CLINICAL PRACTICE GUIDELINE
Guideline coverage includes NICU KEMH, NICU PMH and NETS WA

Cytomegalovirus (CMV) Neonatal Pathway

This document should be read in conjunction with the Disclaimer

Congenital CMV Testing

Universal screening for congenital CMV is not offered – targeted testing should be performed in high risk infants.

Who to Test

1. Clinical suspicion of congenital CMV (unexplained IUGR, thrombocytopenia, petechiae, hepatomegaly, splenomegaly, hepatitis, microcephaly, sensorineural hearing loss (SNHL), chorioretinitis, seizures or indicative CNS radiological abnormalities).
2. Confirmed CMV infection during (or just prior to) pregnancy.
3. Neonates with positive CMV PCR on amniocentesis are considered to have congenital CMV.

How and When to Test

Ideally testing should be performed as early as practical in order to allow for timely decisions to be made around treatment and follow up:

- For infants <3/52 old either urine or saliva CMV PCR is sensitive and specific (more sensitive than testing dried blood spots).
  - Urine for this purpose can be collected using a bag sample(minimum 1ml).
  - Saliva should be taken at least one hour after the last feed using a sterile swab, the tip of which is then placed in viral transport media.
- For infants ≥3/52 old CMV PCR can be performed using the initial newborn screening blood sample (dried blood spot “Guthrie” card) by contacting the WA Newborn Screening Program (phone 6383 4153).
  - Urine / saliva PCR at ≥3/52 cannot differentiate congenital from postnatal infection.

Any infants with a positive CMV PCR on urine or saliva (<3/52 age) or newborn screening blood spot (any age) or positive CMV PCR on amniocentesis, have congenital CMV and require further assessment and follow up by the infectious diseases department.

Diagnosis and management of infants with post-natal CMV infection is discussed separately below.

Congenital CMV Infection

For all neonates with confirmed congenital CMV, thorough clinical assessment and baseline investigations should be performed and follow-up arranged as outlined:

Clinical Assessment

- Growth parameters (length, weight, head circumference).
- Physical examination including: neurological examination, abdominal examination (jaundice, hepatosplenomegaly) skin examination (petechiae).
- Hearing assessment (usually through newborn hearing screening).

Investigations

- Bloods – consider FBC, LFT, conjugated bilirubin +/- CMV viral load (EDTA 2ml).
- *Imaging – early MRI brain to assess for CNS involvement (ideally prior to 4/52 age where possible). MRI is more sensitive for intracerebral calcification than head USS. Where MRI is not possible, consider USS or CT brain.
- *Ophthalmology – early assessment for chorioretinitis.

Treatment – Who?

Discuss all cases considered for treatment with either the ID registrar / consultant or the clinical microbiologist on call through KEMH/PMH switch:

1. Consider treatment of neonates with confirmed congenital CMV infection and moderate to severe CMV disease defined as:
   a) CNS involvement (microcephaly, radiographic changes indicative of CMV CNS disease, chorioretinitis +/- confirmed SNHL).

      AND / OR

   b) Multiple manifestations attributable to congenital CMV (thrombocytopenia, petechiae, hepatomegaly, splenomegaly, IUGR, hepatitis).
2. Treatment is not routinely recommended in mildly symptomatic CMV disease (one or two transient manifestations, e.g isolated thrombocytopenia), congenital CMV with isolated SNHL, or asymptomatic CMV infection.

Treatment – When and How?

Whenever possible patients should be assessed urgently at the Infectious Diseases outpatient clinic at PCH prior to commencing therapy (or discussed with the ID / micro team for NICU patients)

- Commence treatment within the first month of life.
- Treat with oral valganciclovir 16mg/kg twice daily (or IV ganciclovir initially if extreme prematurity or unable to tolerate / absorb oral medications) for a total duration of 6 months, refer to Neonatology Medication Protocols: Valganciclovir.
- All infants commenced on antivirals should have monthly follow up with the Infectious Diseases team at PCH.

Follow Up

All infants with congenital CMV regardless of treatment status should be referred for:

- Audiology follow up at least 6 monthly up to 3 years of age, then annually thereafter until 10 years old.
- Initial paediatric developmental review at 9-12 months (or earlier if concerns - through PMH developmental clinic (att. Dr Paula Holmes) unless patient otherwise qualifies for KEMH developmental follow up i.e. <32/40 gestation).
  - Consider Ages and Stages Questionnaire (ASQ) at 6 months and 12 months.
  - Consider early referral to Child Development Services if concerns identified.
- Early ophthalmology assessment (as outlined above) and follow up thereafter as determined by the ophthalmologist.

Infants with congenital CMV on valganciclovir require:

- Early ID review (1-2 weeks) then 2-4 weekly thereafter – to monitor compliance, side effects and complications, increase dose with growth & coordinate follow up.
- Transaminases (LFT) and EUC – at least monthly throughout therapy.
- Other follow up as above (paediatrics, audiology & ophthalmology).

CMV viral load testing is not routinely required after commencing therapy, except if there are acute septic features or if there are specific concerns about absorption. CMV viral loads are expected to rebound after ceasing therapy and confirmation of this by viral load testing is not warranted.

Post-natal CMV Infection

Infants can acquire CMV infection peri-natally via exposure to maternal genital secretions, or post-natally via blood transfusion, contact with siblings or most commonly through breastfeeding.

Post-natal CMV disease is rare in full-term infants however those born at <32 weeks gestation or with very low birth weight <1500g are at higher risk of symptomatic disease. Manifestations include hepatitis, thrombocytopenia, neutropenia, respiratory distress syndrome and sepsis-like syndrome.

Where CMV disease is suspected, urine or saliva should be collected for PCR testing. A CMV viral load (EDTA tube 2ml minimum) should also be requested.

Treatment (IV ganciclovir / oral valganciclovir) should be reserved for cases of severe disease in discussion with the infectious diseases team.

A low risk of mild neurological and cognitive sequelae in premature infants infected post-natally has been reported although this finding has not been consistent across studies. In contrast to congenital CMV, post-natally acquired CMV infection has not been definitively associated with sensorineural hearing loss. Developmental follow up can be considered on a case-by-case basis.

Overall the risk of severe disease and/or subsequent sequelae in post-natal CMV infection is low and outweighed by the benefits of breastfeeding. This is reflected in the American Academy of Paediatrics 2012 policy statement which recommends breast milk as the enteral feed of choice for preterm infants in CMV seropositive mothers.

Infants with suspected T cell immunodeficiency are at high risk of severe manifestations of post-natal CMV disease and breast feeding should be avoided.

PMH / KEMH - CMV Pathway Checklist

affix patient label here

*please attach a copy to Infectious Diseases referral if applicable Date_____ Age_____

Diagnosis of congenital CMV established by:

CMV +ve PCR on urine / saliva at <3/52 age……. urine ☐ saliva ☐ Date_____

CMV +ve PCR on newborn screening blood spot …. Yes ☐ No ☐ Date_____

CMV PCR +ve on amniocentesis..…..…….. Yes ☐ No ☐ Date_____

Clinical Assessment and Investigations:

Growth parameters…… height (centile) _____ weight (centile) _____

- microcephaly….. Yes ☐ No ☐ HC (centile) _____

Neurological symptoms / exam….. normal ☐ abnormal ☐ details_____

Hepatomegaly/splenomegaly……. Yes ☐ No ☐ details_____

Rash / Petechiae …….. Yes ☐ No ☐ details_____

Thrombocytopenia..…….. Yes ☐ No ☐ details_____

Transaminitis / jaundice……..... Yes ☐ No ☐ details_____

**Head MRI (or other)…….…… normal ☐ abnormal ☐ pending ☐

details / date_____

**ophthalmology examination……. normal ☐ abnormal ☐ pending ☐

details / date_____

**WANHSS / audiology …….. L) ear - pass ☐ refer ☐ R) ear - pass ☐ refer ☐

pending ☐ additional tests_____

Treatment (consider for infants with moderate to severe cCMV disease):

Moderately / severely symptomatic congenital CMV disease?

CNS involvement……. Yes ☐ No ☐ details_____

Multiple manifestations…….. Yes ☐ No ☐ details_____

**Discussed with ID physician…….. Yes ☐

Treatment recommended……... Yes ☐ No ☐ pending ID review ☐

**ID follow up arranged (+ blood forms) Yes ☐ N/A (treatment not recommended) ☐

date_____

Referrals (for all infants with cCMV):

*Audiology (6-9 mo)……. Referral sent ☐

*Developmental follow up (9-12 mo)…. PMH ☐ KEMH (<32/40) ☐ other ☐ details_____

*Ophthalmology …… Referral sent ☐ phone call to PCH registrar ☐

References

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Related policies

Neonatology Medication Protocols: Valganciclovir

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