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Welcome to Mayo Medical Laboratories Hot Topics. These presentations provide short discussion of current topics and may be helpful to you in your practice. Today our topic is enterovirus infection and its association with severe respiratory disease.



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Enterovirus

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Our speaker for this program is Dr. Matt Binnicker, Director of the Clinical Virology Laboratory in the Division of Clinical Microbiology at Mayo Clinic in Rochester, Minnesota.

Dr. Binnicker, thank you for presenting today.

Thanks for the introduction and thanks to each of you for joining me for this presentation. Over the last month, enterovirus has been a common headline in the news and other media outlets as hundreds of patients in the United States have become severely ill from a strain of the virus that is currently circulating in the population. In this presentation, we're going to review some of the important aspects of enterovirus infection, and highlight some of the key features that laboratorians and health care providers should know.

Disclosures

- None

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Before we begin, I just want to mention that I don't have any corporate or financial conflicts of interest to disclose.

Also I'd like to emphasize that we're in a new era of health care and health care delivery in the United States, so as you view this presentation, I would encourage you to consider how the testing we're going to discuss can best be used in your practice, when the tests should be used, and how the results will impact the patients that you're caring for? So let's get started.

## Utilization Message

- As you view this presentation, consider the following important points regarding enterovirus testing:
  - How is the testing going to be used in your practice?
  - When should the tests be used?
  - How will results impact patient management?

The genus enterovirus includes over 60 known serotypes, as well as 12 species. It's because of the large number of serotypes that individuals are susceptible to multiple infections with enterovirus, as the immune response to 1 serotype doesn't necessarily confer protection to other serotypes. There are a number of different viruses that fall into the enterovirus genus, including poliovirus, and nonpolio enteroviruses such as coxsackie virus and echovirus. Enteroviruses have a worldwide distribution and are a very common cause of disease. Enteroviruses are found in a variety of clinical samples, including respiratory secretions and stool, and historically, transmission of the virus has occurred primarily by the fecal-oral route.

## Enterovirus Background and Transmission

- >60 known serotypes
- Enterovirus genus includes 12 species (Enterovirus A-J; Rhinovirus A-C)
- Includes poliovirus, coxsackie A/B, echovirus
- Worldwide distribution / common and ubiquitous
- Found in respiratory secretions and stool
- Transmission occurs primarily via the fecal-oral route

As I mentioned on the previous slide, infection with enteroviruses this is very common, and it's estimated that nonpolio enteroviruses cause 10 to 15 million infections in the United States each year. There is a seasonal incidence associated with these viruses, which is typically late summer to early fall in the United States; however, outbreaks of enterovirus may occur sporadically throughout the year.

## Incidence

- Non-polio enteroviruses cause 10-15 million infections in the United States each year.
- Seasonal incidence is typically late summer to early fall in the United States; however, outbreaks may occur sporadically.

It's important to note that the vast majority of infections with enterovirus are subclinical or asymptomatic. And among those that are exposed, infants, young children, and teenagers are the most likely to become ill due to little or no preexisting immunity to these viruses. If symptoms occur, they may include a fever, runny nose and cough, and in some cases, blisters or sores in the mouth or on the hands and feet. This syndrome, known as hand-foot-and-mouth disease is a relatively common outcome of enterovirus infection in young children. Additional symptoms can include conjunctivitis, and in more serious cases, viral meningitis, encephalitis, or infection of the heart causing myocarditis or pericarditis.

## Clinical Presentation

- Vast majority of infections are subclinical or asymptomatic
- Infants, children, and teenagers are the most likely to become ill due to no preexisting immunity
- Symptoms may include:
  - Fever
  - Runny nose and cough
  - Blisters/sores in the mouth, or on the hands and feet
  - Conjunctivitis
  - Viral meningitis/encephalitis
  - Myocarditis/pericarditis

In mid-August of this year, the Centers for Disease Control was contacted regarding an outbreak of severe respiratory illness in children in the Kansas City, Missouri area. Similar cases were also reported in Chicago, IL and subsequently, in the surrounding cities and states. Clinical samples were submitted to the CDC, and enterovirus species D, serotype 68 was identified as the cause of the disease in these patients. This outbreak was unique in several ways. First, enteroviruses are not a common cause of severe respiratory disease, and second, although this particular serotype had previously been identified as early as the 1960s, it had not been a commonly reported cause of disease in the United States. This outbreak has continued to progress, and to date, approximately 160 cases have been reported.

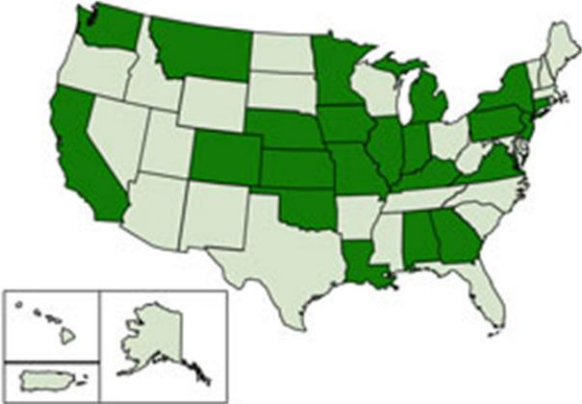
## Enterovirus D68 Outbreak

- In mid-August 2014, the Centers for Disease Control (CDC) was contacted regarding an outbreak of severe respiratory illness in children in Missouri. Cases were also reported in Chicago, IL.
- Enterovirus D68 (species D; serotype 68) was identified.
- This serotype was first identified in California in 1962, but has not been commonly reported until recently.
- To date, >160 cases have been reported in 2014.

As you can see from this map published on the CDC website, the outbreak now involves 22 states around the country, and the distribution of the virus seems to expand on a weekly basis.



# Enterovirus D68 Outbreak



<http://www.cdc.gov/non-polio-enterovirus/about/EV-D68-states.html> Accessed 9.22.14



Enterovirus

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As you can see from this map published on the CDC website, the outbreak now involves 22 states around the country, and the distribution of the virus seems to expand on a weekly basis.

## Enterovirus D68 Outbreak

- The virus is spread through respiratory secretions or when an individual touches contaminated surfaces.
- Enterovirus D68 may cause mild to severe respiratory illness.
  - Many children with severe disease have had a history of asthma
- Symptoms may include:
  - Fever
  - Runny nose and cough
  - Wheezing and difficulty breathing

It's believed that this particular serotype is spread primarily through respiratory secretions or when an individual touches contaminated surfaces and then transmit the virus to mucous membranes, such as the eyes, nose, or mouth. It's important to emphasize that not everyone infected with enterovirus D68 becomes severely ill. In fact, this serotype may cause subclinical or even asymptomatic disease, especially in individuals that are older or have preexisting immunity. However, in young children, especially those with a history of asthma or wheezing, the virus has been shown to potentially cause severe disease, which may require hospitalization. Symptoms may range from a low-grade fever accompanied by a runny nose and cough, to a more significant respiratory condition involving wheezing and difficulty breathing, which may require intubation in some cases.

## Laboratory Testing

- Viral culture – may take 7 to 10 days
  - VRESP / Viral Culture, Respiratory
  - VIRNR / Viral Culture, Non-Respiratory
- Molecular Detection (real-time PCR)
  - **Recommended** for rapid diagnosis
  - LENT / Enterovirus, Molecular Detection, PCR
  - Performed on respiratory samples (throat/nasal swab, nasopharyngeal swab/aspirate, bronchial washing, bronchial lavage fluid)
  - Also performed on CSF or sterile body fluids

In certain patients, especially those requiring hospitalization, laboratory testing may be needed to determine the cause of the infection. If enterovirus infection is suspected, there are several laboratory methods that can be used. First, routine viral culture of either respiratory or nonrespiratory samples can be performed. This approach has several significant limitations, however, including a prolonged turnaround time of up to 7 to 10 days. Another diagnostic option is molecular testing, for example, real-time PCR. This is the recommended approach for a rapid diagnosis, and can be performed on respiratory samples, CSF, and sterile body fluids.

## Laboratory Testing

- Importantly, most laboratory methods do NOT speciate enteroviruses or provide specific serotype information.
- Molecular tests commonly are not able to differentiate enterovirus from rhinovirus.
- A strain of enterovirus D68 was tested by the real-time PCR assay used at Mayo Medical Laboratories and was detected.

It's very important to underscore that most laboratory methods do NOT speciate enterovirus or provide specific serotype information on the virus. In addition, most molecular tests that are commonly performed are not able to differentiate enterovirus from rhinovirus. I should point out that a strain of enterovirus D68 associated with the recent outbreak was tested by the real-time PCR used at Mayo Medical Laboratories and this strain was detected.

## Laboratory Testing

- If specific serotyping is required, samples should be submitted to a state health laboratory that can perform this testing, or the CDC.
- Serotyping is generally performed using viral cell culture and sequencing, which may take weeks to complete.

It's very important to underscore that most laboratory methods do NOT speciate enterovirus or provide specific serotype information on the virus. In addition, most molecular tests that are commonly performed are not able to differentiate enterovirus from rhinovirus. I should point out that a strain of enterovirus D68 associated with the recent outbreak was tested by the real-time PCR used at Mayo Medical Laboratories and this strain was detected.

## Enterovirus D68 – Treatment/Prevention

- There is no specific treatment for enterovirus D68. Treatment is usually supportive.
- Prevention is the key:
  - Wash hands
  - Avoid touching eyes, nose, and mouth with unwashed hands
  - Avoid direct contact (eg, kissing, sharing cups/utensils) with people who are sick
  - Disinfect surfaces (eg, toys, doorknobs) if someone is sick

I wanted to touch briefly on treatment and prevention of enterovirus infection. Unfortunately, there is no specific treatment, such as an antiviral, for enterovirus D68 infection. The treatment is usually supportive and targeted at managing fever, pain and hydration and supporting the airways. Prevention is really the key, and patients should be instructed to wash their hands, avoid touching their eyes, nose, and mouth with unwashed hands, avoid direct contact with people that are sick, and be diligent about disinfecting surfaces if someone in their home, school, or place of work is sick.

## Enterovirus D68 – Summary

- Enterovirus D68 is currently associated with an outbreak of severe respiratory disease.
- Severe disease has been found primarily in children with a history of asthma or wheezing.
- Laboratory testing is not always required, but may be accomplished by:
  - Molecular detection (eg, real-time PCR)
  - Viral cell culture
- Serotyping is performed at select public health laboratories.

In summary, enterovirus D68 is currently associated with an outbreak of severe respiratory disease involving over 20 states in the country. Severe disease has been found primarily in children with a history of asthma or wheezing. Laboratory testing is not always required, but when it is performed, detection of enterovirus may be accomplished by molecular methods, such as real-time PCR, or by routine viral cell culture. Serotyping of the virus is performed at select public health laboratories, and is currently only needed for epidemiologic purposes.



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Thanks again for joining me today for this discussion on enterovirus infection. If you have any questions about the testing that Mayo Medical Laboratories offers for enterovirus, please feel free to contact us.