

## ***Morbidity and Mortality Weekly Report (MMWR)***

# **Notes from the Field: Severe Hand, Foot, and Mouth Disease Associated with Coxsackievirus A6 — Alabama, Connecticut, California, and Nevada, November 2011–February 2012**

*Weekly*

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Hand, foot, and mouth disease (HFMD) is a common viral illness caused by enteroviruses that predominantly affects children aged <5 years. In the United States, outbreaks of HFMD typically occur during summer and autumn months. The most common cause of HFMD in the United States has been enterovirus serotype coxsackievirus A16. Most infections are asymptomatic; persons with signs and symptoms typically have a mild febrile illness with rash on the palms of the hands and soles of the feet, and sores in the mouth. HFMD also has been associated, often weeks after initial symptom onset, with nail dystrophies (e.g., Beau's lines or nail shedding).

From November 7, 2011, to February 29, 2012, CDC received reports of 63 persons with signs and symptoms of HFMD or with fever and atypical rash in Alabama (38 cases), California (seven), Connecticut (one), and Nevada (17). HFMD is not a reportable disease in the United States; the cases were identified as unusual by health-care providers or by a department of health that contacted CDC for diagnostic assistance. Clinical specimens were collected from patients in 34 of the 63 cases. Coxsackievirus A6 (CVA6) was detected in 25 (74%) of those 34 patients by reverse transcriptase–polymerase chain reaction and partial sequencing of the VP1 gene at CDC or at the California Department of Public Health. No enteroviruses were detected in the other nine patients.

Of the 63 patients, 40 (63%) were aged <2 years, and 15 (24%) were adults aged ≥18 years; 44 (70%) of the patients had exposure to a child care facility or school, and eight (53%) of the 15 adults had contact with children in child care where cases of HFMD were reported, or provided medical care or were related to a child with HFMD. Rash and fever were more severe, and hospitalization was more common than with typical HFMD. Signs of HFMD included fever (48 patients [76%]); rash on the hands or feet, or in the mouth (42 [67%]); and rash on the arms or legs (29 [46%]), face (26 [41%]), buttocks (22 [35%]), and trunk (12 [19%]). Of 46 patients with rash variables reported, the rash typically was maculopapular; vesicles were reported in 32 (70%) patients and scabs in 30 (65%) patients. Shedding of nails occurred after initial infection in two (4%) patients. Of the 63 patients, 51 (81%)

**Dept of Health & Human Services – Communicable Disease Prevention & Control**

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sought care from a clinician, and 12 (19%) were hospitalized. Reasons for hospitalization varied and included dehydration and/or severe pain. No deaths were reported.

The age ranges of patients, severity of illness, seasonality of disease, and identification of CVA6 in these cases were unusual for HFMD in the United States. CVA6 has been associated with more severe and extensive rash than HFMD caused by other enteroviruses (1). Since 2008, international outbreaks of CVA6 HFMD in children and adults have been described (1–4), but no outbreaks had been reported in the United States previously. Although all 25 of the CVA6 strains identified in the U.S. cases were genetically closely related (based on partial VP1 gene sequences) to CVA6 strains identified in recent international outbreaks, no epidemiologic evidence (e.g., travel history) has directly linked any of the U.S. cases to importation.

HFMD is spread from person to person by contact with saliva, respiratory secretions, fluid in vesicles, and feces. Transmission of HFMD can be reduced by maintaining good hygiene, including hand-washing and disinfection of surfaces in child care settings (5). CDC continues to receive reports of CVA6-associated HFMD. Persons who suspect a severe case of HFMD should contact their health-care provider. Local or state health departments may contact CDC for assistance with enterovirus laboratory diagnosis.

## Reported by

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## References

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2. Blomqvist S, Klemola P, Kaijalainen S, et al. Co-circulation of coxsackievirus A6 and A10 in hand, foot and mouth disease outbreak in Finland. *J Clin Virol* 2010;48:49–54.
3. Fujimoto T, Iizuka S, Enomoto M, et al. Hand, foot and mouth disease caused by coxsackievirus A6, Japan, 2011. *Emerg Infect Dis* 2012;18:337–9.

4. Wu Y, Yeo A, Phoon MC, et al. The largest outbreak of hand, foot and mouth disease in Singapore in 2008: the role of enterovirus 71 and coxsackievirus A strains. *Int J Infect Dis* 2010;14:e1076–81.
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# HOSPITALIZED ENTEROVIRUS CASE REPORT

|   |     |                       |  |  |                  |  |
|---|-----|-----------------------|--|--|------------------|--|
| Patient Name – Last   |     | First                 | Middle Initial   | Date of Birth<br>____/____/____  | Age<br>_____ yrs | Sex<br><input type="checkbox"/> Male <input type="checkbox"/> Female |
| Address (number, street)  |     |                       | City   | State  | County           | ZIP code   |
| Telephone number – Home ( )   |     |                       |  | Work ( )   |                  | Occupation   |
| Ethnicity (check one)<br><input type="checkbox"/> Hispanic/Latino <input type="checkbox"/> Non-Hispanic/Non-Latino  |     |                       | Race (check all that apply)<br><input type="checkbox"/> African-American/Black <input type="checkbox"/> White <input type="checkbox"/> Native American <input type="checkbox"/> Asian/Pacific Islander <input type="checkbox"/> Other_____ |  |                  |  |
| If Asian/Pacific Islander, check all that apply: <input type="checkbox"/> Asian Indian <input type="checkbox"/> Cambodian <input type="checkbox"/> Chinese <input type="checkbox"/> Filipino <input type="checkbox"/> Guamanian <input type="checkbox"/> Hawaiian<br><input type="checkbox"/> Japanese <input type="checkbox"/> Korean <input type="checkbox"/> Laotian <input type="checkbox"/> Samoan <input type="checkbox"/> Vietnamese <input type="checkbox"/> Other_____ |     |                       |  |  |                  |  |
| Any contact with these settings during 7 days before illness onset? <input type="checkbox"/> Day care/preschool <input type="checkbox"/> School <input type="checkbox"/> Health care <input type="checkbox"/> Other_____  |     |                       |  |  |                  |  |
| <b>DATA ON PRESENT ILLNESS</b>  |     |                       |  |  |                  |  |
| Illness onset date<br>____/____/____  |     | Medical record number |  | Did patient die? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk |                  | Date of death<br>____/____/____                                      |
| Physician name (first, last)  |     |                       | Phone/cell<br>( )  |  | Fax<br>( )       |  |
| Hospital name   |     | City                  | Zip code   | Telephone<br>( )   |                  | Admit date<br>____/____/____   |
| Discharge date<br>____/____/____  |     |                       |  |  |                  |  |
| <b>Signs and symptoms</b>   | Yes | No                    | Unk  | <b>Syndrome(s)</b>   | Yes              | No   |
| Ulcers in throat, mouth or tongue   |     |                       |  | Hand, Foot and Mouth Disease   |                  |  |
| Rash or blisters on palms or soles  |     |                       |  | Flu-like illness   |                  |  |
| Rash on buttocks or groin   |     |                       |  | Aseptic meningitis   |                  |  |
| Other rash (location _____)   |     |                       |  | Encephalitis   |                  |  |
| Fever (max temp _____)  |     |                       |  | Myocarditis  |                  |  |
| Cough   |     |                       |  | Pneumonia  |                  |  |
| Sore throat   |     |                       |  | Pulmonary edema  |                  |  |
| Headache  |     |                       |  | Pulmonary hemorrhage   |                  |  |
| Breathing difficulty  |     |                       |  | DIC  |                  |  |
| Vomiting  |     |                       |  | Acute flaccid paralysis  |                  |  |
| Diarrhea (max stools/24 hrs _____)  |     |                       |  | ICU admission  |                  |  |
| Dehydration   |     |                       |  | Other syndrome <u>OR</u> symptom:  |                  |  |
| Stiff neck  |     |                       |  |  |                  |  |
| Muscle aches  |     |                       |  |  |                  |  |
| Paralysis   |     |                       |  | <b>Clinical history</b>  | Yes              | No   |
| Seizures  |     |                       |  | Diabetes   |                  |  |
| Altered consciousness   |     |                       |  | Hypertension   |                  |  |
| Increased sensitivity to light  |     |                       |  | Immunocompromised  |                  |  |
| Cranial nerve deficits: _____   |     |                       |  | Other:   |                  |  |
| Muscle twitches or jerks  |     |                       |  |  |                  |  |
| <b>Diagnostic and laboratory findings</b>   |     |                       |  |  |                  |  |
| CBC: Date ____/____/____ WBC _____ % Diff: Seg _____ Lymph _____ Mono _____ Eo _____ HCT _____ Platelets _____  |     |                       |  |  |                  |  |
| CSF: Date ____/____/____ OP _____ RBC _____ WBC _____ % Diff: Seg _____ Lymph _____ Mono _____ Eo _____   |     |                       |  |  |                  |  |
| Protein _____ Glucose _____   |     |                       |  |  |                  |  |
| Chest X-ray: Date ____/____/____ <input type="checkbox"/> Normal <input type="checkbox"/> Abnormal Findings _____   |     |                       |  |  |                  |  |
| Lung function tests: Date ____/____/____ <input type="checkbox"/> Normal <input type="checkbox"/> Abnormal Remarks _____  |     |                       |  |  |                  |  |
| Other pertinent labs (E-mix, viral culture, PCR, MRI, CT, etc: provide specimen sources; collection dates; test results) _____  |     |                       |  |  |                  |  |
| Local Health Jurisdiction   |     | Investigator name     |  | Telephone Number   |                  | Date ____/____/____  |
| <b>STATE USE ONLY</b> Case Counted <input type="checkbox"/> Yes <input type="checkbox"/> No Reason for case classification  |     |                       |  |  |                  |  |

# California Department of Public Health – Viral and Rickettsial Disease Laboratory

## ENTEROVIRUS ENHANCED SURVEILLANCE SUBMITTAL FORM

The California Viral and Rickettsial Disease Laboratory (VRDL) is interested in obtaining samples from patients with suspected enterovirus infections, especially unusual presentations of “hand, foot and mouth” disease; patients hospitalized with neurological symptoms where enterovirus is the suspected causative agent and especially any outbreak for which enterovirus is the suspected causative agent.

### Instructions for Submitting Samples

**When to Collect Samples**

The sooner after onset the sample is collected, the greater the probability of obtaining a viral isolate. Ideally specimens should be obtained during the acute phase of illness (within 48-72 hours of onset - when viral excretion is at its peak). Contact your local Public Health laboratory to discuss the utility of viral diagnosis and interpretation of the test results before collecting samples more than one (1) week after onset of symptoms.

**What Samples to Collect**

Overall, throat swabs are the single most useful specimen to detect enteroviruses. When lesions are present, collection of vesicle swabs significantly increases the ability to detect Enteroviruses. We are not recommending collecting stools from acute cases.

**How to Collect Samples**

Throat swabs should be taken with the aid of a tongue depressor, by carefully swabbing the lateral and posterior pharynx without touching the tongue or buccal mucosa.

For vesicle swabs, the skin was cleaned gently with 0.9% sterile normal saline, but not with alcohol, which kills viruses. A sterile 24-gauge needle was used to rupture the vesicle, and a swab was used to absorb the fluid. Alternatively, the swab was gently rolled over the vesicle to squeeze out fluid. Mouth ulcers were sampled by rolling the swab over the floor of the ulcer.

**Storage and Transportation**

Throat swabs and vesicle swabs should be placed in 1-2 ml of Viral Transport Medium (VTM). Samples should be kept at 4°C and transported to the local Public Health Laboratory within 48 – 72 hours.

**Where to Send**

**INSERT LOCAL PUBLIC HEALTH LAB INFO, or  
Viral and Rickettsial Disease Laboratory  
Specimen Receiving- Enterovirus Surveillance  
850 Marina Bay Parkway  
Richmond, CA 94804**

**Send with**

**For each patient, complete the Specimen Submittal Form below and attach either the Hospitalized Enterovirus Case Report or Outpatient HFMD Case Report**

|                                       |                                      |                         |   |  |
|---------------------------------------|--------------------------------------|-------------------------|---|--|
| Patient's last name, first name       |                                      |                         | Patient's Local Health Jurisdiction: _____  |  |
| DOB                                   | Age (with units)                     | Sex (circle):<br>M    F | Reason for submitting sample:<br><input type="checkbox"/> Suspected Enterovirus infection<br><input type="checkbox"/> Patient hospitalized with suspected Enterovirus infection<br><input type="checkbox"/> From a suspected Enterovirus outbreak |  |
| <b>HFMD/ ENTEROVIRUS SURVEILLANCE</b> |                                      | <b>Onset Date:</b>      | <b>This section for Laboratory use only.<br/>Date received and Accession Number</b>   |  |
| 1 <sup>st</sup>                       | Specimen type and/or specimen source | Date Collected          | 1 <sup>st</sup>   |  |
| 2 <sup>nd</sup>                       | Specimen type and/or specimen source | Date Collected          | 2 <sup>nd</sup>   |  |
|                                       |                                      |                         | Viral and Rickettsial Disease Laboratory<br>California Department of Public Health<br>850 Marina Bay Parkway<br>Richmond, CA 94804<br>phone (510) 307-8585                      fax (510) 307-8578  |  |

Type or print submitter's complete mailing address above

Enhanced Enterovirus Surveillance 02/17/2012

If this is an isolate (rather than an original clinical sample), please fill in below:

Submitted as cell culture isolate using passage # \_\_\_\_ of \_\_\_\_\_ cells.     Submitted as Nucleic Acid extract.  
 Source of original clinical sample: \_\_\_\_\_     Outbreak ID (if any) \_\_\_\_\_  
 Identified (or tentatively identified as) \_\_\_\_\_ by \_\_\_\_\_

Contact Name: \_\_\_\_\_ Phone # (\_\_\_\_\_) \_\_\_\_\_ Fax # (\_\_\_\_\_) \_\_\_\_\_

**Questions? Call LOCAL PUBLIC HEALTH LAB (415) 473-6849 or VRDL Medical Records Unit (510) 307-8585**