

NEWBORN HEARING SCREENING AND ASSESSMENT

**Guidelines for the Assessment and Management of
Auditory Neuropathy Spectrum Disorder in Young Infants**

Version 2.2

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NHSP Clinical Group

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Amendment History:

Version	Date	Amendment History
1.0	October 2004	First version created following meeting with national and international scientists/audiologists, and extensive subsequent correspondence and discussion. Edited by Graham Sutton
1.1	May 2008	A number of minor corrections (mostly typographical and to references) made. Addendum on interpretation of CM added.
	September 2011	Separate CM protocol issued (v2.0), replacing old Appendix 2
2.1	September 2012	Complete revision by members of NHSP Clinical Group. Edited by Rachel Feirn
2.2	July 2013	Minor revision to clarify and update some areas

Forecast Changes:

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INTRODUCTION

This document outlines the recommendations of the Newborn Hearing Screening Programme (NHSP) in England for the assessment, diagnosis and management of infants suspected of having Auditory Neuropathy Spectrum Disorder (ANSD). It should be read in conjunction with the NHSP Guidelines for Cochlear Microphonic Testing.¹

This document has been updated in the light of recent work and other published guidelines. Many controversies and areas of uncertainty remain in the diagnosis and management of ANSD. These guidelines are likely to be subject to further revision in the light of new evidence in the future.

Main changes to these guidelines from previous versions:

Changes in version 2.2 (2013) from version 2.1 (2012)

Minor changes have been made to clarify some points. In particular, issues around the definition and initial diagnosis of ANSD in sections 1&2 and the timing of possible cochlear implant referral in section 3.4d have been clarified. Slight changes to section 2 ('Initial Assessment') have also been made for consistency with the 2013 revision of the NHSP Early Assessment guidelines.

Main changes in version 2.1 (2012) from version 1.1 (2008)

- The name used for the condition was updated from 'Auditory Neuropathy / Auditory Dys-synchrony' to 'Auditory Neuropathy Spectrum Disorder', in accordance with recent international guidelines.
- A section on Aetiology was added.
- The section on 'Initial Assessment' was updated in line with the NHSP guidelines for Early Audiological Assessment (2011) and Cochlear Microphonic testing (2011).
- Version 1.1 recommended a repeat ABR assessment at a corrected age of 9-15 months (to test for possible delayed maturation). In versions 2.1 & 2.2 the guidance is to *consider* a repeat ABR at 12-18 months corrected age, depending on the circumstances of the individual case. Appendix 2 discusses the issues around this decision. (Guidance on an earlier repeat ABR at 8-10 weeks corrected age is unchanged.)
- Section 3.4 on Intervention was re-ordered to highlight the importance of early communication support, before the age at which decisions about amplification can be made.
- A brief section on the management of unilateral ANSD was added.
- Some example case scenarios, illustrating the diversity and spectrum of the disorder, are given in Appendix 1.
- Appendices on additional audiological tests (including recent work in electrophysiology) and on medical assessment were added.
- Previous (version 1.1) Appendices 1 (timeline) and 2 (cochlear microphonic testing, plus addendum) were removed. This information is now incorporated into the main document and into the separate 'Guidelines for cochlear microphonic testing'.
- The References section was updated.

1. BACKGROUND

50 1.1 Definitions and Terminology

This document addresses the practical issues in the identification, assessment, diagnosis and management of infants presenting with the following pattern of test results at the initial audiological assessment after the newborn screen:

- 55 • **Auditory Brainstem Response (ABR) absent or with severely abnormal morphology at high stimulus levels^a, with**
- **Otoacoustic emissions (OAEs) and/or cochlear microphonic (CM) present.**

We thus have objective tests that demonstrate the presence of pre-neural responses but absent or abnormal neural responses.

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This suggests relatively normal activity in the outer hair cells, but disruption of transmission at some point from the inner hair cells along the neural pathway to the brainstem. In some cases, the underlying reason for this initial pattern of test results will become evident, whereas in others the underlying reason may not be found. In some cases, neural firing may be occurring but with a lack of synchrony, so that no clear ABR is recordable. In some cases dys-synchrony may also arise due to delayed maturation or myelination of the auditory pathway.

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The term 'Auditory Neuropathy' was originally described by Starr and colleagues in 1996³. Other workers have preferred terms such as 'Auditory Dys-synchrony'⁴, 'Auditory De-synchrony' or 'Auditory mismatch', feeling that these terms better attempt to describe what is happening in the auditory system without implying a particular locus of pathology⁵. To encompass these different opinions, the term 'Auditory Neuropathy/Dys-synchrony (AN/AD)' came into use, and was used in previous versions of the NHSP guidelines.

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At the International Guidelines Development Conference (at Como, Italy, in 2008⁶), a consensus was reached to adopt the term 'Auditory Neuropathy Spectrum Disorder' (ANSD). This term includes both true auditory neuropathy (*i.e.* a true neural abnormality) and other possible underlying mechanisms resulting in neural dys-synchrony, as well as delayed maturation of the lower level auditory pathway. The term ANSD was also considered helpful as it expresses the wide range of presentations, prognoses, and underlying aetiologies associated with the disorder.

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ANSD may affect neural processing of auditory stimuli, which may reduce a child's ability to understand speech and may affect ability to detect sound to various degrees. All such children need to be reviewed and monitored in a similar way, and their management differs

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^aThere is some lack of consensus about the definition of "severely abnormal ABR morphology". We suggest that of Sininger (2002)²: "The neural response (ABR) will be poor or completely absent but will occasionally show a small wave V response [at high stimulus levels]. The majority of cases of [ANSD] have a poor ABR preceded by a large inverting CM that can last up to 5 or 6 ms."

As a guideline for "high stimulus levels" we suggest 75 dB_eHL or above¹. If the audiologist is unsure about ABR morphology then an expert opinion on the traces should be sought.

Occasionally, babies may present with more moderately raised ABR thresholds and TEOAEs present. Our current advice is that such cases should not be labelled as ANSD and that an expert paediatric audiology centre should be consulted.

from that of children with 'conventional' sensorineural or conductive hearing loss in important ways.

90 **1.2 Prevalence**

Sininger² estimates that ANSD occurs in about 1 in 10 children with permanent hearing loss^b, though prevalence estimates vary between studies. The true prevalence of ANSD in the paediatric population with hearing loss has not been determined in large, prospective multi-centre investigations and is therefore uncertain. Initial prevalence figures from the
95 English NHSP are in line with the Sininger estimate. These children, because of absent ABR, might at first sight be thought to have severe/profound sensorineural (cochlear) hearing loss until tests of cochlear function are carried out.

100 Although the majority of ANSD cases occur among special care / neonatal intensive care babies (see section 1.3), some studies have indicated that a significant number may occur in the well baby population². Many newborn hearing screening programmes, including the NHSP protocol, currently only screen for evidence of ANSD in infants admitted to NICU^c, and do not offer ABR screening to all well babies. Cases of ANSD occurring in the well baby population may therefore remain undetected.

105 Cases of ANSD may be referred at a later stage and will need to be investigated, identified and managed following diagnosis. The assessment and management of these older cases is outside the scope of this document.

110 **1.3 Aetiology and Risk Factors**

ANSD is a label for a pattern of test results as defined above. It is not a diagnosis and further investigation is needed to ascertain this.

115 ANSD may arise from a diverse range of aetiologies. Infants with ANSD therefore require assessment, investigation and monitoring of neurodevelopmental progress by a physician with appropriate skills and an understanding of the condition. Diagnosis of the underlying aetiology may determine the most appropriate further management, including specific intervention if indicated.

120 Risk factors for ANSD from the neonatal history include:^{2,7,8,9}

- Extreme prematurity <28 weeks gestation
- Low birth weight / intrauterine growth restriction
- Hyperbilirubinaemia reaching exchange transfusion levels
- Hypoxic ischaemic encephalopathy / intraventricular haemorrhage (as is likely to
125 occur in infants with prolonged assisted ventilation / severe sepsis)

Genetic conditions that may give rise to this pattern of test results include, among others:

- Otoferlin mutations (DFNB9 – autosomal recessive)¹²

^b For the purposes of this document, 'permanent hearing loss' is defined as bilateral permanent childhood hearing impairment averaging ≥ 40 dBHL (0.5-4kHz). This is the definition used by the NHSP.

^c In this document 'SCBU/NICU' means those infants classified as such by the NHSP screening protocol –i.e. those who are admitted to special care / neonatal intensive care for over 48 hours.
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- Pejvakin mutations (DFNB59 – autosomal recessive)¹³
- Familial delayed auditory maturation¹⁴
- Neurodegenerative conditions^d: Charcot Marie Tooth, Friedreich’s Ataxia³
- Metabolic conditions^d e.g. Maple syrup urine disease¹⁵
- Mitochondrial disorders¹⁶

135 Some anatomical anomalies may also give rise to this pattern of test results. These cases should be defined by the abnormality identified, rather than continuing to use the label ANSD. Management of such cases is outside the scope of this document.

Examples include:

- Hydrocephalus^{e 2,7}
- Brainstem anomalies¹⁰
- Auditory nerve hypoplasia or aplasia¹¹
- Other anatomical brain anomalies, e.g. microcephaly, space-occupying lesions such as cerebellar tumours.

145 **1.4 Natural History and Prognosis**

The impact of ANSD on a child’s hearing ability varies amongst individuals. It is not possible to predict either a degree of hearing loss or a prognosis for speech and language development and communication ability based on the diagnosis of ANSD.

- Both ABR and behavioural thresholds are poor predictors of speech discrimination ability.
- The ABR may recover so that it is consistent with the behavioural threshold and has normal morphology^{17,18}. If the problem is due to delayed maturation, recovery would normally be complete by 12-18 months of age (see Appendix 2). It may not be helpful to continue to use the label of ANSD for these cases once maturation of the ABR has been confirmed.
- Behavioural thresholds may improve over the first 1-2 years of life⁸.
- In some cases, the behavioural thresholds may appear to be satisfactory, with age-appropriate speech development, but the child may exhibit features consistent with auditory processing difficulties. There should be a local protocol for the ongoing monitoring of such cases.
- OAEs which are present at initial assessment may disappear over time, whether or not the child is aided.^{2,19,20}

165 Children with ANSD should be monitored carefully. We should guard against giving false hope that the condition will recover, but equally we should be careful to avoid assigning a long-term diagnosis prematurely.

When older, children with ANSD may exhibit some or all of the following features:

- Absent or elevated stapedial reflexes (SRs)

^d These conditions usually give a delayed onset presentation

^e Note that hydrocephalus may interfere with the recording of the ABR so presenting with wave I only. ABR thresholds may improve after shunt insertion and it is therefore advisable to wait until after shunt insertion before performing the ABR assessment.

- 170
- Behavioural thresholds anywhere in the range from normal to profound, and any configuration.
 - Variable responses from one test session to another, but generally reliable within a single session.
 - Speech discrimination poorer than the behavioural audiogram would suggest.
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- Hearing aids may be of less benefit than the behavioural audiogram would suggest.
 - Greater difficulties hearing in competing noise than expected from the behavioural audiogram, and other features indicative of auditory processing difficulties.

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As thresholds usually bear little relationship to speech discrimination ability, management decisions for these children should be guided much more by functional communication development rather than behavioural or ABR thresholds.

185 **2. INITIAL ASSESSMENT**

In the NHSP early audiological assessment protocol²¹, 4kHz tone pip ABR assessment will usually be the first investigation for babies referred following the screen^f. (Note that with babies born prematurely, the initial ABR assessment should not be performed until the baby has reached or is close to term, to allow some time for neural maturation.) Where there is no ABR response at the normal maximum recommended stimulus levels^g, or a severely abnormal response at 75dB_eHL or above, investigations to differentiate between ANSD and sensory (cochlear) hearing loss must be performed.

In an infant, abnormal or absent ABR may be due to:

- 195
- 'Conventional' hearing loss – cochlear, conductive or mixed
 - ANSD due to delayed neural maturation
 - ANSD due to other causes.

200 ANSD must always be excluded before proceeding to hearing aids on the basis of objective test results. The ANSD test protocol should be followed as part of the assessment of every suspected case of permanent hearing loss with absent/severely abnormal ABR, whether or not there are known risk factors for ANSD. Refer to NHSP guidance for the specific tests^{1,22}.

The assessment should include:

- 205
- 1) ABR** – if tone pip ABR responses are absent or very abnormal as described above, a click ABR should be performed, ideally using insert earphones, at 85dB_eHL.
 - 2) Tests of outer hair cell function:** If click ABR is absent or severely abnormal at 75 dB_eHL, perform at least one of the following, as appropriate:
 - a) Diagnostic OAEs^h– transient evoked (TEOAE) are recommended.** If a robust OAEⁱ is found to be clearly present and repeatable, assume ANSD may be present. (Note that OAEs may be absent due to overlying conductive loss^j so the absence of a recordable OAE cannot be taken as evidence for the absence of ANSD)
 - b) Cochlear Microphonics:** Perform click CM with separate runs of condensation and rarefaction at the same stimulus level (not exceeding the NHSP recommended normal maximum stimulus level^g) as was used for the click ABR test, using insert earphones. If a cochlear microphonic (inverting with click polarity) is present and there is still no later true neural ABR response (*i.e.* not inverting with click polarity),
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- 215
- 220

^f For well babies, current NHSP guidance is that it is acceptable to use TEOAEs as the first test. For babies admitted to NICU > 48 hours, and any baby where there is suspicion of, or a possible risk factor for, ANSD, ABR must be performed.²¹

^g Refer to the NHSP 'Guidelines for early audiological assessment'²¹ for guidance on maximum recommended stimulus levels

^h 'Diagnostic OAE' means an OAE carried out in the diagnostic Audiology clinic, with visual display of waveforms, not just on screening equipment.

ⁱ Refer to the NHSP guidelines on TEOAE testing in babies²² for minimum 'pass' criteria

^j Tympanometry (using a 1000Hz probe tone for infants < 6 months) should be performed to aid in the interpretation of an absent OAE.

assume ANSD may be present. Refer to the NHSP ‘Guidelines for Cochlear Microphonic Testing’¹ for detailed notes on CM recording and interpretation.

225 Note that significant overlying conductive loss may prevent the CM from being detected. When abnormal tympanograms are present it is not possible to exclude the possibility of ANSD; however, in cases where there is no other evidence for ANSD this should not delay the management of the child’s hearing loss.

230 If a robust diagnostic OAE^{h,i} has already been recorded, CM testing is not necessary (although it may be useful as confirmation). However, studies show that a substantial proportion of patients with ANSD and present CMs do not have recordable OAEs^k.
Therefore all children with absent or severely abnormal ABR and absent OAE should be tested for a cochlear microphonic.

235 Optionally, particularly for infants aged above about 6 months, include if possible:
3) Stapedial reflexes (SRs)^l

Interpretation:

240	ABR (AC and BC) absent / severely abnormal^a]	
	CM or OAEs present]	implies ANSD
	(SRs absent / elevated)]	
245	ABR (AC and BC) absent / severely abnormal^a]	
	CM and OAEs not recordable*]	implies SNHL^m
250	ABR (AC and BC) present but elevated]	implies SNHL^m
]	- CM test not indicated

*The absence of OAEs and CM does not categorically rule out ANSD, but when both are absent it is reasonable to assume conventional hearing loss and proceed to manage the hearing loss on this basis. However, if robust OAEs and/or CM have been found to be present on one diagnostic test occasion and are not recordable at a future date, the label ANSD should be maintained unless the ABR morphology also improves to become consistent with the behavioural thresholds. There are anecdotal reports that in some cases of ANSD the OAE and/or CM can “burn out” with time. These cases are still likely to have ANSD, although they may additionally have hair cell damage, and should be managed accordingly.

^k In the study by Rance et al⁹ all subjects had evidence of outer hair cell function in the form of the cochlear microphonic but only about half had OAEs; this is presumably because the CM is less affected by middle ear factors.

^l Stapedial reflexes appear to be invariably absent or elevated in cases of ANSD²³. The NHSP team has not previously recommended their use in infants under about 6 months (where high frequency (1000Hz) probe tones must be used), due to doubts about their reliability and a lack of normative data. There is now emerging evidence on reliability and normative data in this young age group^{24,25}, so this test may become a more standard part of the test battery for ANSD at this age in the future.

^m Or mixed SNHL & conductive loss

A key issue with ANSD is **distinguishing long-term ANSD from delayed maturation** particularly in babies who have been in neonatal intensive care. Care should be taken when interpreting ABR results for babies born prematurely or for those who have delays in other aspects of development, as the ABR response may still be maturing. To help differentiate neural maturation changes from other causes of ANSD, whenever possible ABR should be repeated before a definitive initial diagnosis is made; this should preferably be at around 8-10 weeks corrected age (*i.e.* around 2 months after the first ABR).

As improvements in ABR and in behavioural thresholds over the early months of life have been reported in some infants^{8,17,18}, a further repeat ABR at a later age may be helpful in order to confirm the diagnosis. If this is felt to be helpful for the management of the individual case, then a re-test at around 12-18 months of age should be considered. For a discussion of the issues around this decision, see Appendix 2.

Remember that in ANSD, ABR thresholds do not predict behavioural thresholds or functional hearing ability.

3. MANAGEMENT

This section refers primarily to the management of bilateral ANSDⁿ. However, some of this guidance will also be relevant to the management of unilateral ANSD.

285 The management of the child with ANSD requires a multidisciplinary team approach,
working in partnership with the family. As a minimum we suggest the team should include a
Paediatric Audiologist, a medical person (Audiological Physician, ENT consultant or
Paediatrician), a Speech-Language Therapist, a Teacher of the Deaf, and a Neurologist.
290 The timing of involvement of these professionals will depend on the individual case and the
wishes of the family. One member of the team should be designated to take ultimate
responsibility for the management of the case. All the members should be familiar with and
knowledgeable about the condition.

The management of ANSD presents great practical challenges, and the number of cases
295 occurring in any one area is very small. While it is entirely feasible for departments that
perform ABR to carry out CM and OAE testing and raise the initial suspicion of ANSD, we
recommend that those with little or no experience of these cases should seek advice from
centres with high levels of expertise and more experience, to obtain a firm diagnosis and
start the management process. Such centres need to be able to offer support and guidance
300 in diagnosis and management, ensure that families get the best information and advice, and
build confidence in the local staff. In many cases, referral of the patient on to such centres
may be appropriate.

3.1 Information and Support

305 The lack of certainty around prognosis can make ANSD a particularly difficult diagnosis for
parents and families to deal with. In addition, many infants with ANSD will have other
medical issues and/or have had a stormy neonatal course, meaning that hearing may not
initially present a high priority for parents²⁶.

310 The confusion that parents are likely to feel may have a negative impact on the relationship
between parents and professionals. **Ongoing communication, support, encouragement,
and information for parents are critical to successful management.** It is important to
provide written information^o regarding the condition to families as well as to other
professionals involved with the child, such as Health Visitors, GPs and Paediatricians.
315 ANSD should be described specifically, including what is known and not known about the
condition.

It is helpful to cover the following points:

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ⁿ Or bilateral absent / severely abnormal ABR where at least one ear has evidence of ANSD – see section 3.6

^o Helpful sources of written information may include the relevant NDCS factsheet or the leaflet on ANSD produced by Newborn Hearing Screening Wales.
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- The term ANSD is a label for a pattern of test results; it is not a label for a child.
- It is not immediately possible to predict the impact on the child or even the most successful form of treatment.
- An absent ABR does not necessarily imply a profound hearing loss.
- We need to monitor this child closely, as the child may not respond to sound in a typical way.
- Many children with ANSD are able to make good use of their hearing.
- However the majority of children with this pattern of test results do turn out to have hearing problems of some degree.
- While we cannot predict the impact of ANSD on the child at this early stage, by pooling test results and observations from parents, audiologists and other professionals we will be able to do as much for the child as possible.
- Establishing the child's early communication and language skills is important, and use of visual cues is advisable until the child's true hearing ability is known.

Families of children with ANSD should be offered referral for early support. Children with ANSD are at risk for communication difficulties and need to be monitored accordingly. The overall goal is to begin management as soon as the parents/carers feel ready to proceed and to establish a communication method for use by the child and family, and put in place a plan for continuing assessment of hearing and communication.

3.2 Ongoing Audiological Assessment

The audiological profile of children with ANSD may not be stable. Therefore ongoing and regular monitoring of auditory status (behavioural, electrophysiological and middle ear) and hearing, speech, language and general development is required.

Audiological assessments must include:

a) Behavioural thresholds in each ear determined by an age-appropriate method (VRA with insert earphones, Play Audiometry, conventional Pure Tone Audiometry). These can be acquired from a developmental age of around 6 months.

Some children may have complex medical and developmental factors which present a challenge for behavioural testing. Such children must be assessed by suitably experienced and skilled professionals and results should be viewed in the context of the child's developmental status. If reliable results cannot be obtained because of significant developmental delay, Behavioural Observational Audiometry (BOA) and informal observation may be useful in guiding management. Any BOA should be carried out and interpreted with extreme care.²²

b) Electrophysiology: as discussed in Section 2, repeat ABR, CM and OAE recording at 8-10 weeks corrected age. Consider further repeat at 12-18 months, depending on the clinical situation of the individual patient.^P

c) Tympanometry/ Stapedial Reflexes. Monitoring of middle ear status is important as the presence of fluid in the middle ear will affect other tests, and children with ANSD are as likely

^P For a discussion of the relevant issues, see Appendix 2
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as any other to develop middle ear effusion. This should be done in conjunction with other testing. SRs (using both tonal and broad band stimuli) should also be measured, particularly in infants over about 6 months of age.¹

370 Additional tests that may be appropriate in the ongoing assessment of children with ANSD are discussed in Appendix 3.

3.3 Monitoring and Assessment of Communication Development

375 Monitoring and assessment of language and communication development is the key determinant of management options. Close monitoring of communicative and developmental progress by parents and professionals together should be undertaken using the Early Support Monitoring Protocol²⁷ or other appropriate monitoring tools. In addition, regular standardised assessments of language and communication should be undertaken by qualified Teachers of the Deaf or specialist Speech and Language Therapists. The
380 development of more sophisticated monitoring tools would be helpful in the early monitoring and management of infants with ANSD.

3.4 Intervention / Aids to Communication

a) Modes of Communication

385 This should be determined by the needs and desires of the family, taking into account the observed progress of the child. For most children with ANSD, use of a combination of communication systems that incorporates visual support is appropriate (e.g. auditory/aural with lipreading and natural gesture, total communication, sign language). On the other hand, an auditory-only approach (such as auditory-verbal therapy) is very unlikely to be successful.

390 Regardless of communication method, it is important that parents become proficient in the method and use it regularly in the home. Such approaches can be put into place at an early stage, before behavioural thresholds and the child's 'true' hearing ability are known, in order to lay the foundations of communication and language development.

395 **b) Conventional Hearing Aids**
There is increasing evidence that a substantial number of children with ANSD derive benefit from hearing aid fitting if there is a significant behavioural hearing loss. About 50% of the children in one study gained significant benefit⁹, although some clinics report much lower success rates²⁸. Therefore a trial of amplification should be undertaken. However, due to doubt as to the benefit in children where behavioural thresholds are near-normal, **we would only recommend aiding for a child whose behavioural thresholds are reliably elevated**. A number of other considerations and complications apply – for further details and discussion please see reference⁶.

405 **The decision on whether to aid must be based on behavioural results and observations from families and early interventionists regarding the child's responses to sound and early communication development.** If reliable behavioural hearing thresholds are not yet available and there is significant concern from the family and early
410 interventionist, hearing aid fitting can begin based on these concerns and behavioural observation audiometry (unaided and aided) in the test situation.

415 The fitting of hearing aids to children with ANSD should be based on a prescriptive method
specifically developed for infants and young children²⁹ (e.g. DSL). The behavioural
thresholds (not ABR / electrophysiological thresholds) should be used to establish
amplification targets. In order to provide the best chance of benefit, it is important that
optimal audibility of speech sounds above threshold is achieved. Therefore, provided
reliable behavioural thresholds are available, aids should be fitted to target based on these
thresholds, rather than adopting a ‘conservative’ approach.^q

420 Where there is a lack of reliable behavioural thresholds on which to base the prescription, a
conservative approach should be adopted, beginning with low hearing aid gain and
increasing the gain gradually if no responses from the child are observed.

425 DSP hearing instruments should be used, in keeping with MCHAS²⁹ and NHSP³⁰ guidelines.^r

425 Hearing aid benefit should be determined. Benefit is determined primarily based on the
development of speech perception skills, not on aided detection thresholds. Monitoring of
the child’s hearing aid fitting is essential – refer to the appropriate MCHAS guidelines²⁹.

430 Recent studies indicate that the late (cortical) evoked potentials may help to differentiate
those who are able to use hearing aids effectively to understand speech³¹⁻³³. This technique
is discussed further in Appendix 3.

435 **c) FM Systems**

435 FM systems (with or without personal hearing aids) may be beneficial for children with ANSD
who have residual speech recognition in quiet but experience difficulty in noise³⁵. A trial with
an FM system should be considered as part of the hearing aid fitting process, particularly
when the child is involved in a day care or educational setting in which poor acoustic
conditions restrict access to spoken language.

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d) Cochlear Implants (CIs)

445 The literature has shown increasing numbers of children with ANSD who benefit from
cochlear implants^{4,6,28,36}, and this option should be considered when behavioural responses
indicate the child is behaving like a child with a severe/profound hearing loss, and/or when
the child is not making progress with hearing aids (i.e. they show no or very limited speech
discrimination abilities). A trial of conventional amplification is important prior to cochlear
implantation (this is an area where we need more research). Behavioural thresholds are not
a good guide to candidacy, and ANSD patients with even relatively mild hearing losses on
behavioural testing may be CI candidates if they do not show good progress with other
450 interventions.

^q If behavioural thresholds fluctuate from test to test, the “best” thresholds obtained should be used, to avoid risk of over-amplification.

^r Note that current hearing aid technology and prescription techniques (including the use of wide dynamic range compression and advanced signal processing strategies) have generally been developed to address the difficulties typically experienced by patients with conventional sensory hearing loss. Some of these features may be less helpful for patients with ANSD. For example, low frequency information, where temporal cues are most important, may be less useful. Further work is needed in this area.

455 Infants identified with ANSD can be referred to a cochlear implant centre for assessment as soon as there are significant concerns about behavioural responses to sound and/or communication/speech/language development. (It is not appropriate to refer infants with ANSD for cochlear implantation based purely on ABR results, and generally behavioural measures will need to have been obtained). However, in view of the reports of significant improvement in auditory function in some infants with ANSD over time, **the final decision to implant should not be made until audiological test results are stable and demonstrate unequivocal evidence of permanent ANSD.**⁶ (The exception to this is where there is a strong suspicion of a genetic cause for the ANSD known to be associated with profound deafness and good CI outcome^s; such cases can be referred and implanted in a similar timescale to infants with profound conventional SNHL.)

465 Local centres should be able to discuss cases of ANSD with the CI team, and it is important that the CI team are able to accept referrals on the basis of assessment and advice, rather than on the assumption that they will be candidates for surgery. The approach and timescale for assessing such cases will need to be different from that for cases of conventional SNHL (except in the event of a known genetic cause as defined above), and assessment for possible delayed maturation must be carried out as part of the process of CI assessment. It is important to make clear to parents and involved professionals that the referral at this stage is for *assessment* and that it is not yet clear whether the child will turn out to be a candidate for implantation. Responsibility for the ongoing monitoring of hearing and communication development, with appropriate modification of management strategies, also needs to be clearly agreed between the CI team and the local service.

475 Guidelines for cochlear implant assessment of children with ANSD in the UK have now been developed by the British Cochlear Implant Group⁴⁰. Cochlear implant funding bodies in the UK also need to consider their approach to cases referred for ANSD based on the accumulating evidence from around the world.

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3.5 Medical Referral

Ongoing medical / neurological assessment is essential.

485 Some infants may already have an established neurological diagnosis. In others, ANSD identified by newborn hearing screening may be the first indicator of an underlying neurological condition. It is therefore recommended that all children who are diagnosed with ANSD are assessed and investigated by an appropriately skilled and experienced Audiovestibular Physician, Paediatrician or paediatric neurologist.

490 Key elements that should be included in the assessment are listed in Appendix 4.

As with any other child with a hearing problem, ENT involvement may be required to manage any conductive element identified.

495

^s E.g. Otoferlin mutation
NHSP ANSD guidelines v 2.2

3.6 Management of Unilateral ANSD

a) Neonatal tests indicate unilateral ANSD with SNHL in the contralateral ear

500 Cases where the contralateral ear has a severe/profound hearing loss (*i.e.* absent/severely abnormal ABR with no evidence of good outer hair cell function) should be managed with caution, as it is possible that they may in fact be cases of bilateral ANSD. We would advise aiding of the “non-ANSD” ear, but decisions about cochlear implantation of either ear should not be made until there is unequivocal evidence of permanent profound hearing loss or ANSD on behavioural testing.

b) Unilateral ANSD with normal hearing in the contralateral ear

505 There is little consensus about the management of unilateral ANSD in young infants. The effects of unilateral SNHL are fairly well-understood, but the impact on speech/language and educational progress varies between individuals. The effects of unilateral ANSD are less well-understood. As discussed above, monitoring of hearing, communication and
510 speech/language development are important. Children with unilateral ANSD should also receive a medical referral for aetiological investigation.

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520

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635 **Appendix 1: Case Scenarios**

Case example A

History summary:

Born at 26 weeks gestation.

640 Prolonged assisted ventilation; treatment for repeated episodes of sepsis; phototherapy for jaundice.
Home at 5 months on ambulatory oxygen.

Screen: NICU protocol

TEOAE: CR R&L AABR: NCR R&L

645

Initial Audiological Assessment:

8 weeks corrected age, shortly after discharge home. Parents unsure about responses to sound.

(R) ear:

650 4kHz tpABR: no response (RA) at 75 dBeHL
Switched to click ABR using inserts: no response at 85 dBeHL.
CM recorded at same level.

(L) ear:

655 Started with click ABR in view of result obtained on (R) and screen result on (L).
No response (RA) to click at 85 dBeHL
CM recorded at same level.
1kHz tpABR recorded to check for low frequency response: No response (RA) at 90 dBeHL

660 No obvious behavioural responses observed.

Interpretation

- History: high risk for SNHL and ANSD
- ANSD pattern R&L
- Delayed maturation a possibility, though baby is now post-term.

665

Management

- Results discussed with parents, including explanation of ANSD and unpredictable outcome.
- Referral to ToD agreed. Encouraged visual input and close monitoring.
- For repeat ABR 8 weeks later, in view of possibility of delayed maturation.
- Results discussed with neonatal paediatrician.

670

Repeat ABR: 16 weeks Corrected age

TEOAE: present R&L

675 Started ABR with click in view of previous lack of response. Click ABR: repeatable responses present
down to 60 dBeHL R&L though delayed waveforms.
4kHz tpABR: repeatable responses present down to 60 dBeHL though delayed waveforms.
BC 4kHz tpABR: no convincing response at 60 dBeHL.
High frequency tymps: normal R&L

680 *Interpretation*

- Some signs of maturation; need to continue monitoring.

Management

- Results discussed with parents: signs of improvement; still difficult to predict outcome
- Continue ToD support, visual support for communication, and monitoring
- Review in Audiology for behavioural testing.

685

Audiology review: 7 months corrected age (i.e. 10 months chronological age)

Seems to respond well to sound at home; babbling tunefully; good physical development – just sitting unsupported.

690 Conditioned well for insert VRA:

Frequency (kHz)	Minimal response level (dBHL)			
	0.5	1	2	4
(L) ear	30	30	N/T	25
(R) ear	30	25	20	30

Tymps: mobile R&L

Interpretation

695 • Satisfactory VRA responses for developmental age. In view of previous results, need to monitor to ensure good receptive & expressive speech & language development.

Management

- Discussed with parents: encouraging results; responding well to sound; too young to be sure how useful hearing is for speech
- Continued support & monitoring by ToD

Audiology review 6 months later

Seems to hear well at home; responds to quiet sounds.

Producing several recognisable words with meaning.

705 Insert VRA: Minimal response levels at ≤ 20 dBHL R&L at 0.5, 1, 2 & 4 kHz

Ongoing reviews

Repeat ABR successfully obtained under natural sleep at 21 months:

710 4kHz tpABR: CR R&L ≤ 30 dBHL with normal waveform morphology (unable to attempt 1kHz recording as child woke up)

Hearing and speech development monitored at least annually until aged 6 years

Age-appropriate speech and language development.

Interpretation

715 • Was 'transient' ANSD due to delayed maturation. 'ANSD' label no longer appropriate.

Management

- Discharged at 6 years of age after successful start at school. Advised to re-refer if any concerns.

720

Case example B

History summary:

Born at term by emergency caesarean section due to reduced foetal movements.

725 Required intensive resuscitation, followed by assisted ventilation for 5 days.

Developed neonatal convulsions. Cranial ultrasound and MRI demonstrated cortical changes consistent with hypoxic ischaemic encephalopathy.

Home at 6 weeks.

730 Screen: NICU protocol

TEOAE: CR (R), NCR (L) AABR: NCR R&L

Initial Audiological Assessment: Aged 6½ weeks

Parents feel baby sometimes responds to loud sounds.

735 (R) ear:
4kHz tpABR: no response (RA) at 75 dBeHL
Switched to click ABR using inserts: no response at 85 dBeHL.
Cochlear microphonic recorded at same level.
1kHz tpABR attempted to check for low frequency response: RA at 90 dBeHL

740 (L) ear:
4kHz tpABR: no response (RA) at 75 dBeHL
No response (RA) to click at 85 dBeHL
Woke before CM recording could be attempted.

745 Clear TEOAE recorded.

No obvious behavioural responses observed.

Interpretation

- 750
- History: high risk for SNHL and ANSD
 - ANSD pattern R&L
 - Term baby, tested at 6 weeks, so delayed maturation less likely, but wise to repeat ABR to confirm initial diagnosis.

Management

- 755
- Results discussed with parents, including explanation of ANSD and unpredictable outcome.
 - ToD referral offered but parents prefer to wait for now. Encouraged use of visual as well as auditory stimulation.
 - For repeat ABR in 6 weeks
 - Neonatal paediatrician informed of results.

760 Repeat ABR: 12 weeks

Clear TEOAEs recorded R&L

Started with click ABR (inserts) in view of previous results. No repeatable response R or L at 85 dBeHL

765 Baby still sleeping, so CMs recorded R&L (not necessary for diagnosis in view of clear TEOAEs, but useful for learning/training and completeness of results).

High frequency tymps: normal R&L

Interpretation

- 770
- Bilateral ANSD with no indication of maturation so far.

Management

- Discussed results with parents and re-iterated importance of support for early communication as it will be some time before we have an indication of true hearing ability
 - Parents agreed to ToD referral
- 775
- For regular support & monitoring by ToD, with feedback to Audiology. Audiology review for behavioural testing.

Audiology review: 7 months

780 Parents & ToD feel child responds to some louder sounds at home, but little response seen to voices or quieter toys. Some vocalisations but no real babble. Some developmental delay – not yet sitting unsupported.

Unable to successfully condition to VRA. Repeatable responses obtained on a combination of behavioural observation audiometry & distraction testing, as follows:

785

	MRL to soundfield warble tones (dBA)			
Frequency (kHz)	0.5	1	2	4
Presented on (L)	70	80	85	85
Presented on (R)	70	75		80

Responded to voice at 60-70 dBA; no response to 's' or high frequency rattle at 60 dBA. Tymps: mobile R&L.

Interpretation

790

- Behavioural responses and parent/ToD observations consistent with moderate/severe hearing loss, though responses recorded may not yet be quite threshold

Management

795

- Discussed with parents. Agreed to trial hearing aids
- Aids fitted programmed to behavioural responses, slightly conservatively initially in view of lack of precision over thresholds and lack of ear-specific information. Alerted to sound with aids, but no sign of loudness discomfort when checked with loud sounds.

Audiology review 6 weeks later

Conditioned to insert VRA using earmoulds:

800

	Minimal response level (dBHL)			
Frequency (kHz)	0.5	1	2	4
(L) ear	60	60	N/T	70
(R) ear	65	60	70	70
BC	40	60	70	70

Aids re-programmed to these results – now fitted accurately to target.

Ongoing reviews: every 3 months over next year

805

Insert VRA thresholds confirmed on subsequent tests – similar to above, with some variation between assessments.

Parents report good responses to voice with aids. Wearing aids consistently.

Continued support from ToD and Speech & Language Therapist; signing introduced.

Child diagnosed with mild cerebral palsy – under care of paediatric neurologist.

Speech and language development delayed but showing steady progress.

810

At 2 years

Child had GA for orthopaedic procedure – opportunity used to repeat ABR.

No response R or L to 4kHz tp or click ABR at 85 dBeHL.

CMs recorded R&L at 85 dBeHL

815

Interpretation

- Bilateral ANSD confirmed.
- Moderate-to-severe loss on behavioural testing.
- Making good progress with hearing aids.

820

Management

- Continue with aids and ongoing monitoring.

825 **Case example C**

History summary:

Born at 35 weeks gestation. Admitted to NICU for 10 days for temperature maintenance and to establish feeding.

830 Discharged home well. Discharged from further follow-up by neonatal paediatricians after first outpatient review.

1st child. No family history of deafness.

Screen: NICU protocol

TEOAE: NCR R&L AABR: NCR R&L

835

Initial Audiological Assessment:

0 weeks corrected age. Parents concerned about lack of response to sound at home.

Clear TEOAE recorded R&L.

ABR carried out as baby was in NICU > 48 hours:

840

(L) ear:

4kHz tpABR: no response (RA) at 75 dBeHL

Switched to click ABR: no response at 85 dBeHL.

CM not attempted (wanted to move on and ensure 2nd ear tested; clear TEOAE already obtained so

845 CM not necessary).

(R) ear:

4kHz tpABR: no response (RA) at 75 dBeHL

Switched to click ABR: no response at 85 dBeHL.

850 CM recorded at same level.

1kHz tpABR recorded to check for low frequency response: RA at 90 dBeHL

No obvious behavioural responses observed.

855 *Interpretation*

- History: slightly premature and in NICU > 48 hours, but no major risk factors for ANSD
- ANSD pattern R&L
- Delayed maturation a possibility – baby only just term – though was only 5 weeks prem.

Management

860 • Results discussed with parents – fits with their concerns at home. Explained unpredictable outcome.

• Referral to ToD agreed. Encouraged visual input and close monitoring.

• For repeat ABR in 8 weeks.

• Referred to paediatrician and Audiovestibular physician:

865

– Satisfactory general and neurological examination

– Neurological MRI, including internal auditory meati, performed without sedation (under ‘feed and wrap’ protocol). Reported as normal including VIII nerve.

– Possible genetic cause for ANSD considered and referral made to genetic service.

870

Repeat ABR: 8 weeks CA

Still no repeatable response to click ABR at 85 dBeHL

CMs recorded R&L

No repeatable response to 1kHz tpABR at 90 dBeHL

875 No obvious behavioural responses.

Interpretation

- Bilateral ANSD with no evidence of maturation
- Possible genetic cause

Management

- 880
- Parents commenced home sign language tuition
 - For close support & monitoring from ToD
 - Review for behavioural testing as early as possible

Audiology review: 5 months CA

- 885
- Parents & ToD report no observed responses to loud sounds at home.
VRA: Conditioned to vibrotactile stimulation. No response to warble tones using inserts at maximum levels – 100 dBHL at 0.5 kHz and 120 dBHL at 1,2 & 4 kHz R or L.
Tymps: normal R&L.

890 *Interpretation*

- Behavioural testing and parental/ToD observations are all consistent with severe/profound bilateral hearing loss
- Genetic cause suspected in view of lack of other risk factors

Management

- 895
- Discussed with parents and agreed to hearing aid trial. Aids fitted, programmed to behavioural responses.
 - Cochlear implant referral discussed with parents.

At 7 months CA

- 900
- Insert VRA continues to show profound bilateral hearing loss
Limited response to hearing aids
Producing vibrotactile vowel sounds only. Beginning to show understanding of sign.
Satisfactory developmental progress.

905 *Interpretation*

- Bilateral profound hearing loss with no evidence of maturation
- Genetic cause strongly suspected

Management

- 910
- After discussion, referred to cochlear implant programme
 - Appropriate to go ahead with CI referral without further delay.

Appendix 2: Delayed maturation and the timing of repeat ABR testing

915 Version 1.1 of these guidelines recommended carrying out repeat ABR tests at 8-10 weeks corrected
age and 9-15 months to help differentiate long-term ANSD from delayed maturation. Guidance on the
repeat ABR at 8-10 weeks is unchanged, but we have now revised the guidance for the second
repeat ABR. We suggest that a re-test should be considered at 12-18 months of age but that the
920 decision whether or not to carry out this re-test should depend on the circumstances of the individual
case. In making this decision, the following factors need to be taken into account:

i) Age of maturation of ABR

Anecdotally, any maturation of the ABR occurs by around 18 months of age, but there appear to be
few reported studies in the literature. Psaromattis et al¹⁷ reported recovery of the ABR after 4-6
925 months in 12 out of 20 NICU graduates diagnosed with ANSD (original click ABR threshold >
70dBnHL; threshold on re-test \leq 40 dBnHL). Attias& Raveh¹⁸ reported 5 cases of high risk neonates
being considered for cochlear implantation who showed full or partial recovery of the ABR on re-test
7-12 months after diagnosis. Madden et al⁸ reported improved behavioural thresholds 1-15 months
after diagnosis, with a stable audiogram reached by 11-25 months, in 9 out of 18 infants, but do not
930 report whether any changes in ABR were seen.

ii) Practicalities of testing

ABR testing under natural sleep is often difficult to achieve in this older age group, and sedation may
well be required. However co-morbidities in many of these children may mean that sedation is contra-
935 indicated. Sometimes the child may be undergoing sedation or anaesthesia for treatment of some
other condition, and it may be possible to arrange to repeat the ABR at the same time.

iii) Parent counselling

Experience has shown that careful counselling of parents around the repeating of ABR tests is
940 needed. As noted above, sleep can be difficult to achieve and the re-test session may prove to be a
long and difficult one for parent and child. In the case of a child who is showing good behavioural
responses to sound, it can be very discouraging to a parent if the repeat ABR still shows an abnormal
response. It is important that parents understand that active monitoring of the child's behavioural
responses and speech & language development is the key factor in determining their ongoing
945 management and outcome. It helps if these issues have been discussed with parents to prepare
them for the different possible outcomes of the re-test before this is carried out.

iv) Patient management

The practical issues outlined above need to be weighed up against the likely usefulness of the repeat
950 ABR result in management of the patient. For example, if the child at this age is showing convincing
and reliable behavioural responses consistent with a severe/profound hearing loss, and poor speech
& language development, then active audiological management (including consideration of CI referral)
is clearly indicated and a further abnormal ABR test may not add to the picture. Conversely, if the
child is showing good behavioural responses and good speech & language development, whilst it
955 would be informative and encouraging to demonstrate an improved ABR, ongoing follow-up and
monitoring of the child's speech & language development would still be recommended until more
subtle auditory processing difficulties have been ruled out. However, ongoing use of the ANSD label
in these cases may not be helpful.

960 **Appendix 3: Additional Tests**

The following tests may be valuable in the ongoing assessment of infants and children with ANSD.

a) Speech discrimination testing

965 This should be attempted at as young an age as possible, including testing in noise. In addition to
testing in the clinic, speech discrimination ability should also be evaluated in the child's natural
environment (e.g. home, nursery) – this may be done in conjunction with education and/or speech-
language therapy colleagues. Further work is needed on developing age-appropriate tools that are
970 sophisticated enough to look in sufficient detail at early speech/language/communication development
in order to inform the management of young infants with ANSD.

b) Advanced electrophysiological techniques

i) Electrocochleography (ECoChG) and Electrically-Evoked ABR (E-ABR)

975 Recent studies have indicated that these tests may have a role in narrowing down site of lesion and
helping determine cochlear implant candidacy^{37,38}. Studies using trans-tympanic electrocochleography
have identified two abnormal potentials in some ANSD patients: an “abnormal positive potential”
(enlarged summing potential) which has been interpreted as indicating a pre-synaptic disorder and
may give a good CI prognosis, and a “dendritic potential” which has been interpreted as indicating a
980 post-synaptic disorder and therefore likely to indicate poorer CI outcome. At implantation, ANSD
patients with a normal electrically-evoked ABR have gone on to have good post-implant speech
perception ability, whilst those with an abnormal E-ABR have had poor post-implant speech
perception ability. However, these are invasive techniques which are still at a research stage and
further work is needed.

ii) Cortical Auditory Evoked Potentials (CAEPs)

985 There is emerging evidence^{31-34,39} that the presence or absence of auditory cortical responses in
patients with ANSD might provide an insight into the degree of an individual's dys-synchrony and
whether hearing aids are likely to be helpful. The mechanism of this is unclear. Sharma and
colleagues^{33,34} suggest abnormal, or dys-synchronous, patterns of sub-cortical transmission, which
990 occur in children with more disabling degrees of ANSD, have the potential to disrupt normal cortical
development and it is this abnormal cortical development that explains the failure to evoke cortical
responses. An alternative basis for the lack of recordable cortical responses in some patients with
ANSD has been proposed by Neary & Lightfoot³⁹: it requires only a modest degree of temporal dys-
synchrony to “smear” the relatively short latency responses of the ABR but it takes a correspondingly
995 greater degree of dys-synchrony to abolish the longer latency cortical response. So, if both the ABR
and CAEPs are absent then it is reasonable to conclude the dys-synchrony is profound and the
prognosis with amplification may be poor; if the ABR is absent but cortical responses are present the
degree of dys-synchrony is likely to be modest and therefore the prognosis for amplification is better.

1000 Thus, cortical testing may have potential in informing patient management and could guide the
expectations of patients or their parents. The recording of cortical responses to auditory stimuli is
practical in older children and adults but the routine testing of infants is currently not yet standard
clinical practice.

1005

Appendix 4: Medical Assessment

Key elements in the assessment of infants identified with ANSD should include:

- 1010
 - Detailed history, including family history, neonatal factors e.g. gestation, hypoxia, assisted ventilation, hyperbilirubinaemia, intraventricular haemorrhage, hydrocephalus, convulsions
 - Examination, particularly focused on neurological and developmental assessment
- 1015
 - Imaging – MRI brain and internal auditory meati to assess integrity of the VIIIth and VIIth nerves
 - Ophthalmology assessment – particularly looking for evidence of visual cortical dysfunction, optic disc pathology
- 1020
 - Peripheral nerve conduction studies –if generalized neuropathy suspected
 - Referral to a geneticist, particularly if a neurodegenerative condition is suspected, although at the time of publication of these guidelines genetic testing for OTOF or other implicated genes is not available via the NHS in the UK[†].
- 1025
 - Metabolic studies as indicated by relevant clinical features – e.g. urine amino acids

1030 **Acquired ANSD is particularly associated with a neurodegenerative or metabolic aetiology and these children especially require detailed neurological assessment and investigation.**
Neurodevelopmental history, speech and language development, and neurological abnormalities should be noted in detail.

[†]This situation may change in the near future
NHSP ANSD guidelines v 2.2