Transcriptional effects of enterovirus D68 infection

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2014 Outbreak of Acute Flaccid Myelitis (AFM)

Mid-August 2014 – mid-January 2015:

• 120 cases of acute flaccid myelitis/paralysis (AFM) in the US with unknown etiology (Ayscue 2014, Messacar 2015, Van Haren 2015, Greninger 2015)
Acute flaccid myelitis outbreak

Number of confirmed U.S. AFM cases reported to CDC by month of onset,
August 2014 - March 2019

* The data shown from August 2014 to July 2015 are based on the AFM investigation case definition: onset of acute limb weakness on or after August 1, 2014, and a magnetic resonance image (MRI) showing a spinal cord lesion largely restricted to gray matter in a patient age ≤21 years.

† The data shown from August 2015 to present are based on the AFM case definition adopted by the Council of State and Territorial Epidemiologists (CSTE): acute onset of focal limb weakness and an MRI showing spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments, regardless of age.

Mid-August 2014 – mid-January 2015:


- 1,153 confirmed cases of EV-D68 infections, including 14 deaths in the US; likely many more cases of mild EV-D68 infections (CDC)

- EV-D68 etiology
  - 4/10 paralyzed children in CO were EV-D68 positive in respiratory samples
  - 2/23 AFM cases in CA (June 2012 – June 2014) were EV-D68 positive
  - EV-D68 positive AFM cases in Canada, France, Norway, and Australia (Skowronski 2015, Lang 2014, Bragstad 2015, Pfeiffer 2015, Levy 2015)
Enterovirus clinical symptoms

Most infections are asymptomatic or mild respiratory symptoms

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<thead>
<tr>
<th>Genus: EnteroVirus</th>
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<tbody>
<tr>
<td>Enterovirus A</td>
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<td>Enterovirus B</td>
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<td>Enterovirus C</td>
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<td>Enterovirus D</td>
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<td>Enterovirus E</td>
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<td>Enterovirus F</td>
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<td>Enterovirus G</td>
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<td>Enterovirus H</td>
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<tr>
<td>Enterovirus J</td>
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<tr>
<td>Rhinovirus A</td>
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<tr>
<td>Rhinovirus B</td>
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<tr>
<td>Rhinovirus C</td>
</tr>
<tr>
<td>uncultivated Enterovirus</td>
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<tr>
<td>uncultivated Rhinovirus</td>
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<tr>
<td>unknown</td>
</tr>
</tbody>
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**Polioviruses, types 1-3**
Paralysis (complete to slight muscle weakness)
Aseptic meningitis
Undifferentiated febrile illness, particularly during the summer

**Coxsackieviruses, group A, types 1-24**
Herpangina
Acute lymphatic or nodular pharyngitis
Aseptic meningitis
Paralysis
Exanthema
Hand-foot-and-mouth disease (A10, A16)
Pneumonitis of infants "Common cold"
Hepatitis
Infantile diarrhea
Acute hemorrhagic conjunctivitis (type A24 variant)

**Echoviruses, types 1-33**
Aseptic meningitis
Paralysis
Encephalitis, ataxia, or Guillain-Barre syndrome
Exanthema
Respiratory disease
Others: Diarrhea
Pericarditis and myocarditis
Hepatic disturbance

**Enterovirus, types 68-71**
Pneumonia and bronchiolitis
Acute hemorrhagic conjunctivitis (type 70)
Paralysis (types 70, 71)
Meningoencephalitis (types 70, 71)
Hand-foot-and-mouth disease (type 71)

Fields Virology, 2007
Enterovirus D68

*Picornaviridae* family of non-enveloped +ssRNA
Contemporary Circulating Enterovirus D68 Strains Have Acquired the Capacity for Viral Entry and Replication in Human Neuronal Cells

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Transcriptional response to D68 infection

EV-D68 US/MO

1 hr
2 hr
4 hr
8 hr
24 hr

SH-SY5Y

mock
1 hr
2 hr
4 hr
8 hr
24 hr