Royal Devon University Healthcare NHS Foundation Trust

Congenital Cytomegalovirus (cCMV)

Reference Number: RDF1722-23
Date of Response: 15/08/23

Further to your Freedom of Information Act request, please find the Trust's response(s) below:

Please be aware that the Royal Devon University Healthcare NHS Foundation Trust (Royal Devon) has existed since 1st April 2022 following the integration of the Northern Devon Healthcare NHS Trust (known as Northern Services) and the Royal Devon and Exeter NHS Foundation Trust (known as Eastern Services).

Dear Royal Devon University Healthcare NHS Foundation Trust,

The purpose of this FOI request is to ascertain your Trust's approach to screening for and treating congenital cytomegalovirus (cCMV).

If it is not possible to provide the exact information requested, please supply the underlying information in narrative form or whichever format you have available.

Definitions of acronyms and terms used in the FOI request:

- *CMV: cytomegalovirus*
- *cCMV: congenital cytomegalovirus*
- *SNHL: sensorineural hearing loss*
- *'Practices' refers to any standard operating procedures or clinical protocols, guidelines, practices or pathways.*
- *'Information' refers to any recorded information required to be disclosed in response to requests under the Freedom of Information Act.*

If different hospitals or services within your Trust have different Practices or data availability, please provide separate Information or data for each hospital or service (indicating clearly which hospital or service the Information relates to).

Q1. Please provide copies of any Information containing or evidencing Practices used within your Trust whereby newborns who are referred to audiology following their newborn hearing screening test, or newborns/children who demonstrate abnormal hearing at a later stage, are tested for cCMV. Such Practices could include, but are not limited to, early cCMV detection pathways whereby newborns are tested at point of referral to audiology from the newborn hearing screening programme.
Please include details about the intended timescales for testing, carrying out tests and returning test results, if this information is recorded.
Answer: Royal Devon's (RDUH) Eastern Services; Current practice to date: all babies identified with permanent sensorineural hearing loss are referred for paediatric assessment to understand the aetiology of their hearing loss.
Babies under 6 months are prioritised into reserved urgent clinic slots to stream line this process.

At the point of paediatric review urine samples are sent for CMV PCR testing and consent form signed to check the centrally held newborn blood spot card for confirmation of diagnosis as needed as per our local trust guideline on cCMV in newborns.

In older children who will no longer be excreting CMV, reliance is on Guthrie card testing +/- maternal serology to confirm or exclude diagnosis
Turn around for virology samples in the local lab is usually around a week but can be variable over bank holidays.

There is no current practice of national screening for CMV at birth to enable early pick up of CMV within 28 days.

There is no current national support to screen babies for CMV at the time of 'No clear response' on national hearing screen via salivary CMV PCR testing but we at the RDUHT implementing a pilot program to introduce this, alongside Imperial College Hospital, as the most effective means of identifying Congenital CMV within the recommended 28 day treatment window. This is a practice used in other areas of the world but has not been adopted nationally in the UK

Q2. If your Trust does employ Practices whereby newborns/children with abnormal hearing are tested for cCMV, please indicate at which stage samples are taken (you may select more than one):

- *By the newborn hearing screener at the point of referral*
- *By the audiologist at the first appointment after babies have been referred from the newborn hearing screen*
- *By the audiologist at detection of SNHL in a baby referred from the newborn hearing screen*
- *By another healthcare professional (not an audiologist) following detection of SNHL in a baby referred from the newborn hearing screen*
- *At detection of SNHL in older babies and children (i.e. after the newborn hearing screening and testing period)*
- *Unknown*
- *Other, please provide details:*

Answer: Royal Devon's Eastern Services; we do not currently have a practice whereby audiology consent and tests babies directly for CMV at the point of confirmation of hearing loss. Rather at the point of confirmation of hearing loss (usually the second audiology appointment) referral is made for Paediatric assessment and request is made for a urine sample to be brought to that appointment. Consent for testing is taken at that appointment and sample sent.

Testing for older children relies on retrieving the stored Guthrie card at the point of Paediatric assessment with consent form signed and request posted/emailed.

In 2023 we are starting a pilot of salivary CMV testing by the Newborn screening team at the point of first 'No clear response' at the newborn hearing screening, as outlined above.

Q3. If your Trust does employ Practices whereby newborns/children with abnormal hearing are tested for cCMV, please indicate what type of sample is taken (you may select more than one):

- *Saliva swab*
- *Urine*
- *Blood test for the infant*
- *Blood test for the mother*
- *Infant blood spot (Guthrie) card testing*
- *Unknown*
- *Other, please provide details:*

Answer: Royal Devon's Eastern Services; currently urine sampling for CMV PCR with 3 samples to diagnose/ exclude CMV.

With the move to screener testing we are introducing salivary PCR testing. If positive an urgent referral will be sent to paediatrics and a urine sample will be sent to test for CMV for confirmation, blood sent for CMV PCR and newborn blood spot referred for CMV testing if no other samples are available from the first 21 days of life. Very occasionally maternal antibody testing can be useful in older children and/or when Guthrie not available although can be inconclusive.

Q4. Please provide copies of any Information containing or evidencing Practices used within your Trust whereby children under the age of five are tested for cCMV as part of investigations of symptoms (in either the mother or child) that are unrelated to hearing. These could include:

Maternal symptoms of CMV (flu-like symptoms) Symptoms of congenital infection identified before or after birth, such as:

- *Antenatal abnormalities e.g. on ultrasound scan*
- *Characteristic rashes caused by cCMV (petechiae or blueberry muffin rash)*
- *Intrauterine Growth Restriction*
- *Microcephaly*
- *Jaundice*
- *Hepatosplenomegaly*
- *Neonatal visual signs/symptoms*
- *Neonatal seizures*

Symptoms of congenital infection in older children, such as:

- *Neurodevelopmental delays*
- *Special educational needs and disabilities (e.g. autism, ADHD)*
- *Cerebral palsy*
- *Seizures*
- *Visual or sensory impairment*

Answer: Royal Devon's Eastern Services; in our Trust, as advised by neonates and paediatrics, Infants who present with classical features of CMV (eg rash/ hepatosplenomegaly/ microcephaly) are tested for congenital CMV using Urine CMV sampling +/- imaging as appropriate, with management following the local Guidelines for Diagnosis and Management of CMV.
All babies with conjugated hyperbilirubinaemia will be tested for congenital infections including CMV routinely following local guidelines for management of Jaundice in Neonates.
Not all babies with IUGR are currently tested for CMV but are considered on a case by case basis. This has been addressed in more detail in our 2023 cCMV guideline.

In our trust, as advised by community paediatrics, neurodisabiltiy team and epilespy team Children with neurodevelopmental delay/ autism/ ADHD/ cerebral palsy/

seizures or visual impairment are not **routinely** tested for CMV, but investigations will be directed by the individual history and examination findings, +/- imaging findings where deemed clinically appropriate.

Q5. Please provide copies of any Information containing or evidencing Practices used within your Trust following a diagnosis of cCMV in children under the age of five. This could include, but is not limited to:

- *Information about any Practices involving the prescribing of antiviral treatments*
- *Details of the department(s) that the children would be referred to*

Answer: Royal Devon's Eastern Services; please see attached the updated RDUH Guideline for diagnosis and management of congenital CMV and its previous version, as well as the Bristol regional cCMV guideline and the more recent South West neonatal network cCMV guideline, all of which outline our practice. Please note the varying dates of introduction of these guidelines in relation to the timing of the FOI data.

All acutely unwell neonates diagnosed with congenital CMV in RDUH Eastern are referred to our local lead for infectious diseases and discussed with the Bristol regional paediatric infectious diseases team to guide decisions around antiviral therapy. See local guidelines for management of CMV as regard to the pathway on investigations, management and follow up. All infants will be referred for audiology follow up as per national audiology CMV guidance.

In infants in RDUH Eastern who are identified by 'No clear response' on National hearing screen within the treatment window for antiviral therapy are referred for further investigations including blood tests, ophthalmology testing and cranial imaging and referred to our local lead for infectious diseases and discussed with the Bristol regional paediatric infectious diseases team to guide decisions around antiviral therapy. Management decisions relating to treatment and follow up follow the Guidelines available and cases are managed on a case by case basis in discussion with the tertiary team, Bristol paediatric infectious disease.

All children identified with CMV will have regular hearing testing as per guidance and will be offered regular Neurodevelopmental follow up as appropriate to their needs, with regular monitoring of head circumference in infancy.

Questions 6-11 relate to the provision of data for a specific five-year period. If you do not hold data for this time period, please supply data for any period for which you have available data (preferably a recent five-year period) and specify the beginning and end dates. Please indicate if the relevant hospitals or services within your Trust have changed during this time.

Q6. Between 1 January 2018 and 31 December 2022, how many children were diagnosed with cCMV within 28 days of birth, within your Trust? This should include children born outside of your Trust who were diagnosed by services within your Trust.

Answer: Royal Devon's (Eastern & Northern services) data from October 2020 to December 2022:

- ≤5 cases identified who presented with clinical symptoms
- Nil cases identified via newborn hearing screening pathway

In accordance with Section 40 (2) of the Freedom of Information Act 2000, we are unable to provide figures where the number of patients is less than or equal to five and

could risk the identification of those patients and breach Caldicott principles. In these cases ≤5 is used to indicate that a figure between 1 and 5 is being suppressed.

This follows NHS Digital (formerly HSCIC) analysis guidance (2014) which states that small numbers within local authorities, wards, postcode districts, CCG's providers and Trusts may allow identification of patients and should not be published.

The Trust has considered your request for information from January 2018 to October 2020, however to provide you with the information requested would require the manual extraction and manipulation of information from various sources. To carry out this work would exceed the appropriate cost limit as set out in Section 12 (1) of the Freedom of Information Act 2000 and is therefore exempt.

Under the Freedom of Information Act 2000 Section 12 (1) and defined in the Freedom of Information and Data Protection (Appropriate Limit and Fees) Regulations 2004, a public authority is not obliged to comply with a request for information if it estimates that the cost of complying would exceed the appropriate limit. The limit of £450 represents the estimated cost of one person spending two and a half days in determining whether the Trust holds the information, locating, retrieving and extracting that information.

Q7. Of the children who were diagnosed with cCMV within 28 days of birth in this time period (Q6), how many:

a. Previously had a newborn hearing screening test
b. Had been referred to audiology following their newborn hearing screening test
c. Were given antiviral treatment for cCMV following diagnosis

Answer: Please see below.

a) ≤5 had had their screening test prior to diagnosis - if an infant is clinically unwell on neonates hearing screening is deferred as per guidelines.
b) Not Applicable.
c) ≤5 out of the ≤5 received antivirals. ≤5 were fully investigated but after discussion with tertiary care the decision was there was no indication to treat.

Q8. Between 1 January 2018 and 31 December 2022, how many children were diagnosed with cCMV between 28 days and 3 months of age, within your Trust? This should include children born outside of your Trust who were diagnosed by services within your Trust.

Answer: For Royal Devon's Eastern Services; October 2020 to December 2022:

- Nil cases identified who presented with clinical symptoms
- Nil cases identified via newborn hearing screening pathway

Please note this data is obtained from CMV results completed by our local laboratory. It does not capture infants/ children who were diagnosed with cCMV only on newborn blood spot by other practitioners.

The Trust has considered your request for information from January 2018 to October 2020, however to provide you with the information requested would require the manual extraction and manipulation of information from various sources. To carry out this work would exceed the appropriate cost limit as set out in Section 12 (1) of the Freedom of Information Act 2000 and is therefore exempt.

Q9. Of the children who were diagnosed with cCMV between 28 days and 3 months of age in this time period (Q8), how many:

a. *Previously had a newborn hearing screening test*
b. *Had been referred to audiology following their newborn hearing screening test*
c. *Were given antiviral treatment for cCMV following diagnosis*

Answer: Not applicable, see response to question 8.

Q10. Between 1 January 2018 and 31 December 2022, how many children were diagnosed with cCMV between 3 months and 5 years of age, across your Trust? This should include children born outside of your Trust who were diagnosed by services within your Trust.

Answer: From October 2020 to December 2022; please note this data is obtained from CMV results completed by our local laboratory. It does not capture infants/ children who were diagnosed with cCMV only on newborn blood spot.

- Nil cases identified who presented with clinical symptoms
- Nil cases identified via newborn hearing screening pathway

The Trust has considered your request for information from January 2018 to October 2020, however to provide you with the information requested would require the manual extraction and manipulation of information from various sources. To carry out this work would exceed the appropriate cost limit as set out in Section 12 (1) of the Freedom of Information Act 2000 and is therefore exempt.

Q11. Of the children who were diagnosed with cCMV between 3 months and 5 years of age in this time period (Q10), how many:

a. *Previously had a newborn hearing screening test*
b. *Had been referred to audiology following their newborn hearing screening test*
c. *Were given antiviral treatment for cCMV following diagnosis*

Answer: Royal Devon's Eastern Services; of the ≤5 cases identified via Newborn Hearing screen or Audiology referrals:

a) ≤5 had had a newborn hearing screen
b) ≤5 out of ≤5 had 'no clear response/s on screening' on one or both ears so were referred to audiology. ≤5 out of ≤5 had clear response/s on screen so not referred.
c) ≤5 out of ≤5 were treated with antivirals as per our local and regional guideline and in discussion with our regional centre. ≤5 of the ≤5 were recruited to the toddler valganciclovir study.

Royal Devon University Healthcare NHS Foundation Trust

Standard Operating procedure for a Quality improvement project to improve early identification of Congenital Cytomegalovirus (cCMV) infection in babies who demonstrate 'no clear response' on their Newborn hearing screen

Post holder responsible for Procedural Document	
Author of Standard Operating Procedure	[redacted] Staff Grade Paediatrician
Division/ Department responsible for Procedural Document	Paediatric department/ Audiology
Contact details	[redacted]
Date of original standard operating procedure	01/06/ 2023
Impact Assessment performed	
Approving body and date approved	*Paediatric governance and Neonatal governance*
Review date (and frequency of further reviews)	*01/09/2023, then annually*
Expiry date	*Up to 5 years from the date the document became live.*
Date document becomes live	*Date document is published, circulated & put onto the trust intranet*

Please *specify* standard/criterion numbers and tick ✓ other boxes as appropriate

Monitoring Information		**Strategic Directions – Key Milestones**	
Patient Experience	**Yes**	Maintain Operational Service Delivery	
Assurance Framework		Integrated Community Pathways	
Monitor/Finance/Performance		Develop Acute Services	
CQC Fundamental Standards Regulations No:		Delivery of Care Closer to Home	
		Infection Control	
Other *(please specify)*:	European consensus on management of cCMV -recommendation		
Note: This document has been assessed for any equality, diversity or human rights implications			

Full History		Status: Draft	
Version	Date	Author (Title not name)	Reason
1.0	01/ 06 /2023	Paediatric Staff Grade	Quality improvement project to meet recommended standards as laid out in European Consensus on management of cCMV document and to improve early pick up of cCMV

Associated Trust Policies/ Procedural documents:	Guideline for management of Congenital CMV
Key Words:	Congenital Cytomegalovirus (cCMV) Sensorineural hearing loss (SNHL) Newborn hearing screening program (NHSP)
In consultation with and date: Ongoing focus group meetings 2023 Paediatric lead for Aetiology of Hearing loss, Exeter [redacted] NHSP Lead: [redacted] Paediatric Audiology Leads in Exeter CHIME and North Devon, [redacted] (CHIME), [redacted] (ND) Paediatric lead for Aetiology of hearing loss North Devon, [redacted] Microbiology [redacted] Paediatric Infectious disease local lead [redacted] Neonatology (Eastern) [redacted] In addition: Imperial College trust Pilot CMV testing team led by [redacted] and [redacted] Neonatal team RDUH Radiology and Opthalmology RDU and North Devon	
Contact for Review:	[redacted]

Royal Devon University Healthcare NHS Foundation Trust

CONTENTS

KEY POINTS OF THIS PROCEDURAL DOCUMENT:

This document covers the practical aspects of the quality improvement project to achieve early identification of Congenital Cytomegalovirus (cCMV) infection in babies who demonstrate 'no clear response' on their Newborn hearing screen. Our aim is to identify cCMV when present within the 28 day treatment window where possible. This allows for the opportunity to meet with the family and offer investigations to guide decisions about antiviral treatment where appropriate and provide a better patient/ family experience around any diagnosis of cCMV.

The guidance includes neonates > 34 weeks gestation who have no clear responses on the Newborn Hearing Screen program (NHSP). Current targets for NHSP are completion of screening within 4 weeks of birth.

This protocol will cover:

- The taking of the swabs, when and by whom
- Audiological pathway on identification of CMV
- Pathway of samples once taken and directing of results
- Notification of results of screening to both parent and primary care routinely via Audiology Individual management plans
- Clinical management of babies identified has having CMV on screening

This is a joint policy produced and to be used by Newborn hearing screening and paediatric audiology referring into Paediatric infectious disease services over Exeter and North Devon sites.

The aim is to identify cCMV when present before 28 days so that an informed discussion can be had with families to guide further management and allow antiviral therapy to started within the recommended window if appropriate.

1. INTRODUCTION

CMV is a common virus that can affect people of all ages. Most healthy adults and children who become infected show no signs or symptoms and have no long-term effects. However, if CMV is contracted during pregnancy the virus poses risk to the developing baby in the womb (1). Congenital CMV (cCMV) is used to describe CMV that is contracted before birth. Although the majority of neonates with cCMV are asymptomatic, 10-15% of neonates may develop neurological complications later, including onset or progression of sensorineural hearing loss. Sensorineural hearing loss can be bilateral, unilateral, late onset and/or progressive and can be the only marker of cCMV to allow early identification and possible treatment.

Treatment is available for cCMV which may slow the progress of the virus, and may prevent progression of hearing loss, if initiated within the first 4 weeks of life (2). We currently have no evidence that treatment is effective after that time,

We have worked in alliance with our colleagues in Imperial College Hospital Trust to institute a change in practice to allow earlier identification of babies with possible cCMV presenting with sensorineural hearing loss. Current practice leads to identification outside of the treatment window.

We recommend that a salivary swab for cCMV should be offered to all babies who show no clear response on their hearing screening in either or both ears. The CMV swab should be offered at the first appointment where results are indicative of possible sensorineural hearing loss. This swab is sent to virology to be analysed to determine whether CMV is present. If a baby has confirmed cCMV, treatment options will be discussed with the family by the Paediatric team in liaison with our infectious disease lead as detailed below.

Newborn hearing screening programme (NHSP)

The Newborn hearing screening programme (NHSP) offers a hearing screen to all babies born in the UK, and aims to detect permanent hearing loss in the first weeks of life (3/4). To be eligible for hearing screening under national guidance babies must be well and greater or equal to 34 weeks gestation (3). Early detection of hearing loss allows for early intervention to maximise the development of speech, language and communication. In the UK, 1 to 2 in 1000 babies is born with a permanent hearing loss in one or both ears. This increases to 1 in 100 babies who have spent more than 48 hours in intensive care. Congenital hearing loss can be caused by congenital infections. Well babies are not routinely offered a screen for CMV. If a baby has confirmed sensorineural hearing loss identified through newborn screening current National guidance is that testing for cCMV should occur ‘as soon as possible’. Current local established practice of referring to Paediatrics after confirmation of hearing loss at subsequent formal audiological testing is missing the opportunity for identification within the treatment window, outside of which treatment is not yet proven to be effective (5). There is a drive within many centres, including our own in close collaboration with Imperial College Hospital trust to improve service delivery through salivary screening at the time of Newborn screening – we aim to collect data to support a National change of practice

2 PURPOSE

We propose to offer targeted cCMV testing at the point of No clear response on hearing screen at the Newborn hearing screening appointment, with the aim to identify cCMV within the 28 day window where possible. This allows for the opportunity to meet with the family and offer investigations to guide decisions about antiviral treatment where appropriate and provide a better patient/ family experience around diagnosis of cCMV.

3 DEFINITIONS

Congenital infection – infection acquired in utero

Newborn Hearing screening programme – National screening programme to identify hearing loss.

Congenital CMV- Virologically confirmed CMV within 21 days of life

4 STANDARD OPERATING PROCEEDURE: for a quality improvement project to improve earlier identification of congenital CMV via Targeted testing of babies who demonstrate 'no clear response' on their Newborn hearing screen at the screening appointment

Facilities, equipment & special supplies
• Swabs, tubes and specimen bags • Gloves • Hand sanitizing gel • Patient information leaflets

Calibration
No calibration is needed to take a swab.

Quality control
Staff trained and competent to perform the procedure (led by [redacted]). Laboratory testing for salivary swabs for CMV to be validated as per standards prior to issuing of local results (led by [redacted]) Audit of results ([redacted])

Environmental & safety controls
Royal Devon University Healthcare NHS Trust and local policies on hand hygiene and infection control must be followed at all times (6)

4.1 Guidance for Screeners

A salivary swab will be offered for any baby with no clear responses identified on hearing screening, before being referred to Paediatric Audiology for further audiological testing

All screeners will be offered training on how to swab effectively including advice about infection control and safety, prior to taking on the role.

Prior to taking the salivary swab, the screener will give the baby's parent/guardian the information leaflet on Cytomegalovirus infection (see patient leaflet Congenital CMV and Hearing loss – Appendix A).

Explanation should be as follows 'I would like to test your baby for a common virus called CMV, which may affect a baby's hearing. It is important to test for CMV, as treatment with antivirals is available. We can go into more detail if the test results are positive. If the result is positive, you will be contacted by the clinical team by telephone and an appointment for confirmatory testing will be offered. If the result is negative you will be updated by a member of the audiology team within your Individual management plan letter. The test involves putting a small cotton swab in your baby's mouth for up to 60 seconds'. 'The screener will then obtain verbal parental consent for the targeted screen and taking of the salivary swab for cCMV infection. Once the parent has given the consent, the screener can take the salivary swab.

CMV salivary swab packs. These can be prepared in advance and will be provided by Microbiology. They include a Viral swab (initially 2 samples during verification phase in first 12 months) which will need labelled with patient details, a completed form with request identifying 'healthy baby, Newborn screening sample' and a sealable plastic specimen bag. The items are available from microbiology. ***Check the expiry date of the swab to ensure it is in date before use.***

Details of whether the parent/carer accepted or declined the CMV swab should be recorded and included in the referral to Audiology.

Results: The results of the CMV swab can take up to 5 days but may be quicker If the result is positive then the microbiologist will liaise directly with the team agreed, including our Infectious disease lead [redacted], our local Paediatric leads for aetiology of hearing loss [redacted] (Exeter) ad[redacted] (North Devon) and we will be in contact with the family by telephone to arrange a face to face review and appropriate assessments

As a second check all results will be collated in the hearing screening database and any unactioned positive results highlighted to the medical team. The Audiology teams in both Exeter and North Devon will chase results and give written feedback to parents of the result of their babies swab on the Individual audiology action plan. If there is any uncertainty that the result has not been seen or actioned then they will again contact the team.

4.2 Method of taking salivary swab: note during the first 12 month verification period only, 2 swabs will be tested concurrently for lab verification – we will inform screeners when this period is complete

- In a breast-fed baby the swab has to be taken between feeds with an interval of at least one hour, ideally 2 hours. In a bottle-fed baby no visible milk should be seen in the mouth but there is no time limit
- Place the dry swab in the baby's mouth, at the corners of the mouth or under the tongue, resting the swab for as close to a minute as possible until the lower third of the swab is saturated
- You can try to collect for the full 60 seconds at once, or collect in intervals by re-introducing the swab into the mouth as needed (60 seconds total).
- Once the swab of saliva is taken from the baby's mouth, the swab stick may be broken or cut so that it will fit into the tube.
- Enter the baby's details and the date of the sample into EPIC, or on paper form provided. Place the test request for Salivary CMV PCR, with clinical information eg 'Healthy baby , No clear response on newborn hearing screen', print sticker and label sample. (Ensure saliva rather than urine is emphasised as sample type). Seal swab in specimen bag
- Place Sample into internal pod delivery in hospital, or post via internal courier which would arrive the following day. From North Devon it will be forwarded to Exeter Microbiology lab automatically. The sample does not degrade overnight/ over weekend so does not require special storage.

Taking the swab

Swabs should be taken at least 1 hour after breastfeeding, ideally 2 hours. Ensure one hour has passed since the baby was last breastfed and wait if necessary.

Please wear gloves to take a salvia swab.

Swabs, tubes and specimen bags. Please see figure 1.

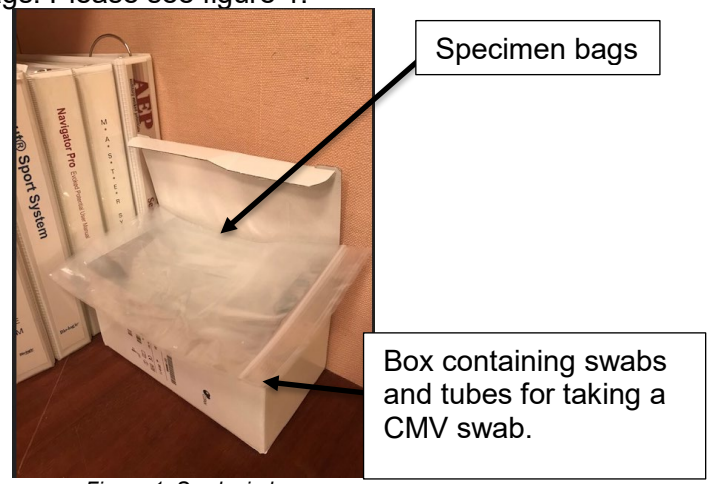

Figure 1: Swabs in box

Take a swab from the box and remove it from the plastic packaging (figure 2).

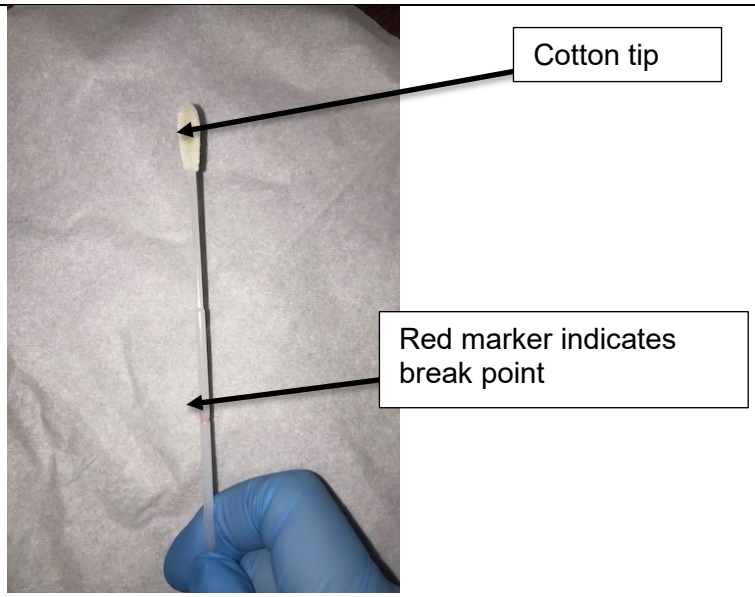

Figure 2: Swab with cotton tip

Gently place the cotton end of the swab into the baby's mouth between their gum and cheek. Allow the baby to 'chew' on the cotton tip for up to one minute until the swab looks wet all over.

When saturated remove the swab from the baby's mouth and carefully snap the swab at the red marker in the middle. Then please the cotton swab into the tube so that the cotton part is in the fluid. (Some viral tubes can be green or yellow-topped) Please see figure 3.

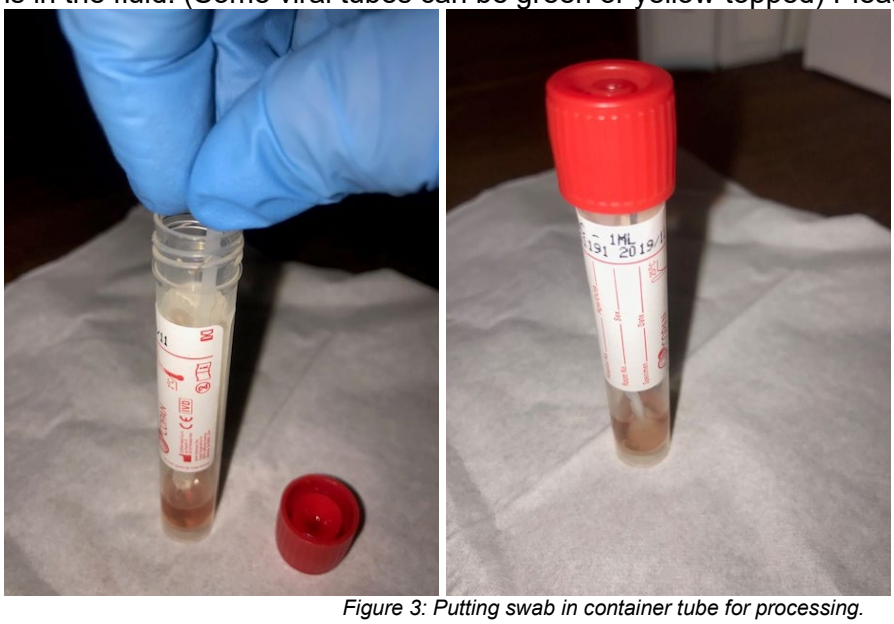

Figure 3: Putting swab in container tube for processing.

Ensure the patient's name and MRN is written on the test tube with the date. Place the sealed tube containing the swab into the specimen bag and seal the bag.

Figure 4: Swab tube in specimen bag.

Ensure you have the correct contact details for the parents and inform them that if the result is positive they will be contacted by a member of the clinical team. This is usually within 2-5 working days. Finish the appointment.

Royal Devon University Healthcare NHS Foundation Trust

4.3 Flowchart of RDUH cCMV salivary screening at newborn hearing screen for infants >34 weeks gestation with 'no clear response'

Patient education on program during pregnancy alongside information on newborn hearing screening

- Verbal and written information given during antenatal care

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Newborn hearing screen appointment: 'no clear response' in either or both ears.
Action by screener:

1. Patient information leaflet given out and procedure discussed prior to taking swab
2. Salivary virology sample taken and sent to microbiology lab (Eastern) to test for CMV PCR
3. For duration of pilot 2 salivary samples required for test validation purposes
4. Referral to audiology
5. Above action documented in newborn hearing screening database including if declined

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CMV PCR salivary testing and dissemination of results

1. Tests salivary sample for CMV PCR
2. For the duration of the pilot the second salivary sample is sent away for second testing
3. CMV PCR result sent to 'CMV result Epic inbox' where a list of named users will be able to review the result from the following departments: paediatrics; newborn hearing screening; audiology; neonatology

↙ ↘

Positive CMV result

- Paediatrician will notify parent/ guardian by phone and organise urgent face to face appointment for medical assessment and further testing as per CMV guideline
- Audiology will ensure prompt assessment
- Newborn hearing screeners will add result to newborn hearing screen database

Negative CMV result

- Parent/ guardian will be notified by audiologist at audiology appointment and result will be given in standard audiology letter
- If hearing loss confirmed to follow usual pathways including referral for paediatric medical assessment
- If normal audiology assessment discharge

4.4 Audiology outcome following (cCMV) screen for Babies Referred From NHSP

Result documentation: The audiology team will check at the first diagnostic ABR appointment whether a salivary sample was taken. They will include documentation within the Individual management plans whether sample positive, negative, missed or Consent withheld. If a positive result noted and not clear on EPIC that the medical team are aware then they will contact the joint team directly via EPIC – [redacted], [redacted] and [redacted]. If no sample was taken and consent given then a salivary test is offered at that point and NHSP Lead informed.

Babies with negative CMV salivary screen and who have normal results on Auditory Brainstem Response (ABR) will be discharged (False positive screen)

Babies with no evidence of cCMV on screening and who have a conductive hearing loss on ABR, will be managed as per the departments audiological protocol.

Where there is POSITIVE evidence of cCMV on screening and normal results on ABR, these cases will be alerted via EPIC to the Paediatric Senior Doctor team. An appointment will be placed with [redacted] via EPIC referral basket. For a baby whose test was taken >3 weeks old, the Guthrie card will be checked for cCMV to confirm whether this is congenital or acquired infection. Appendix B Assessment and discussion will be made as to whether further investigations and treatment are required. Hearing will be monitored routinely until 5 years old as per established hearing pathways for infants with cCMV.
For babies with POSITIVE evidence of cCMV on the salivary swab and abnormal results on ABR, the result will be alerted via EPIC to the Paediatric Senior Doctor team who will be in contact with the family. A consultation will be arranged with the Consultant for Paediatric Infectious Diseases, currently [redacted], to discuss results, arrange further investigations and discuss management options including possible antiviral treatment. This should happen automatically via EPIC basket. Where possible this would be a joint appointment with [redacted] to discuss the wider implications of hearing loss and potential cochlear implantation if appropriate but this can be offered routinely at a later date if not feasable

Where there is NO evidence of cCMV on screening, but babies have a suspected or confirmed sensorineural hearing loss on ABR testing, these cases will be referred to [redacted], Paediatric lead for aetiology of hearing loss, or [redacted], North Devon lead as per current practice. During the verification period a repeat CMV test will be taken. Please refer using EPIC referral system, with Email to [redacted] and secretary as backup. Hearing will continue to be monitored routinely and managed as per current audiology protocols

5 ARCHIVING ARRANGEMENTS

The original of this SOP, will remain with the author [redacted], ***Paediatric Staff grade*** An electronic copy will be maintained on the Trust intranet, P – Policies. Archived electronic copies will be stored on the Trust's "archived policies" shared drive, and will be held indefinitely.

6 PROCESS FOR MONITORING COMPLIANCE WITH AND EFFECTIVENESS OF THE STANDARD OPERATING PROCEDURE/ GUIDELINE

To evidence compliance with this policy, the following elements will be monitored:

Area to be monitored	Methodology	Target	Responsible	Reported to	Frequency
Local Standard: All babies identified as having no clear response on the newborn hearing screening pathway should have a salivary swab for CMV offered within 4 weeks of life	Audit		NHSP lead [redacted]	CHSWG	Annually
Local Standard: All babies with cCMV in the neonatal period (1st 28 days) and hearing loss should have a definitive management decision within 4 weeks of first positive CMV result with treatment commenced as clinically indicated.	Audit		[redacted]		Annually
Audit point:Time taken for action on positive swab results	Audit		[redacted]		Annually

Audit Point: Number of cases of positive CMV diagnosis identified, and number of cases identified with CMV who do not have confirmed permanent hearing loss on AABR in neonatal period	Audit		[redacted]		Annually

References	
1.	CMV Action. The basics about the virus. 2021. Available at: https://cmvaction.org.uk/what-cmv/basics-about-virus [accessed on 26/06/2021].
2	Vossen et al. Congenital cytomegalovirus. A European expert consensus statement on diagnosis and management. https://journals.lww.com/pidj/Fulltext/2017/12000/Congenital_Cytomegalovirus__A_European_Expert.28.aspx
3	NHS England guidance for newborn hearing screening. Last updated September 2021. lhttp://www.gov.uk/government/publications/newborn-hearing-screening-programme-nhsp-operational-guidance/6-patient-journey-from-screen-to-referral
4	Newborn hearing screening-Your pregnancy and baby guide. 2018. Available at: https://www.nhs.uk/conditions/pregnancy-and-baby/newborn-hearing-test/ [accessed on 28/05/2021].
5	Toddler valganciclovir study – Results not yet published but data available and no benefit of treatment established in infants >28days-4yrs (verbal report from study leads – publication awaited
6	Royal Devon University Healthcare trust, Hand hygiene policy (Available via the Hub)
7	Diagnosis and management of Congenital CMV – Royal Devon and Exeter Guidance, (available on the Trust Hub)

Royal Devon University Healthcare NHS Foundation Trust

APPENDIX A: COMMUNICATION PLAN

Royal Devon University Healthcare NHS Foundation Trust

The following action plan will be enacted once the document has gone live.

Staff groups that need to have knowledge of the guideline/SOP	*Newborn screening Team led by [redacted], Microbiology* *Paediatric Audiology – Exeter and North Devon teams* *Paediatric lead for infectious disease – [redacted]* *Paediatric leads for aetiology of Hearing loss in Exeter and North Devon [redacted] and [redacted]* *Neonatal team Exeter* *Neonatology (Eastern)- [redacted]*
The key changes if a revised document	*N/A*
The key objectives	*Early identification of cCMV to allow for early discussion and if appropriate early treatment with antiviral therapy within the 28 day window with the hope of improving long term outcomes*
How new staff will be made aware of the procedure/guideline and manager action	*Ongoing handover within Newborn screening team, Audiology and Paediatric teams* *Royal Devon University Hospital trust guideline for management of Neonatal CMV (7).*
Specific Issues to be raised with staff	*Importance of chasing and sharing of results* *Awareness of the anxiety caused by a diagnosis of congenital CMV when delivering results – however balanced against the significant benefits of early diagnosis*
Training available to staff	*Training will be available for the screening team and delivered internally with video support*
Any other requirements	
Issues following Equality Impact Assessment (if any)	*N/A*

Royal Devon University Healthcare NHS Foundation Trust

Location of hard / electronic copy of the document etc.	[redacted] *Governance team*

APPENDIX X: EQUALITY IMPACT ASSESSMENT TOOL

Name of document	Standard Operating procedure for a Quality improvement project to improve early identification of Congenital Cytomegalovirus (cCMV) infection in babies who demonstrate 'no clear response' on their Newborn hearing screen
Division/Directorate and service area	Child and Woman's health
Name, job title and contact details of person completing the assessment	[redacted], Paediatric SAS grade doctor and lead for Aetiology of hearing loss
Date completed:	

The purpose of this tool is to:

- **identify** the equality issues related to a policy, procedure or strategy
- **summarise the work done** during the development of the document to reduce negative impacts or to maximise benefit
- **highlight unresolved issues** with the policy/procedure/strategy which cannot be removed but which will be monitored, and set out how this will be done.

1. What is the main purpose of this document?

We propose to offer targeted cCMV testing at the point of No clear response on hearing screen at the Newborn hearing screening appointment, with the aim to identify cCMV within the 28 day window where possible. This allows for the opportunity to meet with the family and offer investigations to guide decisions about antiviral treatment where appropriate and provide a better patient/ family experience around diagnosis of cCMV.

2. Who does it mainly affect? *(Please insert an "x" as appropriate:)*

Carers ☐ Staff ☒ Patients ☒ Other (please specify) Parents

3. Who might the policy have a 'differential' effect on, considering the "protected characteristics" below? (By *differential* we mean, for example that a policy may have a noticeably more positive or negative impact on a particular group e.g. it may be more beneficial for women than for men)

Please insert an "x" in the appropriate box *(x)*

Protected characteristic	Relevant	Not relevant

Age	☐	x☐
Disability	☐	x☐
Sex - *including: Transgender, and Pregnancy / Maternity*	☐	x☐
Race	☐	x
Religion / belief	☐	x☐
Sexual orientation – *including: Marriage / Civil Partnership*	☐	x☐

4. Apart from those with protected characteristics, which other groups in society might this document be particularly relevant to… (e.g. those affected by homelessness, bariatric patients, end of life patients, those with carers etc.)?

This testing will be offered to all patient groups
Babies born prematurely before the age that newborn hearing screening is felt to be a true guide of permenant hearing loss are therefore not elligable for early CMV targeting testing though this pathway. Discussions about how to identify CMV early in this group are on going but need to be guided by National Neonatal standards of care

5. Do you think the document meets our human rights obligations? ☒

Feel free to expand on any human rights considerations in question 6 below.

A quick guide to human rights:

- ***Fairness –*** *how have you made sure it treats everyone justly?*
- ***Respect –*** *how have you made sure it respects everyone as a person?*
- ***Equality –*** *how does it give everyone an equal chance to get whatever it is offering?*
- ***Dignity –*** *have you made sure it treats everyone with dignity?*
- ***Autonomy –*** *Does it enable people to make decisions for themselves?*

6. Looking back at questions 3, 4 and 5, can you summarise what has been done during the production of this document and your consultation process to support our equality / human rights / inclusion commitments?

1) *We aim to ensure testing is available to all patient groups and geographical areas inclusively. We are aware that Premature infants require special consideration but are currently out of the remit of this document due to Newborn hearing screening standards. We will encourage local Neonatal services to review CMV testing guidance in Premature infants*

2) *CMV action are an active National patient group keen to push forward with increased understanding of CMV for parents and earlier testing and are in support of this method of care. We have also listened to local feedback in support of earlier testing*

7. If you have noted any 'missed opportunities', or perhaps noted that there remains some concern about a potentially negative impact please note this below and how this will be monitored/addressed.

"Protected characteristic":	*See comments re Premature infants*
Issue:	
How is this going to be monitored/ addressed in the future:	
Group that will be responsible for ensuring this carried out:	

RDUH cCMV salivary screening at newborn hearing screen for infants >34 weeks gestation with 'no clear response': Quality improvement pilot program

Background

CMV is the commonest congenitally acquired infection and congenital CMV (cCMV) is a leading cause of sensorineural hearing loss in childhood. Kimberlin et al (2015) showed in an RCT that treatment of congenital CMV with 6 months of valaciclovir is beneficial if started prior to 28 days of life in terms of improved hearing and neurodevelopmental outcomes. This included infants whose only presenting feature of cCMV is sensorineural hearing loss. The national newborn hearing screening program screens all newborns in the first few weeks of life. If an infant has 'no clear response' the existing pathway is referral to audiology for formal testing and if hearing loss diagnosed referral to paediatrics for medical assessment for causes of hearing loss. However, this time window does not allow for diagnosis of cCMV within 28 days of life. Therefore, we propose a quality improvement pilot program to identify these infants earlier to allow time to start treatment with antivirals if indicated within 28 days. Salivary CMV screening at the point of 'no clear response' on newborn hearing screen has previously evaluated (Kadambari 2015) and shown to be feasible and successful. Whilst the national screening committee do not currently formally recommend national targeted screening; multiple centres across the UK are now implementing this to improve the quality of care for these infants (personal correspondence). The paediatric infectious diseases team at Imperial Hospital and the virology department at St Georges Hospital are implementing targeted salivary cCMV screening and at RDUH we have been working with these departments to introduce this locally.

Aim

To implement salivary CMV screening at the point of 'no clear response' at newborn hearing screen at the RDUH (Eastern and Northern) to facilitate earlier diagnosis of congenital CMV to allow for earlier antiviral treatment if indicated.

Methods

This is a multidisciplinary team project which has been planned by the following members of staff at RDUH:

Paediatrics- [redacted]

Newborn hearing screening program (NHSP)- [redacted]

Audiology (Eastern)- [redacted]

Audiology (Northern)- [redacted]

Microbiolgoy- [redacted]

Neonatology- [redacted]

The RDUH MDT is in liaison with the team the following teams who are implementing a similar pathway:

Paediatric Infectious Diseases team Imperial- [redacted]

Virology St Georges Hospital

The pathway has been written and agreed by the RDUH MDT from January 2023- current with monthly MDT meetings for detailed planning of pathway including educational program alongside

Flow chart of planned intervention: (for full plan see SOP and guideline in key documents)

Flowchart of RDUH cCMV salivary screening at newborn hearing screen for infants >34 weeks gestation with 'no clear response'

Patient education on program during pregnancy alongside information on newborn hearing screening

- Verbal and written information given during antenatal care

↓

Newborn hearing screen appointment: 'no clear response' in either or both ears. Action by screener:

1. Patient information leaflet given out and procedure discussed prior to taking swab
2. Salivary virology sample taken and sent to microbiology lab (Eastern) to test for CMV PCR
3. For duration of pilot 2 salivary samples required for test validation purposes
4. Referral to audiology
5. Above action documented in newborn hearing screening database including if declined

↓

CMV PCR salivary testing and dissemination of results

1. Tests salivary sample for CMV PCR
2. For the duration of the pilot the second salivary sample is sent away for second testing
3. CMV PCR result sent to 'CMV result Epic inbox' where a list of named users will be able to review the result from the following departments: paediatrics; newborn hearing screening; audiology; neonatology

↙ ↘

Positive CMV result

- Paediatrician will notify parent/ guardian by phone and organise urgent face to face appointment for medical assessment and further testing as per CMV guideline
- Audiology will ensure prompt assessment
- Newborn hearing screeners will add result to newborn hearing screen database

Negative CMV result

- Parent/ guardian will be notified by audiologist at audiology appointment and result will be given in standard audiology letter
- If hearing loss confirmed to follow usual pathways including referral for paediatric medical assessment
- If normal audiology assessment discharge

Key documents- please see the following

Standard operating procedure of targeted salivary cCMV screening

Guideline on management of cCMV

Education pack for newborn hearing screeners on how to take salivary samples

Patient information leaflet

Planned evaluation of the pilot project

The initial pilot will run for 12 months. 10 months into the pilot data of all infants screened and results and outcomes will be collated and written up in a report and presented. Audit against audit outcomes documented on SOP. This will be used to inform the continuation of the project.

References

Chung PK et al. Targeted screening for cCMV infection: clinical, audiological and neuroimaging findings. ADC Fetal and Neonatal Edition. 2023;108:F302-F308

Kimberlin DW, Jester PM, Sánchez PJ, Ahmed A, Arav-Boger R, Michaels MG et al. Valganciclovir for Symptomatic Congenital Cytomegalovirus Disease. Kimberlin DW et al. N Engl J Med 2015; 372(10): 993-943. doi: 10.1056/NEJMoa1404599

Kadambari et al. Evaluating the feasibility of integrating salivary testing for congenital CMV into the Newborn Hearing Screening Programme in the UK. Eur J Pediatr. 2015 Aug;174(8):1117-21. doi: 10.1007/s00431-015-2506-8. Epub 2015 Mar 7.

Shah T, Luck S, Sharland M, Kadambari S, Heath P, Lyall H. Fifteen-minute consultation: diagnosis and management of congenital CMV. Archives Disease inof Childhood Education and Practice volume 101, issue 5.

Hearing loss and congenital CMV infection: a systemic review. Goderis J et al. Pediatrics 2014 Nov; 134 (5): 972-982.

Bristol Royal Hospital for Children guidelines on congenital CMV

UK Standards for Microbiology Investigations, Investigation of cytomegalovirus infection. Public Health England. 28 (4).

The European Society for Pediatric Infectious Disease (ESPID). Congenital Cytomegalovirus. A European Expert Consensus Statement on Diagnosis and Management. The Pediatric Infectious Disease Journal 2017;36(12):1205-1213.

Flowchart of RDUH cCMV salivary screening at newborn hearing screen for infants >34 weeks gestation with 'no clear response'

Patient education CMV avoidance pregnancy alongside information on newborn hearing screening

- Verbal and written information given during antenatal care

↓

Newborn hearing screen appointment: 'no clear response' in either or both ears. Action by screener:

1. Patient information leaflet given out and procedure discussed prior to taking swab
2. Salivary virology sample taken and sent to microbiology lab (Eastern) to test for CMV PCR
3. For duration of pilot 2 salivary samples required for test validation purposes
4. Referral to audiology
5. Above action documented in newborn hearing screening database including if declined

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1. Tests salivary sample for CMV PCR
2. For the duration of the pilot the second salivary sample is sent away for second testing
3. CMV PCR result sent to 'CMV result Epic inbasket' where a list of named users will be able to review the result from the following departments: paediatrics; newborn hearing screening; audiology; neonatology

↙ ↘

Positive CMV result

- Paediatrician will notify parent/ guardian by phone and organise urgent face to face appointment for medical assessment and further testing as per CMV guideline
- Audiology will ensure prompt assessment
- Newborn hearing screeners will add result to newborn hearing screen database

Negative CMV result

- Parent/ guardian will be notified by audiologist at audiology appointment and result will be given in standard audiology letter
- If hearing loss confirmed to follow usual pathways including referral for paediatric medical assessment
- If normal audiology assessment discharge

Clinical Guideline for:
Diagnosis and Management of Congenital Cytomegalovirus (CMV) Infection

Summary

This guideline outlines the process of investigation, diagnosis and management of congenital CMV infection for use on the Neonatal Unit.

Key Points

1. Congenital CMV is the commonest congenitally acquired infection, and the estimated cause of approximately 25% of sensorineural hearing loss in childhood.
2. Only 5-10% will show symptoms at birth, and most will remain symptom free. However, 10-15% of those initially asymptomatic may develop complications later in life.
3. Congenital CMV is diagnosed from positive CMV PCR in the first 21 days of life from a salivary, urine or blood sample
4. If it the infant is older than 21 day of life the diagnosis can be made retrospectively using the newborn blood spot card taken from all infants at 5 days old
5. Diagnosis can be made antenatally using amniocentesis or fetal blood DNA PCR.
6. 6 months of treatment should be commenced if symptomatic with CNS or focal organ disease.
7. Please see Appendix 1 for quick reference diagnosis and management flow sheet.
8. Please see Appendix 2 for flow chart of cCMV screening at 'lack of clear response' at newborn hearing screen

CONTENTS

1 BACKGROUND

CMV is the commonest congenital infection, with an incidence of between 7 per 1000 live births. It can result from both primary and recurrent maternal infection.

Only 5-10% of infected babies show symptoms at birth, and most babies will remain symptom free. However, 10-15% of asymptomatic infants will develop complications later in life, particularly that of sensorineural deafness and developmental problems.

Congenital CMV infection is the leading cause of acquired sensorineural hearing loss, accounting for an estimated 25% of cases.

Early diagnosis is key, as treatment has been shown to improve symptoms, and the determination between congenital and acquired CMV is important, as management approaches will differ.

Intrauterine mother to infant transmission rate is 30-40% in primary disease. The risk to the infant is much lower with reactivation (~1%). Transmission of CMV may also be intrapartum, through vaginal secretions, or postnatal through breast milk, blood products or close personal contact.

2 PRESENTATION

Antenatal ultrasound features which may suggest cCMV

- Intrauterine growth restriction (IUGR)
- Ventricular dilatation
- Periventricular calcification
- Microcephaly

Neonatal features which may suggest cCMV

- Sensorineural hearing loss (can be present at birth, or later in life)
- Blueberry muffin rash
- Intrauterine growth restriction (IUGR)
- Microcephaly
- Hepatosplenomegaly
- Petechiae
- Jaundice
- Intracranial calcification
- Chorioretinitis
- Lymphadenopathy

Laboratory features most commonly found

- Conjugated hyperbilirubinaemia
- Thrombocytopaenia
- Elevated hepatic transaminases

Some symptoms can overlap with other congenital infections, in particular neurological symptoms and toxoplasmosis; and hepatosplenomegaly, rash and thrombocytopenia with Syphilis. Therefore a full TORCH screen should be done if depending on the clinical picture.

In addition to those with clinical features of congenital infection, investigations for CMV should be done on infants born to a mother with documented recent infection, inconclusive results or with typical fetal ultrasound findings such as IUGR, microcephaly, ventricular dilatation and intracranial calcification

Premature infants have been shown to have a higher incidence of congenital CMV infection, so a lower threshold for testing is appropriate.

3 DIAGNOSIS

Antenatal

Congenital CMV may be diagnosed in pregnancy from the following:
Positive CMV PCR from fetal blood/ amniocentesis
Positive maternal IgM
Evidence of maternal IgG seroconversion, with or without detectable IgM, or presence of low avidity (less mature) CMV IgG in pregnancy

Congenital CMV can be excluded in pregnancy if mother is CMV IgG negative

If CMV is diagnosed antenally in mother, the infant needs a full diagnostic work-up for CMV as per section below

Neonates and infants up to 6 months old

The following infants should be tested for cCMV:

- Antenatal USS features suggestive of cCMV
- Infants with clinical symptoms suggestive of cCMV
- IUGR (<2nd centile) especially if
    - Preterm (as have increased incidence of cCMV)
    - Symmetrical
    - Unknown cause
- Infants with ‘no clear response’ on newborn hearing screening (see flowchart appendix 2 and SOP)

Congenital CMV infection can be confirmed or excluded by testing 2 urinary samples for CMV DNA PCR within the first three weeks of life. Whole blood and saliva may be tested by a negative result does not exclude congenital CMV infection.

Samples after 3 weeks of age cannot distinguish congenital from postnatal or perinatal infection. Therefore, if congenital CMV is suspected after three weeks of life, the newborn blood spot card should be traced and tested for CMV DNA PCR. Please email: [redacted] to request this. Written parental consent from parents is required. See proforma in Appendix 3. Please note sensitivity for this test is 45-75%. Alternatively, if any samples exist from the first three weeks of age, these should be used.

Infant CMV IgG may represent transplacental transfer of maternal antibodies so if present should be followed by sending 2 infant urine samples for CMV PCR as above.

Further investigations if clinical symptoms/ signs of CMV or positive CMV PCR

- Full clinical examination
- Confirmatory testing of CMV: urine, blood +/- newborn bloodspot card if older than 21 days old and no other sample taken <21 days old available
- Bloods for Full Blood Count, Urea and Electrolytes and Liver Function Tests.
- Neuroimaging: cranial ultrasound scan or MRI brain are necessary at diagnosis as any intracranial abnormalities related to congenital CMV would lead to the neonate being treated as symptomatic. The sensitivity of MRI is higher but often detects subtle abnormalities no linked to cCMV infection, causing diagnostic difficulties and parental anxiety.
- Abdominal ultrasound scan is necessary if hepatosplenomegaly is detected clinically to confirm CMV infection or to rule out other pathology
-
- Hearing assessment at diagnosis and repeated regularly
- Ophthalmology assessment at diagnosis and repeated regularly. [redacted] (Eastern) and [redacted] (Northern).

Children identified with cCMV beyond the age of 6 months

Consideration for further investigations (blood tests and neuroimaging) on a case by case basis
These children will need regular audiology, opthalmology and paediatric neurodevelopmental follow up, frequency depending on the individual case

4 MANAGEMENT

Neonates and young infants with cCMV need urgent assessment to consider urgent antivirals. Please refer to [redacted]), paediatric infection clinic if outpatient. Antiviral treatment has been shown to reduce neurological damage, developmental delay and hearing loss. All cases are managed on a case by case basis with discussion with microbiology and the Bristol paediatric infectious diseases team

Infants diagnosed with congenital CMV prior to 28 days old should be started on antiviral treatment if symptomatic with CNS and/or focal organ disease (including sensorineural hearing loss) as follows:

- Valganciclovir orally (16mg/kg BD) for 6 months, or
- Ganciclovir IV (6mg/kg BD) if not fully enterally feeding and switch to valganciclovir to complete 6 month course once tolerating enteral feeding

If congenital CMV is diagnosed in infants after the neonatal period, after 30 days of age, treatment is not yet routinely recommended but is sometimes considered up to 6 months of life depending on the specific case

5 FOLLOW UP of infants with cCMV

Paediatric infection clinic monthly follow up whilst on antivirals for clinical review, weight and dose adjustment and blood testing monitoring for toxicity and compliance:

Monitoring required for infants on antiviral treatment:

If on Ganciclovir: FBC, LFT and U&E weekly

If on Valganciclovir: FBC, LFT and U&E weekly for the first 2 weeks then every 2 weeks. If stable then monthly till completion of treatment

Viral load (urine preferably) tested in first month whilst on antiviral therapy. Re-test viral load oif there is a need for treatment interruptions

Therapeutic drug monitoring if:

Viral load not dropping, consider resistance if normal therapeutic levels

Toxicity is suspected

Abnormal renal function or preterm (<36 weeks gestation)

Audiology follow up - regularly until at least 6 years old (i.e until child is verbal)

Ophthalmology follow up - regularly until at least 5 years old

Neurodevelopmental follow up- whilst on antivirals. Then at 12-24 months old for formal neurodevelopmental assessment

6 POSTNATAL ACQUIRED CMV

6.1 To only treat if patient is at risk of developing severe complications of CMV (immunosuppression, preterm or rare cases when symptomatic). To discuss with Bristol paediatric infectious diseases team. If indicated treatment would be 2-3 weeks of antivirals as for cCMV.

7 SAFETY INFORMATION

7.1 Please note Valganciclovir and Ganciclovir can be teratogenic and mutagenic, so it is advisable to avoid all contact with skin when administering, skin should be washed immediately if contact occurs, gloves are often advised.

7.2 Reconstitution of Ganciclovir and Valganciclvir is best done in the pharmacy aseptic/ production units as gloves and goggles should be used when reconstituting. Speak to pharmacy for more information.

8 INFECTION CONTROL

8.1 Babies known to be shredding CMV in urine do not have to be isolated, but routine infection control precautions need to be followed.

8.2 Pregnant staff should not look after babies with congenital CMV as a precaution.

9 RESOURCES FOR PARENTS

9.1 Website for parents: https://cmvaction.org.uk

10 MONITORING COMPLIANCE WITH THIS GUIDELINE

10.1 Any concern or non-compliance with this guideline that is identified through the investigation of clinical incidents, claims or complaints will be reviewed as per the Trust Policies regarding Incidents, Claims and Complaints, and may result in an audit and/or amendment to the guideline.

10.2 Relevant Policies:

- Incident reporting policy and procedure
- Claims management policy and procedure
- Policy and Procedure for the Management of Complaints, Concerns, Comments and Compliments

11 ASSOCIATED CLINICAL GUIDELINES OR POLICIES

South West Neonatal Network Guideline. Diagnosis and management of Congenital and Acquired CMV Infection.Ratified by the SW Neontal ODN Membership Board on Nov 2019. Review date July 2025.

The European Society for Pediatric Infectious Disease (ESPID). Congenital Cytomegalovirus. A European Expert Consensus Statement on Diagnosis and Management. *The Pediatric Infectious Disease Journal* 2017;36(12):1205-1213.

12 PUBLICATION DETAILS

Author of Clinical Guideline	[redacted], [redacted]
Division/ Department responsible for Clinical Guideline	Specialist Services/CWH/NNU
Contact details	[redacted]
Version number	2.0
Replaces version number	1.0
Date written	June 2023
Approving body and date approved	Neonatal Management and Governance Meeting, Paediatric Governance Meeting DD/MM/2023
Review date	DD/MM/YYYY
Expiry date	DD/MM/YYYY
Date document becomes live	DD/MM/YYYY

APPENDIX 1: Flow Chart for diagnosis and management of Congenital CMV Infection in the first 6 months of life

Virology confirmed diagnosis within 21 days of birth = Congenital CMV Infection. Diagnosis from-

CMV PCR (Urine) x 2- Gold standard
CMV PCR saliva x 1 with confimatory urine sample
CMV PCR blood[1]
Retrospective diagnosis on dried newborn blood spot

↓

Further investigations within 28 days of life:

- Clinical examination
- FBC, U&E, LFT
- Audiology assessment (newborn hearing screen or formal assessment if failed newborn hearing screen)
- Ophthalmology assessment
- Brain imaging:
  - 1st line: Cranial ultrasound scan
  - 2nd line: consider MRI[2]

Notes:
1.Baseline Blood CMV PCR should be taken as soon as possible after diagnosis
2. MRI if CrUSS abnormal or if clinical concerns

↙ ↘

SYMPTOMATIC: Focal organ or CNS disease

Antiviral treatment to be started within 30 days of birth for 6 month course:
Valganciclovir 16mg/kg/dose BD PO OR
Ganciclovir 6mg/kg BD IV if not fully enterally fed (switch to valganciclovir when achieved enteral feeding)

Monthly review in paediatric infection clinic for weight and dose increase; clinical review; blood test monitoring:

- FBC, LFT and U&E weekly for the first 2 weeks, 2 weekly. If stable move to monthly
- Viral load every 2 weeks for first month, then monthly

Audiology follow up
Opthalmology follow up

ASYMPTOMATIC

Ensure all investigations are normal within 28 days old
No antiviral treatment
Audiology follow up until child is verbal

APPENDIX 2: Flowchart of RDUH cCMV salivary screening at newborn hearing screen for infants >34 weeks gestation with 'no clear response' (see SOP for full details)

Patient education on program during pregnancy alongside information on newborn hearing screening

- Verbal and written information given during antenatal care

↓

Newborn hearing screen appointment: 'no clear response' in either or both ears.
Action by screener:

1. Patient information leaflet given out and procedure discussed prior to taking swab
2. Salivary virology sample taken and sent to microbiology lab (Eastern) to test for CMV PCR
3. For duration of pilot 2 salivary samples required for test validation purposes
4. Referral to audiology
5. Above action documented in newborn hearing screening database including if declined

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CMV PCR salivary testing and dissemination of results

1. Tests salivary sample for CMV PCR
2. For the duration of the pilot the second salivary sample is sent away for second testing
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↙ ↘

Positive CMV result

- Paediatrician will notify parent/ guardian by phone and organise urgent face to face appointment for medical assessment and further testing as per CMV guideline
- Audiology will ensure prompt assessment
- Newborn hearing screeners will add result to newborn hearing screen database

Negative CMV result

- Parent/ guardian will be notified by audiologist at audiology appointment and result will be given in standard audiology letter
- If hearing loss confirmed to follow usual pathways including referral for paediatric medical assessment
- If normal audiology assessment discharge

APPENDIX 3

Use of newborn blood spot Card for Confirmation of Congenital CMV Infection.

Please email: [redacted] or discuss directly with the

Newborn Screening Laboratory on [redacted] . Written parental consent is required using the form below:

Newborn Screening Bloodspot Card - Consent for Further Tests

I consent for the Newborn Screening Blood spot sample from my child:

……..……. DOB ……

to be released for further tests (please specify):

..……..……

……..……..……

as explained to me by:

……..……..……

Name of Parent/Guardian:……..……..

Signature:……..……

Date:……..…….

Name of child's Consultant: ……..……..

Signature of Doctor obtaining consent: ……..……..

Contact details: ……..……...

13 REFERENCES

- Chung PK et al. Targeted screening for cCMV infection: clinical, audiological and neuroimaging findings. ADC Fetal and Neonatal Edition. 2023;108:F302-F308

- Kimberlin DW, Jester PM, Sánchez PJ, Ahmed A, Arav-Boger R, Michaels MG et al. Valganciclovir for symptomatic congenital cytomegalovirus disease. Kimberlin DW et al. N Engl J Med 2015; 372(10): 993-943. doi: 10.1056/NEJMoa1404599

- Shah T, Luck S, Sharland M, Kadambari S, Heath P, Lyall H. Fifteen-minute consultation: diagnosis and management of congenital CMV. Archives Disease in Childhood Education and Practice 2016;101 (5):232-5

- Hearing loss and congenital CMV infection: a systemic review. Goderis J et al. Pediatrics 2014 Nov; 134 (5): 972-982.

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Clinical Guideline for:
Diagnosis and Management of Congenital Cytomegalovirus (CMV) Infection

Summary

This guideline outlines the process of investigation, diagnosis and management of congenital CMV infection for use on the Neonatal Unit.

Key Points

1. Congenital CMV is the commonest congenitally acquired infection, and the leading cause of acquired sensorineural hearing loss in childhood.
2. Only 5-10% will show symptoms at birth, and most will remain symptom free. However, 10-15% of those initially asymptomatic may develop complications later in life.
3. Gold standard diagnosis of congenital CMV is 2 positive neonatal urine samples for CMV DNA PCR or positive CMV PCR in the blood in the first 21 days of life.
4. Congenital CMV is excluded by 2 negative urine samples for CMV in the first 21 days of life.
5. If investigation is after 21 days old, CMV DNA PCR can be performed on the 5 day newborn blood spot to diagnose congenital CMV retrospectively.
6. Diagnosis can be made antenatally using amniocentesis or fetal blood DNA PCR.
7. 6 months of treatment should be commenced if symptomatic with CNS or focal organ disease.
8. Please see Appendix 1 for quick reference diagnosis and management flow sheet.

CONTENTS

1 BACKGROUND

1.1 CMV is the commonest congenital infection, with an incidence of between 3-5 per 1000 live births. It can result from both primary and recurrent maternal infection.

1.2 Only 5-10% of infected babies show symptoms at birth, and most babies will remain symptom free. However, 10-15% of asymptomatic infants will develop complications later in life, particularly that of sensorineural deafness and developmental problems.

1.3 Congenital CMV infection is the leading cause of acquired sensorineural hearing loss.

1.4 Early diagnosis is key, as treatment has been shown to improve symptoms, and the determination between congenital and acquired CMV is important, as management approaches will differ.

1.5 Intrauterine mother to infant transmission rate is 30-40% in primary disease. The risk to the infant is much lower with reactivation (~1%). Transmission of CMV may also be intrapartum, through vaginal secretions, or postnatal through breast milk, blood products or close personal contact.

2 PRESENTATION

2.1 Neonatal features

- Sensorineural hearing loss (can be present at birth, or later in life)
- Blueberry muffin rash
- Intrauterine growth restriction (IUGR)
- Microcephaly
- Hepatosplenomegaly
- Petechiae
- Jaundice
- Intracranial calcification
- Chorioretinitis
- Lymphadenopathy

2.2 Laboratory features most commonly found

- Conjugated hyperbilirubinaemia
- Thrombocytopaenia
- Elevated hepatic transaminases

2.3 Ultrasound features

- Intrauterine growth retardation (IUGR)
- Ventricular dilatation
- Intracranial calcification
- Microcephaly

2.1 Some symptoms can overlap with other congenital infections, in particular neurological symptoms and Toxoplasmosis; and hepatosplenomegaly, rash and thrombocytopenia with Syphilis. Therefore a full TORCH screen should be done if features of suspected congenital infection are present.

2.2 In addition to those with clinical features of congenital infection, investigations for CMV should be done on infants born to a mother with documented recent infection, inconclusive results or with typical fetal ultrasound findings.

2.3 Premature infants have been shown to have a higher incidence of congenital CMV infection, so a lower threshold for testing may be appropriate.

3 DIAGNOSIS

3.1 In pregnancy:

3.1.1 If the mother is CMV IgG negative after birth, congenital infection is excluded.

3.1.2 If maternal IgG is reactive, with positive or negative IgM, congenital infection is possible but the results are inconclusive.

3.1.3 If an amniocentesis or fetal blood PCR are positive the diagnosis in pregnancy is confirmed, but the infant would still need to be investigated and diagnosis confirmed after delivery.

3.1.4 These tests may also be helpful in determining if the infection is a re-activation or primary source.

3.2 In Newborn:

3.2.1 Congenital CMV infection can be confirmed or excluded by testing urine for CMV DNA PCR within the first three weeks of life.

3.2.2 Whole blood (EDTA/purple top) can also be tested but a negative result may not exclude congenital infection. However a positive test is diagnostic. Positive results should be confirmed with a further repeat sample.

3.2.3 Obtaining two serial negative urine CMV DNA PCR results is recommended to fully exclude congenital CMV infection. Therefore 2 urine samples, taken at different times, should always be requested to diagnose or exclude CMV.

3.2.4 Samples after 3 weeks of age, cannot distinguish congenital from postnatal or perinatal infection. Therefore, if suspected after three weeks of life, the Guthrie card should be traced and tested for CMV DNA PCR. Alternatively, if any samples exist from the first three weeks of age, these should be used. See proformas in Appendix 2 and 3.

3.2.5 Once confirmed, a baseline CMV DNA PCR on blood should be obtained for all.

3.2.6 Infant CMV IgG (TORCH Screen) may represent transplacental transfer of maternal antibodies so if present should be followed by urine testing for CMV PCR as above.

3.2.7 Further investigations at diagnosis:

- Full clinical examination
- Bloods for Full Blood Count, Urea and Electrolytes and Liver Function Tests.
- Brain imaging, cranial USS or MRI, are necessary at diagnosis to separate symptomatic and asymptomatic infants.
- MRI sensitivity is higher but can also detect subtle abnormalities not linked to CMV infection, creating diagnostic difficulties and parental anxiety. Therefore, Cranial USS is first line, and MRI only if USS is abnormal or there are clinical concerns.
- Lumbar puncture is suggested if all other investigations are normal as if there is positive CSF for CMV DNA, treatment is advised.
- Hearing assessment
- Ophthalmology assessment

4 MANAGEMENT

4.1 Infants diagnosed with congenital CMV prior to 30 days old should commence treatment if symptomatic with CNS and/or focal organ disease as follows:

- Valganciclovir orally (16mg/kg BD) for 6 months, or
- Ganciclovir IV (6mg/kg BD) if not fully enterally feeding and switch to valganciclovir to complete 6 month course once tolerating enteral feeding

4.2 Treatment has been shown to reduce neurological damage, developmental delay and hearing loss.

4.3 Asymptomatic patients DO NOT require treatment.

4.4 Please discuss with microbiology and [redacted] (local paediatrician lead for infectious diseases) and/or the Bristol Paediatric Infectious Diseases team (bleep [redacted] via Bristol Children's Hospital switchboard).

4.5 If congenital CMV is diagnosed in infants after the neonatal period, after 30 days of age, treatment is not yet routinely recommended but results of the Toddler Valganciclovir study evaluating these infants is awaited.

5 FOLLOW UP

5.1 Monitoring required:

- If on ganciclovir: FBC, LFT and U&E weekly
- If on valganciclovir: FBC, LFT and U&E at week 2 and 4, then monthly till completion of treatment
- Viral load (urine preferably) every 2 weeks for the first month, then monthly whilst on antiviral therapy
- Therapeutic drug monitoring if:
  1. Viral load not dropping, consider resistance if normal therapeutic levels
  2. Toxicity is suspected
  3. Abnormal renal function or preterm (<36 weeks gestation)

5.2 Paediatric follow up:

[redacted]Paediatric clinic (WON CHEEM INFEC) follow up for monitoring of infection, medication side effects; and development progress.

- Within first month of diagnosis
- 6 months age
- 12 months of age

5.3 Audiology follow up - regularly until at least 6 years old.

5.4 Ophthalmology follow up - regularly until at least 5 years old.

6 SAFETY INFORMATION

6.1 Please note Valganciclovir and Ganciclovir can be teratogenic and mutagenic, so it is advisable to avoid all contact with skin when administering, skin should be washed immediately if contact occurs, gloves are often advised.

7 INFECTION CONTROL

7.1 Babies known to be shredding CMV in urine do not have to be isolated, but routine infection control precautions need to be followed.

7.2 Pregnant staff should not look after babies with congenital CMV.

8 RESOURCES

8.1 Website for parents: https://cmvaction.org.uk

9 REFERENCES

- Valganciclovir for Symptomatic Congenital Cytomegalovirus Disease. Kimberlin DW et al. N Engl J Med 2015; 372: 993-943
- Shah T, Luck S, Sharland M, Kadambari S, Heath P, Lyall H. Fifteen-minute consultation: diagnosis and management of congenital CMV. Archives disease of childhood Education and Practice volume 101, issue 5.
- Hearing loss and congenital CMV infection: a systemic review. Goderis J et al. Pediatrics 2014 Nov; 134 (5): 972-982.
- Bristol Royal Hospital for Children guidelines on congenital CMV
- UK Standards for Microbiology Investigations, Investigation of cytomegalovirus infection. Public Health England. 28 (4).

10 MONITORING COMPLIANCE WITH THIS GUIDELINE

10.1 Any concern or non-compliance with this guideline that is identified through the investigation of clinical incidents, claims or complaints will be reviewed as per the Trust Policies regarding Incidents, Claims and Complaints, and may result in an audit and/or amendment to the guideline.

10.2 Relevant Policies:

- Incident reporting policy and procedure
- Claims management policy and procedure
- Policy and Procedure for the Management of Complaints, Concerns, Comments and Compliments

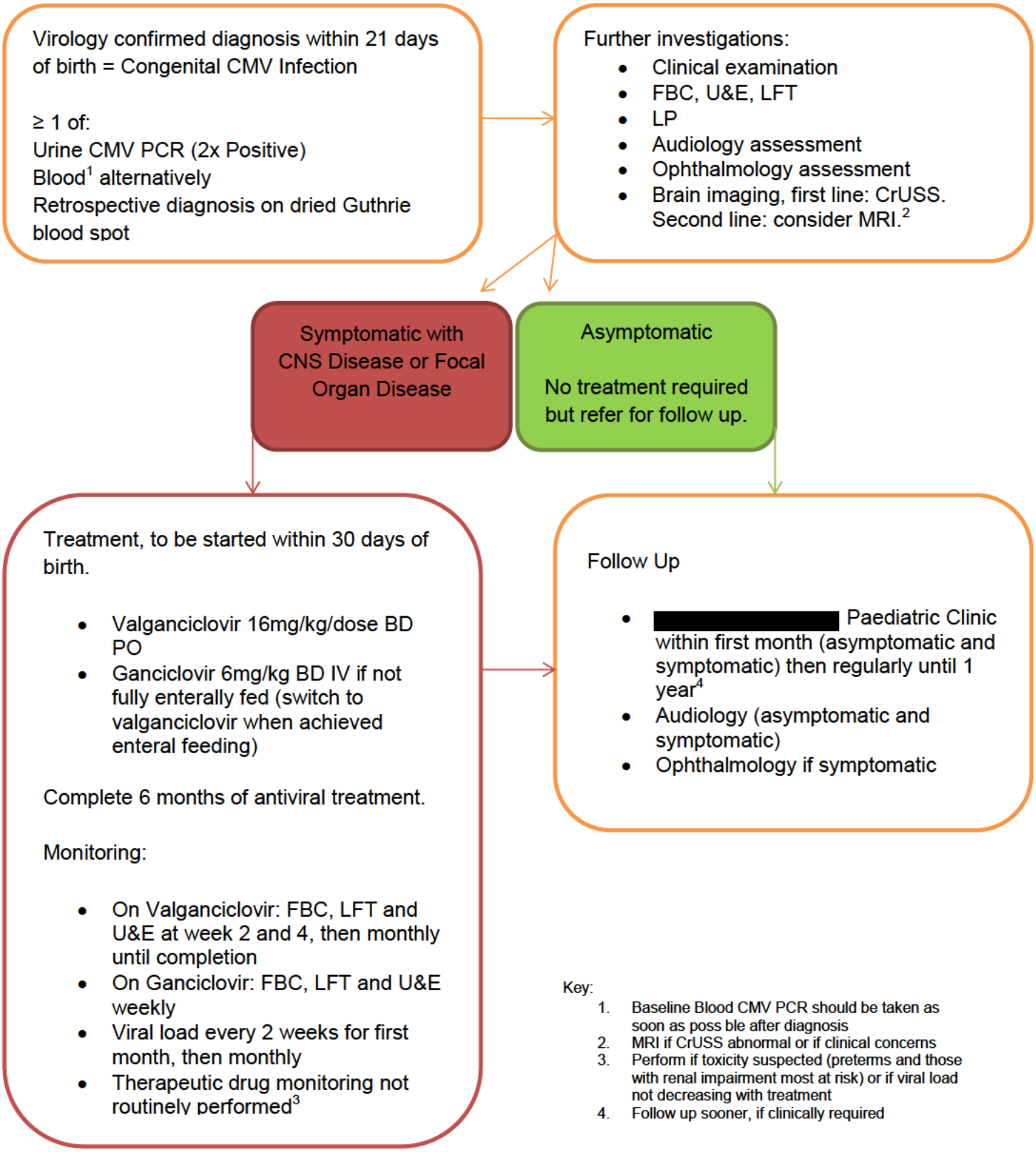
11 ASSOCIATED CLINICAL GUIDELINES OR POLICIES

12 PUBLICATION DETAILS

Author of Clinical Guideline	[redacted]
Division/ Department responsible for Clinical Guideline	Specialist Services/CWH/NNU
Contact details	[redacted]
Version number	1.0
Replaces version number	N/A – New Guideline
Date written	December 2020
Approving body and date approved	Neonatal Governance & Management Meeting 12/12/2020
Review date	12/09/2024
Expiry date	12/12/2024
Date document becomes live	16/12/2020

APPENDIX 1:

Flow Chart for diagnosis and management of Congenital CMV Infection



Key:

1. Baseline Blood CMV PCR should be taken as soon as poss ble after diagnosis
2. MRI if CrUSS abnormal or if clinical concerns
3. Perform if toxicity suspected (preterms and those with renal impairment most at risk) or if viral load not decreasing with treatment
4. Follow up sooner, if clinically required

APPENDIX 2:

Use of Guthrie Card for Confirmation of Congenital CMV Infection

As previously discussed, when CMV DNA samples from urine, or blood are taken after 3 weeks of age, it is not possible to distinguish between congenital or postnatally acquired infection, and it is unsafe to assume. Therefore, use of the Day 5 Guthrie (Blood Spot) Card for testing of CMV DNA PCR should be sought, and can usually resolve the diagnostic question.

This test is also recommended by the Newborn Hearing Screening Programme, in England, for investigation of sensorineural hearing loss.

These cards are stored in the Newborn Screening Laboratory at Southmead, in Bristol.

The following are required for it's request:

1. Consent form signed by the parent.
2. Requesting letter to [redacted], please find example letter below.
3. Laboratory request form for the Royal Free Hospital, please find here https://www.google.co.uk/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwialrPWqbrtAhUCQxUIHTmGBqYQFjABegQIAxAC&url=http%3A%2F%2Fs3-eu-west-1.amazonaws.com%2Ffiles.royalfree.nhs.uk%2FRFH_Guthrie_Cards.docx.doc&usg=AOvVaw3zNN_-JfF7ljwLixO-YSfV

Please send both a signed copy of the consent form, laboratory request form, and covering letter to to:

[redacted]

Director of Newborn Screening

Department of Clinical Biochemisty

Pathology Sciences Laboratory

Southmead Hospital

Bristol

BS10 5NB

Please note, if for any reason the sample you are requesting is greater than one year old, the Bristol Laboratory will require an address to send the invoice for retrieval to.

Any queries can be discussed with our Microbiology department, or the Newborn Screening Laboratory directly on [redacted]

[redacted]

Director of Newborn Screening

Department of Clinical Biochemisty

Pathology Sciences Laboratory

Southmead Hospital

Bristol

BS10 5NB

Dear [redacted],

Patient:

DOB:
Hospital No.:

NHS No.:

I would be most grateful for your help with … who presented with … . Virology tests show that he/she is infected with CMV but unfortunately, due to the timing of samples, it is not possible to say with certainty whether the infection was acquired congenitally or postnatally. I would therefore be grateful if the Guthrie card of … could please be made available for testing for CMV DNA PCR at the Royal Free Hospital.

I enclose a signed consent form, together with a laboratory referral form. Please could you arrange for the Guthrie Card and referral form to be sent on to the address on the form?

Many thanks for your help.

Yours sincerely,

APPENDIX 3:

Newborn Screening Bloodspot Card - Consent for Further Tests

I consent for the Newborn Screening Blood spot sample from my child:

…….. DOB …….

to be released for further tests (please specify):

……..……

……..……

as explained to me by:

……..……

Name of Parent/Guardian:……..……..

Signature:…….……

Date:…….…….

Name of child's Consultant: ……..……..

Signature of Doctor obtaining consent: ……..……..

Contact details: ……..……...

Clinical Guideline

CMV – DIAGNOSIS AND MANAGEMENT OF CONGENITAL AND POSTNATALLY ACQUIRED CYTOMEGALOVIRUS (CMV) INFECTION

SETTING	Bristol Royal Hospital for Children, Neonatal medicine - St Michael's Hospital and Southmead Hospital
FOR STAFF	Doctors and midwives
PATIENTS	Neonates and Children with suspected CMV infections – congenital or postnatally acquired, including premature babies.

CONGENITAL CMV – see flowchart

Congenital CMV is the commonest infection to be passed from mother to baby during pregnancy in the Western world (6/1000). We know that only 10% of infected babies show signs at birth. Although most infected babies will remain symptom-free and have no further problems, some (around 15% of babies) develop problems with their hearing and development later in childhood. It is the leading non-genetic cause of sensorineural hearing loss.

An accurate diagnosis has to be made within the first three weeks from birth to distinguish between congenital and acquired CMV, this is important as it changes the management of the baby.

Acquisition:

1. Intrauterine (primary infection, reactivation or reinfection)
2. Intrapartum (vaginal secretions)
3. Postnatal (breast milk, blood products, close personal contact)

Clinical presentation:
Most commonly CMV infection is asymptomatic (90%). Listed are the most common signs of CMV infection:

- Sensorineural hearing loss (can be present at birth or present later in life)
- Blueberry muffin rash
- Petechiae
- Jaundice
- Intrauterine growth restriction (IUGR)
- Microcephaly
- Hepato-splenomegaly
- Lymphadenopathy

The most common laboratory abnormalities are:
- Conjugated hyperbilirubinaemia,
- Thrombocytopaenia
- Elevated hepatic transaminases

The most common abnormalities on USS – non-specific as present in other congenital infections

- Periventricular calcifications
- Ventriculomegaly

Premature infants appear to have a higher incidence of congenital CMV infection and a lower threshold for CMV testing may be appropriate

Diagnosis:

In pregnancy: If the mother is CMV IgG negative after birth of the baby, congenital infection is excluded. If the maternal IgG are reactive with positive or negative IgM, without an amniocentesis, congenital infection is possible but the results are inconclusive, if the amniocentesis or fetal blood are PCR positive the diagnosis in pregnancy is confirmed, but it is worth noting we would still want to investigate the neonate even if amniocentesis positive.

Newborn: A diagnosis of congenital CMV infection can be made or excluded by testing urine for CMV DNA by polymerase chain reaction (PCR) within the first three weeks of life. Whole blood (EDTA/purple top) can also be tested but a negative result may not exclude congenital infection; a positive result is diagnostic. Positive results should be confirmed with a further repeat sample. Obtaining two serial negative urine CMV DNA results is recommended to fully exclude congenital CMV infection.
If congenital CMV infection is suspected after the first three weeks of life, the Guthrie card should be traced and tested for CMV DNA. Alternatively effort should be made if any historical samples exist from the first three weeks of age.

Other investigations:

- A Hearing test needs to be arranged at diagnosis and repeated regularly.
- Ophthalmology investigation should be arranged at diagnosis and repeated yearly
- Brain imaging: Head USS or MRI brain are necessary at diagnosis to separate symptomatic from asymptomatic infants. The sensitivity of MRI is higher but often detects subtle abnormalities not linked to the CMV infection, creating diagnostic difficulties and parental anxiety.
- Lumbar Puncture (LP): An LP is suggested if all the other investigations are normal as if there is positive CSF for CMV DNA, treatment is advised.
- Abdominal USS is necessary if hepatosplenomegaly is detected clinically to confirm CMV infection or rule out other pathology.

Management

Congenital CMV
For babies diagnosed in the neonatal period: Valganciclovir orally (16mg/kg BD) for 6 months; Ganciclovir iv (6 mg/kg BD) if the baby is not feeding enterally.
Discuss each case with Paediatric Infectious Disease (PID) team.
As valganciclovir and ganciclovir can be teratogenic and mutagenic it is advised to avoid all contact with skin when administering. Use gloves and if contact with skin does occur wash immediately. Reconstitution of ganciclovir and valganciclovir is best done in the pharmacy aseptic/production units as gloves and goggles should be used when reconstituting. Speak to the pharmacy team or on call Pharmacist for more information.

All congenital CMV children will routinely need hearing and ophthalmology assessment and will therefore need to be discussed or referred to the infectious diseases team to ensure appropriate follow up.
Currently the "toddler valganciclovir study "evaluates treatment with valganciclovir in children with congenital CMV diagnosed outside the neonatal period (the estimated closing date to recruitment is February 2020). (http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=17418)

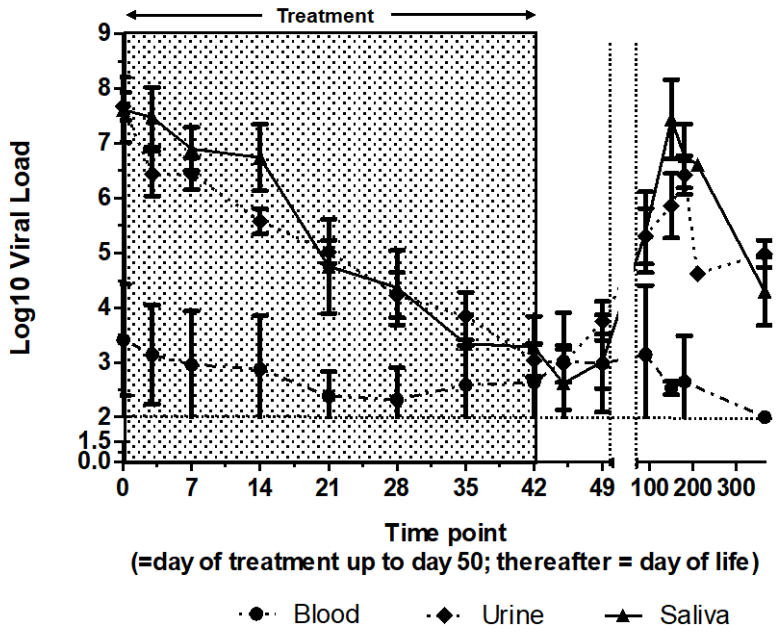
Postnatally Acquired CMV
Discuss with PID, to treat only if the patient is at risk of developing severe complications of CMV (immune suppressed, preterm babies or in rare cases when symptomatic). The treatment choices are as above.

Infection control
Babies known to be shedding CMV in urine DO NOT have to be isolated but routine infection control precautions need to be followed.
In addition, infection control guidelines recommend that pregnant staff do not look after babies with congenital CMV, as a precautionary measure.

Clinic Follow up
In babies on treatment perform the following:

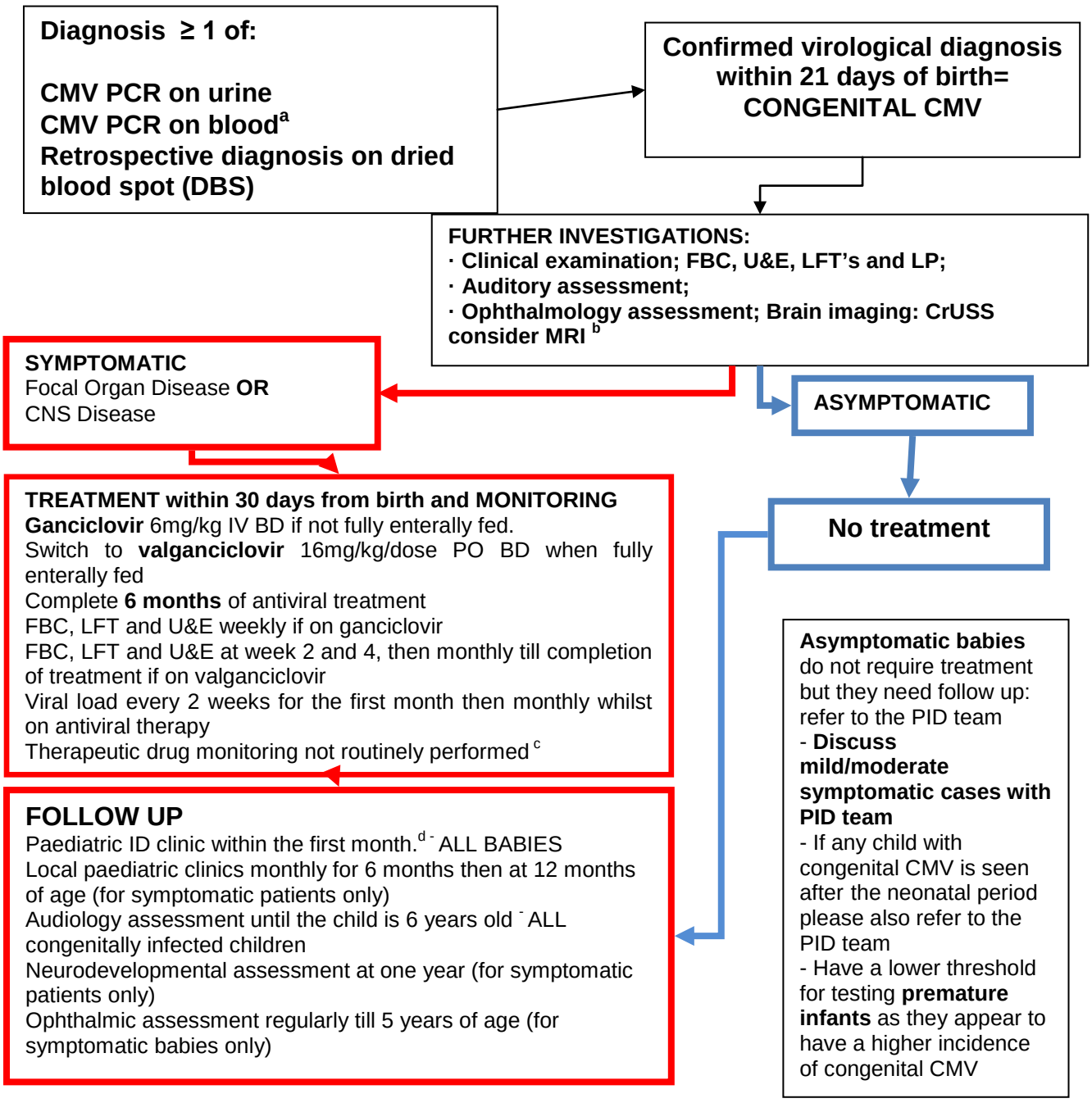
- If on ganciclovir: FBC, LFT and U&E weekly
- If on valganciclovir: FBC, LFT and U&E at week 2 and 4, then monthly till completion of treatment course
- Viral load (VL) every 2 weeks for the first month then monthly whilst on antiviral therapy (urine preferably)
- Therapeutic drug monitoring (TDM) if:
    - VL not dropping (if TDM normal think about resistance)
    - Toxicity is suspected
    - Abnormal renal function or preterm babies (<36 weeks gestation)

Figure 1: Mean viral load over time in different body fluids in 17 babies treated for congenital cytomegalovirus.



CMV viral load was measured in blood, urine and saliva using quantitative real-time PCR.
Treatment was with either ganciclovir or valganciclovir in all babies and for a duration of 42 days +/- 1 day in 16/17 babies.

Flow Chart for the Diagnosis and Management of CONGENITAL CMV infection



Key:

[a] Baseline CMV PCR on blood should be taken as soon as possible after initial diagnosis

[b] Cranial Ultrasound performed in first instance. MRI if the CrUSS is abnormal or there are clinical concerns

[c] Perform only if toxicity is suspected (more likely if prematurity <36 weeks, abnormal renal function) or if viral loads increasing during treatment

[d] Follow up should be sooner if clinically required

** Children diagnosed in the neonatal unit need to be discussed with the PID team ([redacted] or [redacted]) for consideration of treatment and the paediatric infectious diseases nurses need to be notified (ext [redacted] or [redacted] or [redacted]) .

Website for parents: **cmvaction**.org.uk
CMV leaflet available for pregnant women with a diagnosis of CMV infection

References

1. Pediatrics. 2014;134(5):972.
2. Early Human Development 87 (2011) 723–728
3. N Engl J Med. 2015
4. London Congenital CMV guidelines in press

RELATED DOCUMENTS	CMV in pregnancy leaflet DMS address ie http://nww.avon.nhs.uk/dms/download.aspx?did=nnnn
AUTHORISING BODY	Paediatric Immunology Governance Group
SAFETY	Infection control guidelines recommend that pregnant staff does not look after babies with congenital CMV. As valganciclovir and ganciclovir can be teratogenic and mutagenic it is advised to avoid all contact with skin when administering. Use gloves and if contact with skin does occur wash immediately. Reconstitution of ganciclovir and valganciclovir is best done in the pharmacy aseptic/production units as gloves and goggles should be used when reconstituting. Speak to the pharmacy team or on call Pharmacist for more information.
QUERIES	During working hours the paediatric infectious diseases service can be contacted on bleep [redacted] and the virology department on ext. [redacted]. Out of hours please refer to switchboard for the on call paediatric infectious diseases or virology team.