

# Non-Polio Enterovirus Infections in the Neonate

## Introduction

Enterovirus (EV) infections are common in the neonatal period with most cases being asymptomatic or minimally symptomatic and without long-term sequelae. However, in a minority of cases, characterized by hepatic, myocardial or central nervous system involvement, EV infections can be severe and sometimes fatal. Understanding the correlates of severe disease may help clinicians suspect the illness, investigate and treat appropriately.

The **purpose** of this fact sheet is to:

- Inform health care professionals of the risks of enterovirus infection to the neonate and the need for rapid diagnosis
- Highlight appropriate laboratory testing, including RT-PCR on blood and CSF, on neonates with severe disease consistent with enterovirus infection
- Review the clinical presentation and treatment options

## Correlates of Severe Enterovirus Neonatal Infections

- Maternal history of viral illness or chorioamnionitis around the time of birth
- Prematurity (< 37 weeks)
- Early onset of illness (< 2 weeks of age)
- High white blood cell count (> 15000)
- Low haemoglobin level (< 10 g)

## Clinical Presentations

- **Non-specific Febrile Illness**
  - Fever, irritability, poor feeding, cough, lethargy and rash
- **Aseptic Meningitis**
  - Meningitis the sole clinical manifestation
- **Severe Neonatal Enterovirus Infection (EVs most often encountered are echoviruses 6, 11, 20, 30; Coxsackie virus B3, B4; and EV71)**
  - Hepatic necrosis and coagulopathy (HNC)
    - Presents within the first week of life
    - Clinical findings of HNC are non-specific. The case fatality rate is 24–31%
    - Echovirus 11 is most commonly associated
  - Myocarditis
    - Coxsackie B viruses is the usual cause
    - Fatality rate 74%
  - Encephalitis or meningo-encephalitis
  - Encephalitis or CNS involvement as part of a multisystem disease (e.g. encephalomyocarditis) – more dire prognosis

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## Diagnosis

### Clinical – Differential Diagnosis

- Suspect Enterovirus infection on history and clinical assessment, including:
  - geographic location and season of the year
  - exposure – careful history of the symptoms of viral illness in mother, family member or minor illness in nursery personnel
  - clinical signs and presentation
  - incubation period
- Exclude bacterial sepsis
- Exclude other viral infections e.g. Herpes Simplex
- Exclude congenital heart disease

### Laboratory Tests

**Submit all specimens for viral studies to ProvLab on a properly filled out requisition, label sample and type of specimen and specify viral study requested:**

- CSF – submitted to ProvLab for viral studies is automatically tested for enteroviruses, herpes simplex (HSV) and varicella zoster (VZV).
- Blood can be tested by RT-PCR for enteroviruses and by PCR for HSV/VZV, upon special request by discussion with the Virologist on Call – PH: Edmonton 780-407-7121; Calgary 403-944-1200.
- Conjunctiva and buccal lesions swabs – viral testing automatically includes enteroviruses.
- Stool samples – tested by RT-PCR for enteroviruses upon explicit request.
- Respiratory samples – tested using the RVP panel, include testing for enteroviruses and rhinoviruses, but cannot distinguish between enteroviruses and rhinoviruses.
- Specific molecular typing request for enterovirus – must be done by contacting the Virologist on Call (VOC) at ProvLab – PH: Edmonton 780-407-7121; Calgary 403-944-1200.

## Treatment

**Consult with a pediatric infectious disease specialist for infants presenting with symptoms of severe disease.**

- **Treat with broad spectrum antibiotics** until bacterial sepsis has been excluded. Treat with Acyclovir until Herpes Simplex infection has been excluded (CSF tested negative for HSV by PCR does not rule out HSV infection).
- **Intravenous Immunoglobulin (IVIG)** – In severe catastrophic and generalized neonatal enterovirus infections it is likely that the infant received no specific antibody to that particular virus from his mother. Evidence for efficacy is scant but it is reasonable to give high-dose IVIG in these cases.
- Avoid corticosteroids.
- Clinical trials are in progress to determine efficacy of treatment with the antiviral drug pleconaril.

### Resources:

- 1) *Infectious Diseases of the Fetus and Newborn Infant*. Remington & KleinWilson, Nizet, Maldonado Elsevier Saunders. Seventh Edition. 2011. Chapter 24. 759-799.
- 2) *Non-polio enterovirus infection in the neonate and young infant*. Hawkes MT, Vaudry W. *Paediatr Child Health*. Vol 10 No 7. September 2005. 383-388
- 3) *Enteroviruses*. Romero JR, Chapter 45 in *Clinical Virology 3<sup>rd</sup> ed*, Rochman DD, Whitley RJ, Hayden FG eds, ASM Press 2009.
- 4) *Presentation, Diagnosis, and Management of Enteroviruses Infections in Neonates*. Abzug MJ *Paediatr Drugs* 2004; 6: 1-10.
- 5) *Enterovirus Infection in Neonates*. Tebruegge M, Curtis N. *Seminars in Fetal and Neonatal Medicine* 2009; 14: 222-227.
- 6) *Pleconaril enteroviral sepsis syndrome*. National Institute of Allergy and Infectious Diseases (NIAID). *Clinical trials.gov* identifier: NCT00031512.

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