

GUIDELINES FOR INVESTIGATING INFANTS WITH CONGENITAL HEARING LOSS IDENTIFIED THROUGH THE NEWBORN HEARING SCREENING

BEST PRACTICE GUIDELINES PRODUCED BY BAAP/BAPA

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Introduction

This document applies to cases of bilateral permanent hearing loss averaging over 40dB in the better ear, identified through newborn hearing screening. It was originally prepared in consultation with doctors involved with the 23 first phase sites for the National Newborn Hearing Screening Programme (NHSP) in England.

It has been revised by the British Association of Paediatricians in Audiology (BAPA), endorsed by the British Association of Audiological Physicians (BAAP) and provides guidance for the doctors who undertake aetiological investigation of all bilateral permanent hearing loss in infants identified through newborn hearing screening.

These guidelines complement those issued by the professional bodies, i.e. BAAP and BAPA (British Association of Paediatricians in Audiology) previously called BACDA¹ (British Association of Community Doctors in Audiology), and take into account issues relevant to the diagnosis in infancy. These guidelines are recognised by the Newborn Hearing Screening Programme (England) and will be reviewed and revised regularly as new evidence emerges.

It should be noted that:

- Investigation for the cause of unilateral hearing loss is outside the scope of this document.
- BAAP is in the process of preparing guidelines for the investigation of mild and moderate hearing loss, and unilateral hearing loss for children of all ages.

The process of aetiological investigation:

- Takes a systematic approach that will maximise the opportunity to arrive at an (aetiological) diagnosis of the hearing loss.
- Includes explaining to and discussing with families the aims and possible outcomes of investigations and potential impact on subsequent management of their child
- Recognises that the choice lies with the parents but it is the responsibility of the doctor on the team to provide parents with accurate and unbiased information so that they can make an informed decision.

- Acknowledges that some parents may decide against investigations and their views should be fully respected.

General guidance

- Medical investigations including those designed to search for the cause of deafness must be available to families of infants with significant hearing loss.^{2,3} Investigation into the aetiology of sensorineural hearing loss in children is a part of the medical support and management for families of hearing impaired children. The investigating doctor should have appropriate training and competency to understand the associated developmental and medical issues. Duplication of tests must be avoided wherever possible by working together with other professionals involved in the care of the child.
- Parents must be given comprehensive, up-to-date and unbiased information about proposed medical investigations that may help in identifying the cause of hearing impairment and the likely diagnoses as well as treatment of any co-existing conditions, including both the benefits and disadvantages of the tests. This information should be in an accessible format e.g. National Deaf Children's Society (NDCS) Fact Sheet "Why does my child have a hearing loss" (www.ndcs.org.uk), so that parents feel that they can make an informed decision.
- Parents should be given every opportunity to further discuss their views and concerns with the doctor so that they can decide whether they want their child to have the investigations and if so, the nature and timing of any tests.
- There must be at least one doctor in the local NHSP Team, with appropriate level of knowledge and competence⁴ in explaining the investigations to parents and answering their queries with comprehensive and up to date knowledge of the causes of hearing loss in children and neonates, interpretation of test results and appropriate management of any abnormality found^{5,6,7}. The doctor should be trained and competent in the comprehensive history and clinical examination (not confined to ears and mouth) of infants and children from neonate onwards. This may include onward referral for further assessments and the doctor should also have sufficient knowledge of paediatrics and child development to be able to recognise abnormal development and distinguish it from normal variations. The doctor should take the responsibility for review of the aetiological diagnosis and further investigation as and when required. S/he should be carrying out the process of aetiological investigation of deafness and examination of babies and children sufficiently often to be thoroughly familiar with the process. In services covering smaller number of births, it is advised that this is achieved by being part of a local network through regular peer review, case discussion and regional audit. Additional quality control and clinical governance could be achieved by participating in National Audits such as those conducted by BAAP and BAPA.

- It is suggested that the Medical Lead for the local NHSP team must have the above competencies and skills.
- It is the responsibility of the doctor to keep the parents informed at every stage of the investigation process and to convey the results. The parents should have reasonable access to the doctor for further explanation and information as required. The investigations should be reviewed and discussed with the parents not only in the light of new evidence, but also as the child matures.

Benefits of investigations

For parents, the child and professionals

- Provides an opportunity to explore the cause of the hearing loss
- Allows professionals to give better advice with regard to possible progress and outcomes. If the medical diagnosis is known, then the doctor can provide better advice to parents, e.g. progression of hearing loss due to wide/dilated/enlarged vestibular aqueduct (EVA) or in congenital Cytomegalovirus infection.
- May help monitor, treat or prevent complications in some patients e.g. those with cardiac conduction defects
- May help prevention of further deterioration of hearing loss in a child with e.g. Cytomegalovirus (CMV) or m.1555A>G mitochondrial mutation.
- Facilitates better planning of future health care for the child
- Enables better medical and audiological management of the child's hearing loss
- Allows improved information and advice for the family
- Enables more informed genetic counselling

Timing of investigations

Investigations should be offered as soon as possible so as to maximise the chance of arriving at a diagnosis, but taking into consideration parental readiness, choice and the general health of the baby. It should be recognised that there may be only a small time window for diagnosing certain conditions e.g. viral infections, while other conditions may take years to manifest e.g. retinitis pigmentosa in Usher's syndrome or goitre in Pendred's syndrome but can be predicted earlier by accurate medical investigation.

Aetiological diagnosis is an ongoing process. It should be reviewed and parents informed as new scientific and clinical information emerges.

One positive investigation suggesting a cause does not exclude other causes and further investigations should still be considered

Reasons for carrying out aetiological investigations early

- To maximise the chances of arriving at an aetiological diagnosis
- To give an opportunity for the parents to understand the cause of their child's deafness
- To provide better advice to parents especially with regard to future planning of their family
- To provide an opportunity to treat and thereby prevent hearing loss or its deterioration e.g. in CMV
- To successfully treat and therefore prevent serious complications e.g. conduction defects leading to cardiac arrest in Jervell Lange-Nielsen (JLN) syndrome
- To provide better advice to parents that may lead to reducing the chances of further deterioration of hearing loss in their child or extended family e.g. enlarged vestibular aqueduct (EVA, WVA), avoiding exposure to aminoglycosides in m.15555A>G mitochondrial mutation
- To identify associated pathology early so that appropriate management can be instituted e.g. renal anomalies in Branchio-Oto-Renal (BOR) syndrome or refraction errors
- To determine best management options for rare conditions such as severe cochlear dysplasia or hypoplastic (or aplastic) auditory nerves
- To enable some investigations to be carried out under natural sleep whilst baby is still very young e.g. MRI

The yield from and usefulness of certain investigations can depend on age, ethnicity and the presence of other deaf people in the family

Discussion about each individual investigation and the reason for or against it should be clearly stated in the notes

The following are investigations that are recommended and of these Level 1 investigations must be carried out in all cases and Level 2 investigation should be carried out in specific conditions

History

General history (Level 1)

Comprehensive general medical history must be recorded and should include details of pregnancy and maternal health, birth, postnatal period and infancy. These could be obtained from parents and detailed examination of the mother's and child's medical notes and parent held record

Suspicion of infections especially within the first trimester, use of potentially ototoxic medication during the pregnancy (including alcohol), placental insufficiency and intrauterine growth retardation are all important to note. Any adverse perinatal events such as significant hypoxia, hyperbilirubinaemia and treatment with ototoxic medication in the newborn, treatment in a Neonatal Intensive Care Unit (NICU), prolonged ventilation, and postnatal infection especially bacterial meningitis should be recorded.

Examination of maternity and perinatal notes will also provide useful additional information, e.g..Rubella status, medication in pregnancy.

Examination of neonatal notes will provide information on severity and duration of hypoxia, acidaemia, hyperbilirubinaemia, and ototoxicity.

Family history (Level 1)

Detailed family history of hearing loss or risk factors associated with hearing loss in at least 3 generations to include siblings, parents and grandparents, uncles, aunts and first cousins should be recorded wherever possible.

Use of a genetic pedigree tree is helpful in updating this information on a regular basis. Each update should be clearly identifiable as such and should be initialled and dated

Examination (Level 1)

It is essential that a full physical examination be performed, including the head and neck, in particular eyes and ears, and otoscopy, examination of the palate. Further, examination of the rest of the body, limbs including hands and feet, skin and nails, chest, abdomen, spine and cardiovascular system for any dysmorphic features or abnormalities. It is also important to perform or arrange an age appropriate developmental assessment.

Family audiograms (Level 1)

It is recommended that an age appropriate hearing assessment of first degree relatives is carried out even if there are no concerns about the hearing in other relatives, as previously unsuspected abnormalities may be present.⁸ It is important that each Paediatric Audiology Department has a policy with clear guidance for management of any hearing loss identified in the family members.

Specific Investigations

The following investigations are recommended:

1. **Imaging:** Includes imaging the ear and any other parts of the body that may be affected.

Radiology of the Head and Neck.^{5,9,10,11,24}

- a. **Magnetic Resonance Imaging (MRI)** of the inner ears and internal auditory meatus (IAMs) is the first line radiological investigation in children. It will show most structural abnormalities except those of the ossicular chain. MRI, which does not involve radiation, will show soft tissues, e.g. brain, VIIth and VIIIth nerves and membranous labyrinth including the endolymphatic sac but takes much longer (up to 30 minutes) compared to CT of petrous temporal bones. **(Level 1)**
- b. **Computerised Tomography (CT)** of petrous temporal bones will clearly show the bony structures including middle ear ossicles and should be considered when information of the bony structures is needed. However CT scans do not show the nerves and involves radiation that can be up to 100 times that of a chest X-ray. **(Level 2)**

General Principles

- i. Particular expertise is required in interpreting images
- ii. It is important to give a clinical summary and specify any suspected anomaly so that the radiologist can select the optimal scan protocol
- iii. All patients should be offered MR imaging in the first weeks of life to avoid sedation or anaesthetic later on
- iv. MRI should be considered urgent if:
 - meningitis is the cause of deafness
 - hearing loss is progressive or fluctuating
 - recurrence risk and genetic diagnosis is important to parents and doctors
- v. In all cases this should follow discussion with parents and be decided on a case by case basis

- vi. CT and MRI may be carried out from birth and the timing depends on when the parents are ready and what action is planned. Infants and children over 3 months will normally need sedation for radiological investigations and children over 2 years may require a general anaesthetic, but may vary according to local protocols.
- vii. The advantages of a definitive diagnosis in infancy should be weighed against the risk of radiation exposure from CT scans.

If it is likely that the child will need cochlear implantation it may be better to leave the imaging to the Cochlear Implant Team. This needs to be a local decision taken with the relevant Cochlear Implant Team

Renal Ultrasound is indicated if Branchio-Oto-Renal Syndrome is suspected (i.e. conductive hearing loss with pre-auricular pits, branchial sinuses) or if there are multiple or multi-system abnormalities, or a family history of renal problems **(Level 2)**

2. **Electrocardiography (ECG)**^{12,13,14,15,16,17}

The only known association between ECG abnormalities and hearing loss is in Jervell Lange-Nielsen Syndrome (JLNS) which is a very rare condition (1 in 160,000 to 1 in 600,000) with long QT interval and profound sensorineural hearing loss, sometimes with a family history of syncope or sudden death. Delay in motor milestones is also seen in these children. Babies with a corrected QT interval (QT_c) greater than that expected for their age need to be reviewed by a paediatric cardiologist. Computerised calculations should not be relied upon. Only 12 lead ECG must be used. The ECG should be repeated if the first one was done under 4 months corrected age. **(Level2)**

3. **Genetics**^{18,19,20,21,22,23}

All genetic tests, their purpose, process and possible outcomes, implications for other family members, as well as advantages and disadvantages of each test must be discussed clearly and in detail with the family. Every opportunity should be given for the family to understand the tests and take an informed decision as to whether they would prefer for their child to be investigated or not. The possibility that blood samples could be stored with consent for future investigation needs to be discussed with parents.

Written consent must be obtained when genetic tests are carried out²⁴

The following tests are recommended:

a. Test for **Connexin 26 and 30** mutations (**Level 1**)

A negative result does not exclude other types of hearing loss due to other genes

Referral to a clinical geneticist should be discussed with the family

- If the result of the test is not clear cut
- If an autosomal recessive condition is suspected and there is only one mutation found
- If sequence variants are of unknown pathogenicity
- If there are two different variants in the Connexin 26 gene
- To confirm that one mutation comes from each parent
- To offer the option of further discussion

b. Test for m.1555A>G mitochondrial mutation where there is a family history of hearing loss through maternal inheritance or hearing loss following exposure to aminoglycosides,. Consider other mitochondrial mutations, depending on the family history (**Level 2**)

c. Test for **chromosome abnormalities** and **microdeletions** where there is suspected developmental delay or dysmorphic features (**Level 2**)

d. Test for the Pendrin gene in cases of enlarged vestibular aqueduct and/or Mondini anomaly?²⁵ (**Level 2**)

Referral for genetic counselling should be dependent on local protocols which should be developed with the geneticists, i.e. Some may prefer to request molecular tests once they have seen the family.

In the case of a positive test result, parents should be given written information on the implications for their child and any future children. e.g. "Understanding the Deafness: A Guide for Patients and Families. Harvard Medical School Centre for Hereditary deafness"

(<http://hearing.harvard.edu/info/GeneticDeafnessBookletV2.pdf>)

4. Congenital Infection ^{26,27,28,29,30,31}

a. **CMV (Level 1)**

This is the commonest intrauterine infection causing hearing loss in the UK although in majority of cases the child is asymptomatic. i.e. there may be no obvious symptoms in the mother or baby when born. Congenital CMV is found in up to 0.5% of all births in the UK and about 4% of these will be deaf at birth. CMV can cause progressive hearing loss, so the figure rises to about 8% by the age of 5.

In babies < 1year of age:

Urine or saliva CMV DNA PCR x 2 (separate occasions)

Consider maternal IgG

In babies >1year of age:

Urine or saliva CMV DNA PCR x 2 (separate occasions)
CMV IgG if taking blood anyway

If either is positive, request Guthrie (Blood spot) card for CMV DNA testing.

It requires:

Mother's name at time of birth

Baby's name at time of birth

Mother's address during the first few weeks of baby's life

Signed parental consent

Newborn screening laboratory address:

<http://www.newbornscreening.org/laboratories.asp>

Signed parental consent is needed if you wish to retrieve the Guthrie card from the Regional centre

b. Rubella (Level 1)

From birth to 3 months. IgM will be present in clotted blood sample in all cases of congenital infection, and 90% between 3 and 6 months.

Maternal immunisation status may not be significant

c. Toxoplasma (Level 1)

If IgM is present in baby's blood up to 6 months of age, this indicates a congenital Toxoplasma infection.

d. Syphilis (Level 1)

Serology can be carried out at any time. Maternal screening is no longer carried out. The implications on the family need to be considered carefully prior to requesting this test.

5. Ophthalmology^{32,33,34,35,36} (Level 1)

40% of children with permanent congenital hearing impairment have ophthalmic conditions. Eye problems may include non-specific problems of squint and refractive errors. In some children the eye examination may help to make or clarify a diagnosis such as CHARGE association, Usher syndrome or congenital CMV or Rubella.

- All children should be offered referral for detailed assessment by a paediatric ophthalmologist at the time of diagnosis to ensure correct visual acuity and to exclude associated pathology.
- The timing of further assessments is detailed in Vision Care for Deaf Children and Young People, NDCS/Sense Quality Standards 2004³⁵

Always ask about any visual problems at follow-up visits

6. Blood tests (Level 2)

It may not be possible to obtain large amounts of blood from a small baby and it must be remembered that some of these tests may have been carried out as part of general paediatric management

a. Haematology

Full blood count, haemoglobinopathy screening and ESR rarely provide answers to the cause of a hearing loss, so these tests should carry very low priority

b. Biochemistry

Urea and electrolytes and **serum creatinine** may be useful to assess renal function when the child is older if conditions like Alport or Alstrom syndromes are suspected

Thyroid function: Check the outcome of Neonatal Blood Spot before requesting tests for Congenital Hypothyroidism.

7. Urine examination^{37,38} (Level 1)

Dipstick for blood and protein: can be done easily. This may not rule out Alport as the renal symptoms and signs may develop later and haematuria can be intermittent.

Metabolic Screen: may be useful as part of a wider search for a cause when a metabolic condition is suspected or where there is faltering growth or developmental delay.

Explaining the results of the investigations, the interpretation and making an aetiological diagnosis at the appropriate time is the responsibility of the doctor. Parents must be given adequate information in oral and written format, through an interpreter if necessary, so that they can understand the reasons for carrying out the investigations, advantages, disadvantages and possible outcomes.

These guidelines must be reviewed regularly as new evidence may emerge which may lead to a change in practice

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