to white mothers.

Another large population study to include childhood hearing impairment was the Third National Health and Nutrition Examination Survey (NHANES III), which used a 40,000-person sample with characteristics representative of the US population as a whole over 1988–1994. Niskar et al. report on children aged 6 to 19 who were asked about their hearing status and screened using pure-tone audiometry in a mobile examination centre. Self-report of ‘hearing difficulties’ (not necessarily permanent) was 34 per 1,000 children. They screened using frequencies representing speech (0.5, 1 and 2 kHz) and at higher frequencies (3, 4 and 6 kHz), and defined hearing loss as average thresholds for either frequency above 15 dB HL. A hearing loss in at least one ear was present in 149 per 1,000 children (14.9%), most of which was unilateral and slight in severity, and some of which was likely to have been temporary or fluctuating. However, by extrapolating from their data, the authors estimate that there are 7 million US children at any one time that may need extra help in the classroom due to a hearing impairment. An accurate count of how many children nationwide are getting extra funding for special education can be obtained from the reports of the Individuals with Disabilities Education Act Program (IDEA-B). Data for the 2005 report are broken down by disability and age for children aged 3 to 16. The number of children aged 3 to 16 for whom special education is funded due to a hearing impairment alone (there will also be children with PCHI in ‘deaf-blind’ or ‘multiple disabilities’ categories) was 70,702 – ranging from 2,174 aged 3 to 6,269 aged 12.

Universal hearing screening was taken up at differing rates across the United States, and a number of groups have published results from the early years of screening in individual hospitals and states – a selection of which is shown in Table 1.2. Once again, there is great diffi-
difficulty comparing between studies, and further difficulty in generalising from these yields to prevalence across the country since these pioneering programmes were likely to have taken place in large, well-resourced or well-motivated hospitals, many of whom had a large proportion of babies in NICU. As part of EHDI, data are being collected by the Centers for Disease Control and Prevention (CDC). The annual data for 2005 show that of nearly 4 million births in states who were screening, 91.5% of babies were screened. Unfortunately, of the 64,421 babies referred for further screening or investigation, outcomes are only known for 43.5%, the majority of the rest being lost to follow-up or lost to documentation. The incidence of unilateral or bilateral PCHI of any severity reported to CDC is 0.92 per 1,000 babies screened, but this seems likely to be a vast underestimate of the actual rate.

Norton et al. and Johnson et al. have both re-screened babies at high risk of hearing impairment to test the sensitivity of newborn screening protocols. They found that although they are very good at detecting hearing loss of moderate severity or above, they miss a large proportion or slight and mild impairments. This must be clear to parents, professionals and those who plan provision for children with hearing loss.

### Other ‘developed’ countries

Martin et al. performed an ascertainment study of hearing-impaired children in the European Community (nine countries) who were born in 1969, were eight years old at the time of the study and who had a hearing impairment of at least 50 dB HL. They found a prevalence rate of 0.9 per 1,000. They also reported that 29% of the children had additional disabilities. These figures agree well with similar studies in the United States. More recently, epidemiologists from European countries have compared prevalence of hearing loss from cohorts of children in the 1980s with the data from the Trent study in the UK. In Denmark, Davis and Parving reported on the prevalence of bilateral sensorineural or mixed PCHI of at least moderate severity (average threshold >40 dB HL), and the prevalence is shown by severity profile in

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### Table 1.2 Selected results from US screening programmes showing large variation in definition and rates.

<table>
<thead>
<tr>
<th>Citation</th>
<th>Site</th>
<th>Definition</th>
<th>Rate per 1,000 screened</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barsky-Firsker and Sun 1997</td>
<td>Tertiary referral centre, New Jersey</td>
<td>Sensorineural. Bilateral or unilateral. Not including babies from NICU.</td>
<td>2.1</td>
</tr>
<tr>
<td>Vohr et al. 1998</td>
<td>Rhode Island (statewide)</td>
<td>Sensorineural and permanent conductive</td>
<td>2.0</td>
</tr>
<tr>
<td>Mason and Herrmann 1998</td>
<td>University hospital, Honolulu, Hawaii</td>
<td>Bilateral loss requiring amplification</td>
<td>1.4</td>
</tr>
<tr>
<td>Finitzo et al. 1998</td>
<td>Texas (multi-site)</td>
<td>Detectable permanent.</td>
<td>3.14</td>
</tr>
<tr>
<td>Dalzell et al. 2000</td>
<td>New York (statewide)</td>
<td>Bilateral or unilateral</td>
<td>2.0</td>
</tr>
<tr>
<td>Stewart et al. 2000</td>
<td>Kentucky (multi-site)</td>
<td>Sensorineural</td>
<td>2.7</td>
</tr>
<tr>
<td>Mehl and Thomson 2002</td>
<td>Colorado (multi-site)</td>
<td>Sensorineural or permanent conductive. Bilateral</td>
<td>1.39</td>
</tr>
<tr>
<td>Connolly et al. 2005</td>
<td>Tertiary referral centre, Jackson, Mississippi</td>
<td>Detectable permanent.</td>
<td>4.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Country</th>
<th>40–130 dB HL</th>
<th>70–130 dB HL</th>
<th>95–130 dB HL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denmark</td>
<td>1.45</td>
<td>0.86</td>
<td>0.54</td>
</tr>
<tr>
<td>England</td>
<td>1.32</td>
<td>0.59</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Table 1.3 where it is compared with figures generated from the Trent study. Approximately 90% of hearing impairment reported was congenital in both studies. It can be seen that there were significantly more severely and profoundly hearing-impaired children in Denmark than in England. When risk factors were investigated it was found that significantly more congenitally hearing-impaired children had an NICU history in England (33%) than in Denmark (17%), whereas more hearing-impaired children had a family history of hearing impairment in Denmark (40%) than in England (27%). Further work by Uus and Davis, centred around the same issues in Estonia, reported that the prevalence of hearing impairment in Estonia (1.72 per 1,000) was higher than that of England (1.32 per 1,000) and Denmark (1.45 per 1,000).

Data from universal screening in parts of some countries are also available. Results from groups in Paris and Siena show rates of bilateral permanent hearing impairment >40 dB of 1.4 and 1.42 per 1,000 babies screened, respectively, which are slightly higher than the rate of 1.0 per 1,000 from the pilot sites in England, despite the fact the Paris study did not include babies from NICU. In Western Australia, the yield was found to be 0.68 per 1,000. Out of 28,708 babies screened over 7 months, only nine babies were diagnosed with permanent bilateral hearing loss and eight of these had known risk factors for PCHI. This was seen to represent a poor detection rate, and universal screening was subsequently stopped, with a return to targeted screening. In Asia, the yield of bilateral PCHI detected per 1,000 children screened was 2.8 in a university hospital in Hong Kong and 2.0 in a university hospital in Japan. It is not immediately clear whether the difference in yields between countries, has to do with the performance of the screening programmes, the prevalence of risk factors or some specific environmental / genetic influence on the population. In Taiwan, two studies looked at the feasibility of screening in two environments: a hospital in Taipai and a community-based screen in Tainan. They achieved similar yields of 1.3 and 1.5 confirmed bilateral cases of hearing loss per 1,000 babies screened, but the lack of babies from NICU and the need for parents to choose to pay for the test makes the figures difficult to compare with those from England.

Prevalence rates in disadvantaged countries

In order to obtain local data from developing countries, there have been some attempts to screen children, mainly of school age, in their communities, see Table 1.4. These have generally taken the form of pure-tone audiometry with or without otoscopy and tympanometry. Once again, the inconsistencies between the studies makes it difficult to compare them, and difficult to compare estimated prevalence with estimates from studies in developed countries. Neverthe-
Table 1.4  Selected results from child hearing screening studies in disadvantaged countries showing the differences in definitions and results.

<table>
<thead>
<tr>
<th>Study and location</th>
<th>Population</th>
<th>Definition of case</th>
<th>Cases per 1,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdel–Rahman et al. 2007&lt;sup&gt;61&lt;/sup&gt; Ismailia, Egypt</td>
<td>Secondary school children</td>
<td>Sensorineural hearing loss ascertained by Rinne and Weber tests</td>
<td>222</td>
</tr>
<tr>
<td>Sobhy 1998&lt;sup&gt;62&lt;/sup&gt; Alexandria, Egypt</td>
<td>School children</td>
<td>Excluding wax occlusion and OME Bilateral Average thresholds &gt;25 dB Bilateral Average thresholds &gt;40 dB Bilateral Conductive and sensorineural Unilateral or bilateral</td>
<td>1.17–2.59</td>
</tr>
<tr>
<td>Seely et al. 1995&lt;sup&gt;63&lt;/sup&gt; Pangama, Sierra Leone</td>
<td>Children</td>
<td>Bilateral Average thresholds &gt;30 dB Sensorineural only Unilateral or bilateral Average thresholds &gt;30 dB Bilateral</td>
<td>6.5</td>
</tr>
<tr>
<td>Olusanya et al. 2000&lt;sup&gt;64&lt;/sup&gt; Lagos, Nigeria</td>
<td>School children (mainstream school)</td>
<td>Bilateral Average thresholds &gt;30 dB</td>
<td>139</td>
</tr>
<tr>
<td>Hatcher et al. 1995&lt;sup&gt;65&lt;/sup&gt; Kiambu, Kenya</td>
<td>School children</td>
<td>Bilateral Average thresholds &gt;30 dB Sensorineural only Unilateral or bilateral Average thresholds &gt;30 dB Bilateral</td>
<td>22</td>
</tr>
<tr>
<td>Westerberg et al. 2005&lt;sup&gt;66&lt;/sup&gt; Zimbabwe</td>
<td>Primary school children</td>
<td>Bilateral Average thresholds &gt;30 dB Sensorineural only Unilateral or bilateral Average thresholds &gt;30 dB Bilateral Middle-ear disease with hearing loss (conductive, mixed or sensorineural) Unilateral or bilateral</td>
<td>10</td>
</tr>
<tr>
<td>Swart et al. 1995&lt;sup&gt;67&lt;/sup&gt; Swaziland</td>
<td>First year school children</td>
<td>Bilateral Average thresholds &gt;30 dB Sensorineural only</td>
<td>10</td>
</tr>
<tr>
<td>Swart et al. 1995&lt;sup&gt;67&lt;/sup&gt; Swaziland</td>
<td>First year school children</td>
<td>Bilateral Average thresholds &gt;30 dB Sensorineural only</td>
<td>10</td>
</tr>
<tr>
<td>Minja et al. 1996&lt;sup&gt;68&lt;/sup&gt; Rural Dar es Salaam, Tanzania</td>
<td>Primary school children</td>
<td>Sensorineural only</td>
<td>141</td>
</tr>
<tr>
<td>Minja et al. 1996&lt;sup&gt;68&lt;/sup&gt; Urban Dar es Salaam, Tanzania</td>
<td>Primary school children</td>
<td>Sensorineural only</td>
<td>77</td>
</tr>
<tr>
<td>Elahi et al. 1998&lt;sup&gt;69&lt;/sup&gt; Rural areas, Pakistan</td>
<td>Children</td>
<td>Sensorineural or permanent conductive Bilateral Average thresholds &gt;30 dB Sensorineural or mixed Unilateral or bilateral Average thresholds &gt;30 dB</td>
<td>39</td>
</tr>
<tr>
<td>Rao et al. 2002&lt;sup&gt;70&lt;/sup&gt; Rural south, India</td>
<td>First year school children</td>
<td>Sensorineural or mixed Unilateral or bilateral Average thresholds &gt;30 dB</td>
<td>32</td>
</tr>
<tr>
<td>Liu et al. 2001&lt;sup&gt;71&lt;/sup&gt; Sichuan, China</td>
<td>Children &lt;15 y</td>
<td>Average thresholds &gt;30 dB Unilateral or bilateral Average thresholds &gt;30 dB</td>
<td>2.6</td>
</tr>
<tr>
<td>Mencher and Madriz Alfaro 2000&lt;sup&gt;72&lt;/sup&gt; Costa Rica</td>
<td>School children</td>
<td>Bilateral Permanent Average thresholds &gt;30 dB</td>
<td>1.50–1.63</td>
</tr>
</tbody>
</table>

less, there is a consensus that the levels of PCHI are greater in underdeveloped countries, with Davidson et al.<sup>59</sup> estimating that sensorineural loss is twice as common. Evidence also seems to point towards a higher rate of hearing impairment amongst disadvantaged communities in richer countries.<sup>18,34</sup> with Niskar et al.<sup>37</sup> finding that children from families with incomes at or below the national poverty line were significantly more likely to have a hearing impairment when screened. The World Health Organization in its report on chronic diseases<sup>60</sup> views the
process from poverty to chronic diseases as ‘interconnected in a vicious cycle’, as poor people
have greater exposure to risks and decreased access to health services.

Alberti\textsuperscript{73} estimated that half of all disabling hearing loss worldwide was preventable by
primary means, from vaccination to better protection from noise exposure. Consanguinity is
a common risk factor in some communities.\textsuperscript{69} There also seems to be an increased prevalence
of middle-ear disease in disadvantaged communities and this can be aggressive, becoming
chronic suppurative otitis media (CSOM) or leading to cholesteatoma.\textsuperscript{74} The presence of recurrent
or chronic middle-ear disease is highly correlated with a permanent hearing loss in this
population because of the reduced access to effective treatment.\textsuperscript{69,75}

There is some impetus for an increased effort of identification of PCHI in developing
countries, and this seems to be backed by the opinion of mothers.\textsuperscript{76} Trials of UNHS at immuni-
sation clinics have been undertaken in Nigeria and South Africa and were successful in terms
of coverage, but the attendance at follow-up was poor. Swanepoel et al.\textsuperscript{77} report that out of 68
subjects (14\% of screened sample), only 40\% returned for the second follow-up and 44\% for
the third follow-up. Some argue that primary prevention strategies should take priority, as the
current high prevalence would overwhelm the capacity for early intervention.\textsuperscript{78} Others would
argue that with facilities available for deaf and hearing-impaired children throughout the world,
children worldwide should be identified to take advantage of those facilities.\textsuperscript{79}

**RISK FACTORS**

Risk in this context refers to an increased probability that an event will occur; in this case,
that a child will have a hearing impairment. Factors that increase the likelihood can be non-
specific, i.e. affecting a whole population but not by much, or can be specific to the child. The
former is important to know for planning services, and examples might be poverty or being
aged less than 9 years old. This section will concentrate more on the latter. Specific risk factors
– the most notable being a family history of permanent hearing impairment present since
childhood in a parent, sibling, grandparent, great-grandparent, aunt, uncle, nephew, niece or
cousin or a lengthy stay in NICU – can be used for targeted screening during universal screen-
ing. The practice of targeted screening in babies was common between the invention of the
technology for newborn screening and the infrastructure being put into place for UNHS. An
example of this was in the Redbridge District of London, where there was a targeted newborn
hearing screen for 10 years between 1990 and 2000.\textsuperscript{80} From the 32,890 babies born, 3.5\% were
identified before discharge from hospital as high-risk using the appropriate JCIH guidelines at
the time, and screened using ABR. The yield was 1.6 per 1,000 babies screened for bilateral
impairment 40 dB HL (17 children, or 0.52 per 1,000 live births). By the time these children
and their peers started primary school, they made up only 40\% of all cases of bilateral PCHI
40 dB HL; 18\% had risk factors at birth but had not been screened and 42\% had no obvious
risk factors. This is a compelling argument for universal over-targeted screening.

Some risk factors have come from understanding the aetiology of PCHI, conversely the
aetiology has sometimes been worked out after observational studies showed something as a
risk factor. This is a continuing reason for studying risk factors – in order to understand more
about what might be causing hearing loss. Other reasons are that the high risk may extend
beyond the neonatal period, indicating the need for further observation of a child as he or she
develops, and to help parents who encounter one of these risk factors understand the increased
risk their children may face.
A frequently quoted list of risk factors is published by the Joint Committee on Infant Hearing. Some are highlighted as particularly relevant when thinking about progressive or delayed-onset cases, and they recommend that any child who has these risk factors is seen by an audiologist before 30 months old if the newborn screen is clear. The Newborn Hearing Programme (NHSP) in the UK publish their own guidelines on the management/surveillance of high-risk individuals. It is recommended that any neonates with meningitis are referred straight to audiology without a screen, and children who recover from meningitis be offered an audiology appointment within 4 weeks of discharge from hospital. Babies born with cranio-facial abnormalities (including cleft palate) or Down syndrome should be screened again at eight months. Other babies who should be offered an assessment at eight months and at intervals throughout their childhood are those with: a family history of PCHI; assisted ventilation in NICU for >5 days; neonatal jaundice to a level needing exchange transfusion; congenital infection with toxoplasmosis, rubella, cytomegalovirus (CMV) or herpes; and developmental delay associated with a neurological disorder. They recommend audiological testing for babies who have had high levels of ototoxic drugs and caution strongly against their use if there is a family history of hearing loss after antibiotics.

Weichbold et al. examined the histories for 23 9-year-old children who had developed bilateral PCHI after a clear newborn hearing screen. Eleven children had risk factors (as defined by JCIH 2000): three had a family history of hearing loss; two had recovered from meningitis; two had a cranio-facial malformation; one had persistent pulmonary hypertension; one had a congenital CMV infection; one received extracorporeal membrane oxygenation; and one had recurrent otitis media with effusion. They also found that five children had received ototoxic therapy (not on the list of risk factors at the time) and two had been born before the 33rd gestational week (one child had a combination of the last two). Six children (26%) showed no risk indicators for post-natal hearing loss.

**AETIOLOGY**

The major aetiological classification system suggested by Davidson et al. has been used in most recent studies. The categories are:

- genetic;
- prenatally acquired;
- perinatally acquired;
- post-natally acquired;
- cranio-facial anomalies; and
- other.

Unfortunately, it is common for a large percentage of children in epidemiological studies to have an unknown aetiology, referred to as ‘missing’. In a selection of recent studies stating the aetiology of PCHI for different populations, there are reports of 16 to 55% of unknown origin (see Table 1.5).

Several studies have looked at ways of finding the underlying aetiology in missing cases, both as a way of improving epidemiological data and for clinical reasons. In the Trent study, 41% of children did not have an identifiable aetiology. Nevertheless, it was possible to impute aetiology from other data such as medical notes, and this reduced the percentage of people who
Table 1.5  Selection of cross-sectional cohort studies with percentage of cases from each aetiological category, showing differences across time and study.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort (N)</td>
<td>(100)</td>
<td>(228)</td>
<td>(653)</td>
<td>(130)</td>
<td>(17 160)</td>
<td>(301)</td>
</tr>
<tr>
<td>Category</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genetic</td>
<td>13</td>
<td>36</td>
<td>45</td>
<td>43</td>
<td>30</td>
<td>23*</td>
</tr>
<tr>
<td>Prenatal</td>
<td>7</td>
<td>16</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Perinatal</td>
<td>–</td>
<td>14</td>
<td>17</td>
<td>15</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td>Post-natal</td>
<td>24†</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>CFA</td>
<td>1</td>
<td>–</td>
<td>3</td>
<td>12</td>
<td>–</td>
<td>7</td>
</tr>
<tr>
<td>Other</td>
<td>–</td>
<td>–</td>
<td>2</td>
<td>–</td>
<td>2</td>
<td>9**</td>
</tr>
<tr>
<td>Missing</td>
<td>55</td>
<td>27</td>
<td>25</td>
<td>16</td>
<td>49</td>
<td>32</td>
</tr>
</tbody>
</table>

* Including ‘known syndrome’ (12) ‘family history’ (11) ** congenital abnormality, other
† Including 13 cases of Hib meningitis.
Epidemiology of permanent childhood hearing impairment

had no aetiological information to approximately 25%. Taking this one step further, Parker et al. report investigating 82 children from the Trent study using a questionnaire, home visit and genetic test for the most common genetic mutation causing hearing impairment (Connexin 26 35delG, see Genetic hearing impairment–non-syndromic below). They found eight children had a genetic syndrome not previously assigned and seven further cases had the Connexin 26 35delG mutation. Parving found that aetiology was significantly more likely to be found if a child with PCHI had a non-audiological examination in addition to a standard audiological exam (37/61 vs. 61/117). Peckham et al. suggested that congenitally acquired CMV might be responsible for a large proportion of children for whom no other obvious cause is found for PCHI. Their study found that such children were twice as likely to have CMV excreted in their urine than children with normal hearing (13% vs. 7%). There are a number of guidelines now available for clinicians investigating the cause of hearing loss in individual children with core investigations that all children with PCHI should receive; additional tests are suggested depending on the circumstances (Table 1.6).

The BAAP give several reasons for investigating the cause of hearing loss:

- To try to answer parents who ask ‘why is my child deaf?’
- To help identify, monitor, treat or prevent associated medical complications in some patients.
- To help prevent further deterioration of hearing loss in some patients.
- To enable better-informed genetic counselling.
- To inform epidemiological research.
- If the diagnosis is known, then the doctor can provide better advice to parents, such as assisting the family in making decisions about the most appropriate communication mode, about educational placement and about cochlear implantation.

Table 1.6  The recommended history and examination for a child with PCHI – this may help discover aetiology.

<table>
<thead>
<tr>
<th>Core</th>
<th>Additional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal history: pre- and perinatal problems, general development, general health and head injury.</td>
<td>Genetic tests: Chromosomal examination (karyotyping) if developmental delay or dysmorphic features; Connexin 26 and 30 gene testing for common mutations if PCHI severe or greater; testing for other mutation, including mitochondrial, as suggested by the history.</td>
</tr>
<tr>
<td>Family history: looking back three generations, including congenital and acquired hearing loss.</td>
<td>Renal ultrasound: If syndrome with multi-system abnormalities suspected, or if family history of renal problems.</td>
</tr>
<tr>
<td>Imaging of head and neck: Computerised Tomography (CT) or Magnetic Resonance Imaging (MRI) scans.</td>
<td>ECG, as some syndromes are associated with dangerous cardiac conduction abnormalities.</td>
</tr>
<tr>
<td>Infection screen: for CMV and rubella</td>
<td>Infection screen: toxoplasmosis and syphilis tests if indicated.</td>
</tr>
<tr>
<td>Ophthalmology: may show changes due to a syndrome such as Usher or congenital rubella. Also important for ascertaining extra needs for children with hearing impairment.</td>
<td>Blood tests and urine examination: if syndromes involving kidneys are suspected, such as Alport or Alstrom syndromes.</td>
</tr>
<tr>
<td>Thyroid function: usually done at birth.</td>
<td></td>
</tr>
</tbody>
</table>
The presence of one possible aetiology does not exclude other causes. For example, it is increasingly recognised that some mutations do not in themselves cause hearing loss, but lower than the threshold for environmental insults pre, peri and post-natally. Such mutations include the A1555G mitochondrial gene mutation, which predisposes to hearing loss when a child takes aminoglycoside antibiotics, such as gentamicin. There is also a controversy over whether perinatal problems, often cited as the cause of congenital defects, are actually the effect of pre-existing developmental anomalies. Children with a sensorineural hearing loss can be more at risk of conductive problems such as chronic otitis media, something that can potentially be treated to improve hearing.

As might be expected for a condition with such a variety of causes, the frequency of occurrence of some causes of PCHI varies over time and geographical areas. Parving and Hauch looked at the ascribed causes of hearing loss in children attending the School for the Deaf in Copenhagen in 1993–1994 in comparison to causes evaluated 10 and 40 years previously. They found that the frequency of congenital inherited hearing impairment increased steadily with time, whilst between 1953 and 1983 there had been a significant increase in prenatal infections, which then declined between 1983 and 1993. Admiraal and Huygen in the Netherlands found a similar decrease in prenatal infectious causes from 1988 to 1998, whilst the proportion of PCHI thought to have a perinatal cause had increased.

The changes in the developed world over the last few decades have shown the success of primary prevention. Measles, mumps, rubella and meningitis are all implicated in PCHI, and all have been the subject of immunisation programmes. Secondary prevention has also helped, with better nutrition and treatment leading to better outcomes from infections such as measles and meningitis. Meanwhile there has been a rise not just in the proportion of genetic cases but in the actual numbers. In some cases this is due to better neonatal care leading to the survival of babies with life-threatening syndromes, in others it is due to the increase in prevalence of particular mutations. Nance and Kearsey suggest that the frequency of PCHI caused by Connexin 26 or 30 mutations may have doubled in the last 200 years due to the establishment of a ‘Deaf community’ leading to healthier hearing-impaired adults. These adults go on to have children and this decreases genetic selection for the unmutated forms of the Connexin gene.

In contrast, Dunmade et al. looked at the aetiologies of sensorineural hearing loss in children in Nigeria, comparing aetiologies of hearing loss in 1980 and 2000, and found there had been no significant decrease in infectious causes. The figures for the 115 children studied in 2000 showing some common causes were febrile illness (18.3%), measles (13.9%), meningitis (8.7%) and mumps (6.9%). Saunders et al. offered the Connexin 26 35delG genetic test to children with PCHI in an audiology clinic in Jinotega in Nicaragua and found that despite a family history of hearing loss in 33%, this mutation, so common in the UK, was not present in any of their children. Another difference he found was in the unmonitored use of ototoxic antibiotics, which are cheaper than their alternatives.

**GENETIC HEARING IMPAIRMENT**

At least half of all cases of PCHI are known to have a genetic cause. However, despite significant advances in the understanding of the molecular basis of hearing loss, identifying

*The use of the capital D indicates the community of deaf people who use BSL as their language and identify with other deaf people who share their language, culture and history.*
the precise genetic cause in an individual remains difficult. Using systematic investigation, such as that described in Table 1.6, will increase the chances of finding the aetiology, but it is estimated that a mutation in one of between 300 and 500 genes (around 1% of the total number of genes) can cause hearing loss. Approximately 120 of these genes have been identified so far – around 80 causing syndromes that include hearing loss and over 40 responsible for ‘non-syndromic’ hearing loss. Most of these genes are located on the autosomal chromosomes, up to 20% on the X-chromosome and up to 20% in the maternally inherited mitochondrial DNA. This confirms the findings from the questionnaire section of the Parker et al. study based on the Trent cohort: the families of 526 hearing-impaired children (aged 4–13) were sent questionnaires asking about any family history of hearing loss, the results pointing towards different genetic disorders with autosomal dominant, autosomal recessive and sporadic inheritance.

**Syndromic PCHI**

If hearing loss is one of several clinical findings, the disorder is described as a syndrome. Approximately 30% of genetic hearing impairment is syndromal. Over 400 syndromes featuring PCHI have been described and many of the genetic abnormalities responsible identified. Syndromal hearing impairment can be sensorineural or conductive, due to structural anomalies of the auditory system. McClay et al. report that the presence of any congenital syndrome significantly increased risk of an abnormality of the temporal bone involving the cochlear or vestibular system visible on a CT scan. This risk was found to be elevated regardless of the presence of PCHI, but higher still if PCHI was present. The presence of a genetic syndrome in children with PCHI should not be overlooked as it can be important in determining prognosis and intervention measures – as well as for estimating the recurrence risks in the family.

Chromosomal syndromes may occur either during meiosis or mitosis, resulting in too much or too little genetic material, and many increase the risk of PCHI. Two of the most common syndromes caused by chromosomal abnormalities are Down and Turner syndromes. Maatta et al. studied 129 individuals (mainly children) with Down syndrome, and found that one-third of the sample had hearing impairment or recurrent ear infections. Overall, the risk of sensory impairments increased with increasing levels of intellectual disability.

Genetic syndromes caused by mutations, deletions or additions on the autosomal chromosomes can be inherited in a recessive or dominant manner. The majority of syndromal genetic hearing impairments are inherited in an autosomal recessive way and are detectable at birth. Recessive inheritance occurs when both parents – who may not necessarily exhibit the trait – carry a mutated gene that may cause a genetic syndrome. If both parents carry one normal copy of the gene and one mutated copy of the gene, there is a 25% chance of the child inheriting both of the mutated genes (one from each parent) and manifesting the genetic disorder. There is also a 50% chance that the child will inherit one of the mutated genes and become a carrier for that disorder but not manifest the syndrome. Such disorders include Usher syndrome, Cockayne syndrome, Pendred syndrome, Jervell and Lange-Nielsen syndrome, Hurler syndrome and Alstrom syndrome. Usher syndrome is one of the most studied of these syndromes. It was formally classified into three clinical types and was expected to be caused by three corresponding mutations. However, recent work reported by Cohen et al. suggests that there are more than three genetic causes of Usher syndrome, each having different potential effects in different individuals with very little evidence for phenotypic–genotypic correlations.
For dominant inheritance, only one mutated copy of the gene is required for a syndrome to be manifest. Usually, one parent will have the syndrome, and there is at least a 50% chance of the child inheriting the gene and manifesting the genetic disorder. If both parents exhibit the trait, there is a 75% chance of the child manifesting the disorder. Hearing impairment inherited in this way usually manifests itself after the neonatal period, either because it is congenital and progressive or because it is late-onset. Examples of autosomal dominant syndromes include Marshall-Stickler syndrome, Waardenburg syndrome and Treacher Collins syndrome.

Syndromes carried on the X-chromosome affect males predominantly because they have only one X-chromosome. Females ‘carry’ the mutated syndrome-causing gene but are unaffected if they have a normal copy on their other X-chromosome. Any male children of a carrier will inherit the genetic material for their X-chromosome from their mother (their father contributing the Y-chromosome instead), with a 50% chance that this will include the mutated gene. If this occurs, since there is no copy of the gene on the Y-chromosome, the syndrome will be manifest. Examples of X-linked syndromes include Hunter syndrome, Alport syndrome and Norrie syndrome, all of which do not manifest at birth but develop in early infancy. It is a mutation in an X-linked gene that is responsible for ‘deafness with fixation of the stapes’, which gives a progressive hearing loss of sensory and conductive types. Although this mutation is very rare, diagnosis is important because if this is not recognised, there can be further damage to hearing if surgical methods to release the stapes are not attempted.

Mitochondria are small organelles located within the cytoplasm of the cell and have their own DNA (mDNA), which is independent of the nuclear DNA. Mitochondria are inherited from the mother only. Thus, a mother who has hearing loss from a mutation on her mDNA will pass this mutation onto her children of whatever sex, but a father with the same mutation will not pass it on. There are multiple copies of mDNA in each mitochondrion, and, therefore, expression of a syndrome-causing gene is not inevitable. Thus the clinical phenotype is extremely variable. An important syndrome to recognise is the MELAS syndrome, where permanent hearing loss may be the first manifestation; and recognition allows better management of subsequent complications.

Non-syndromic

Autosomal recessive non-syndromic hearing impairment is the most common form of genetic deafness, accounting for around 80% of all cases. Thus, it can be estimated to account for around 40% of all profound PCHI. Numerous non-syndromal recessive hearing impairment genes have been localised, with Petersen and Willems reporting 85 loci on 39 different genes. Autosomal dominant inheritance is thought to account for approximately 15% of the cases. X-linked inheritance accounts for approximately 2–3% of the inherited hearing impairments (but 5% of those affecting males).

Mutations in the GJB2 gene are responsible for as much as 50% of autosomal recessive non-syndromic PCHI. This gene codes for a protein called Connexin 26, a gap junction protein regulating the passage of ions in and out of the cell, and was identified in 1997. As with the mutations responsible for Usher syndrome, it has become obvious that genotype–phenotype relationships are more complex than once thought. Green et al. studied the prevalence of mutations in the GJB2 gene in 52 people with congenital sensorineural hearing loss at a clinic in Iowa. Twenty-two were found to have GJB2 mutations, 19 of whom had a mutation on both chromosomes. Of the 41 abnormal copies of GJB2, 29 had the same mutation – 35delG.
The siblings of these 52 people were also screened, and it was found that all those who had two abnormal copies of the gene also had PCHI. A total of 560 unrelated children were also screened and there were 14 in whom one copy of the GJB2 gene had a mutation. This gives a carrier rate of 3.0% (probable range 2.5–3.6%). It is important to remember that this carrier rate will be specific for this particular population — mid-western United States. Pandya et al. searched the DNA of children from the Annual Survey of Deaf and Hard of Hearing Children and Youth, conducted at the Research Institute of Gallaudet University, and found that GJB2 mutations accounted for 22.2% of deafness in the overall sample but differed significantly amongst Asians, African Americans and Hispanics. Ethnic differences are particularly marked where there is a small founder population, such as in some Jewish communities.

PRENATAL FACTORS

Infections

Infections are considered to be the main cause of prenatally acquired hearing impairment. In the 1970s–1980s, congenital rubella was the single most common reported cause of sensorineural hearing impairment in childhood, accounting for 16–22% of cases of hearing impairment in babies. If infected during the first month, there is a 50% chance of the developing fetus being affected such that congenital rubella defects are detectable. This risk declines throughout pregnancy to an approximate 6% chance in the fifth month and beyond. Problems associated with congenital rubella (CRS) include learning disability, heart disease, cataracts, microcephaly, hepatomegaly, splenomegaly, bone lesions, purpura, glaucoma and hearing impairment. Hearing impairment is the most common permanent manifestation and affects 68 to 93% of children with congenital rubella. The hearing impairment is usually severe to profound sensorineural hearing impairment and can be progressive.

Congenital rubella was a devastating syndrome that became a major public health issue. A rubella vaccine was first licensed in 1969. By 1999, 105 (49%) of the 214 countries and territories reporting to WHO had introduced the rubella vaccine in their national immunisation programme. In the UK, the rubella vaccine was offered to schoolgirls in the United Kingdom from 1970, and post-partum susceptible women shortly after. Mass vaccination with MMR (measles–mumps–rubella vaccine) of babies was introduced in 1988. Schoolgirl vaccination was discontinued in 1996, although post-partum vaccination of susceptible women identified through antenatal testing continues. Reported cases of CRS declined from about 50 a year in 1971–1975 to just over 20 a year in 1986–1990. About 40 infants with CRS were reported over all of the next 12 years. Women living in the UK who were born abroad have much higher rubella susceptibility rates than UK-born women, and two-thirds of the CRS cases since 1991 have been to mothers born outside the UK. The previously high coverage of children interrupted the epidemic transmission (which was mainly in children), but concerns over the safety of MMR have led to a decrease in immunity amongst children. If an epidemic of rubella occurred in the UK, women born in places without vaccination will be at increased risk of acquiring infection in pregnancy. The likelihood of importation of infection is high, as the developing world still has endemic rubella. Rittler et al. found 43 cases of CRS recorded from the records of 3,883,165 live births collected by the Latin-American Collaborative Study of Congenital Malformations, World Health Organization (WHO) Collaborating Centre for
the Prevention of Birth Defects (ECLAMC), which suggests a prevalence of CRS in Latin America of around 1:100,000 live births.

Another prenatal infection that causes congenital abnormalities is toxoplasmosis. Sever et al.\textsuperscript{121} studied 23,000 mothers and children from around 20 weeks gestation until 7 years old. Of these mothers, 38.7% had antibodies to toxoplasmosis during pregnancy, and children born to these mothers had double the risk of developing PCHI by age 7 (0.4% vs. 0.2%, \( p = 0.01 \)).

Cytomegalovirus CMV is a common chronic asymptomatic infection in adults, which can cross over the placenta to affect the developing fetus and child. Roizen\textsuperscript{117} has observed that CMV infection occurs in 2.2% of all newborns, making it the most common intrauterine infection. Lipitz et al.\textsuperscript{122} report that from their sample of 18 babies with confirmed CMV, four (22%) had neurological problems at birth. Fowler and Boppana\textsuperscript{123} summarised seven studies between 1982 and 2004, and found that the risk of PCHI was 22–65% in those babies symptomatic at birth and 6–23% in those asymptomatic at birth. Amongst those affected by PCHI, there were progressive, fluctuating and delayed-onset cases. They were unable to identify any way of predicting which babies were more at risk of PCHI from asymptomatic CMV infection, and they flag up the fact that UNHS may miss many babies with PCHI due to CMV because of its variable course. It is not yet established how much CMV infection contributes to the overall prevalence of PCHI, as studies vary in their method of investigating infection. In the meta-analysis by Morzaria et al.\textsuperscript{124}, the mean of cases reportedly due to CMV in the studies from 1990 to 2002 was 0.92% (s.d. 1.07) of the total, but Peckham et al.\textsuperscript{88} reported that 14% of those diagnosed with PCHI of unknown aetiology excreted CMV in their urine (compared with a base rate of 7%), and Barbi et al.\textsuperscript{125} reported that of 130 children with PCHI, 24.7% had CMV in blood retained from a sample at birth (base rate not given). Given the availability of an antiviral treatment for CMV,\textsuperscript{126} there is an argument for screening newborn babies for CMV.\textsuperscript{125,127}

**Maternal drug therapy**

Maternal drug therapy during pregnancy can also contribute to congenital hearing impairment. Some substances may permanently injure or destroy the hair cells of the cochlea resulting in a sensorineural PCHI. For example, alcohol, streptomycin, quinine and chloroquine phosphate may destroy neural elements of the inner ear.\textsuperscript{128} The loss is usually triggered by the ingestion of ototoxic drugs during the first trimester, with damage to the auditory system occurring especially in the sixth or seventh week after conception. Conductive PCHI can also result from ototoxicity, primarily as a result of ossicular malformations of the middle ear. Brent\textsuperscript{91} emphasises the gene–environment interaction involved in teratogenic drugs.

**Perinatal factors**

Perinatal factors which may predispose to PCHI include prematurity, hyperbilirubinaemia (kernicterus), anoxia (including apnoea and cyanosis), severe neonatal sepsis, rhesus incompatibility, low birth weight and trauma.\textsuperscript{129} Some perinatal problems that were known to cause neurological damage have been much diminished in the modern maternity hospital, for example, the introduction of photosynthetic lights to reduce jaundice (hyperbilirubinaemia) to non-toxic levels and rhesus inoculation to prevent rhesus incompatibility in future pregnancies. On the
other hand, medical advances have ensured that more premature, anoxic and low-birth-weight (LBW) babies survive, leading to more babies graduating from NICU with a hearing impairment. Davis and Wood showed that a baby admitted to NICU for any reason had a risk of developing PCHI by 3 years old that was seven times higher than those who had not. Razi and Das showed that even in children who had a hearing threshold within the normal range, the mean high-frequency threshold was higher in children who had experienced an adverse perinatal event.

Prematurity is a risk factor for PCHI, but it is not clear whether this itself is the causal factor or whether the causes are factors associated with prematurity such as anoxia, hyperbilirubinaemia, increased bacterial and viral infections, treatment with ototoxic drugs and/or LBW. Veen et al. concluded that in their study of 890 5-year-olds who had very LBW or had been very premature, the prevalence of sensorineural hearing impairment was 15 times higher than the average Dutch population of 5- to 7-year-olds. Van Naarden and Decoufle studied 320,000 children born in Georgia US in 1991–1993 and found that by age 3, 169 children had developed PCHI, of which 17 had been amongst the 3,362 children who had been born weighing less that 1,500 g. This gives a relative risk of 13.9 (95% CI 8.2–23.4). In this group of very low weight babies, it is hard to identify the precise cause of hearing impairment due to the sheer numbers of possible complications those infants may experience.

Children with adverse perinatal events are also at risk of having other developmental disabilities, making them particularly high need. Van Naarden and Decoufle estimated that for a child who was born weighing less than 1,500 g, the risk of developing a hearing impairment plus another disability was 27.8 times (95% CI 11.6–66.5) that of a child born weighing over 3,000 g. Davis and Wood found NICU babies with a hearing impairment were considerably more likely to have another disability (odds ratio 8.7 to 1). Yoon et al. suggest that UNHS may not pick up all of the NICU graduates who develop PCHI due to the high incidence of middle ear problems and delayed-onset sensorineural hearing loss.

**Post-natal factors**

It is possible for post-natal causes of acquired PCHI to be genetic due to delayed onset of hearing impairment, but most acquired cases are caused post-natally by infection, ototoxic agents or trauma. Otitis media should be included even though permanent hearing impairment secondary to otitis media is uncommon in the developed world, because it may delay the detection of permanent hearing impairment. Systemic and neurological infections that have been linked with PCHI are bacterial meningitis, measles, mumps, HIV and CJD. Thanks to a successful vaccination programme and better general health, new-onset measles and mumps-related hearing loss is now rare in the developed world.

Bacterial meningitis is a serious infectious disease both in the neonatal period and throughout childhood. It can be caused by a variety of pathogens, including *Haemophilus influenzae* type b (Hib), *Streptococcus pneumoniae* (pneumococcus) and tuberculosis (TB). For children who survive meningitis, there are often sequelae, which include learning disabilities, hydrocephalus, motor abnormalities, vestibular deficits, psychosis, hyperactivity and visual and sensorineural hearing impairments. Reports have indicated that acquired hearing impairment represents 9.5% of total PCHI, with 6.5% of these cases being caused by meningitis. Meningitis-induced hearing impairment is often bilateral, severe or profound and rapid in onset. Clinical and experimental studies have shown that the loss results from direct damage to the
cochlea by the infection, but it may be exacerbated by additional cochlear damage resulting from any ototoxic drugs used to treat the disease.\textsuperscript{136} Children who have lost their hearing to meningitis are often considered to be amongst the best candidates for cochlear implants due to their previous experience with language and their total loss of any auditory neural function. The incidence of post-meningitic hearing impairment varies from 7 to 31\%, depending on the type of meningitis and type of hearing impairment included.\textsuperscript{137–141} Wellman et al.\textsuperscript{140} and Kutz et al.\textsuperscript{141} also compared the complication rate between Hib and pneumococcus, finding the latter significantly more likely to lead to hearing impairment. In 2004, a Hib vaccine was added to the routine childhood vaccination schedule in England, and from 2006, a vaccine against invasive pneumococcal disease was also added. It is hoped that this will reduce the incidence of acquired PCHI.

Children may be given a number of ototoxic treatments, for example, aminoglycosides (such as gentamicin) for severe infections or those resistant to penicillin; platinum-containing chemotherapy such as carboplatin for retinoblastoma a childhood cancer of the eye, and radiotherapy for tumours in the glands of the neck. Many of these treatments are the best available\textsuperscript{142} but often the adverse effects can be minimised by action such as co-administering aspirin with gentamicin,\textsuperscript{143} careful dosing of carboplatin\textsuperscript{144} and well-placed radio-opaque shields.\textsuperscript{145}

CONCLUSION

Hearing impairment is the most frequent sensory impairment in humans, with significant social and psychological implications. In the light of the impact that PCHI can have on children and their families, the importance of epidemiological studies cannot be underestimated. In developed countries, around 1 in 1,000 babies is born with at a serious permanent bilateral hearing loss, and permanent hearing loss becomes more common as children grow older.

In developing countries, the prevalence may be higher and in some countries it may be considerably higher, but there is a lack of large-scale, robust epidemiological studies.

Epidemiological data were at the forefront of public health and audiological arguments for universal hearing screening, and have also been used to plan and monitor primary prevention such as vaccination. This chapter explained the difficulties in collecting data on incidence, prevalence and aetiology. Recent results of studies from throughout the world on the prevalence and aetiology of deafness have been presented that show the changing nature of deafness throughout the world. Clearly, a greater emphasis on collecting routine data on the pattern, degree, aetiology and natural history of children with deafness is needed throughout the world. It is only by recording these data that we will understand the extent and nature of childhood deafness and propose realistic public health plans to provide support for these children and their families.

REFERENCES