# Hand, Foot, and Mouth Disease Outbreak and Coxsackievirus A6, Northern Spain, 2011

**To the Editor:** Hand, foot, and mouth disease (HFMD) is an acute, febrile viral infection characterized by vesicular exanthema on the palms of the hands, soles of the feet, and oral mucosa. The infection is transmitted through oral and respiratory secretions, vesicular fluid, and/or feces of affected persons. The most common etiologic agents are coxsackievirus (CV) A16 and human enterovirus (HEV) 71, but other HEVs, mainly belonging to species A, have also been associated with illness (*1*). HFMD mainly affects infants and children <5 years of age.

On May 10, 2011, an outbreak of HFMD was reported in a daycare center in the city of Irun in Basque Country, Spain. Monitoring subsequently was conducted for HFMD cases among children in the health district that contained the daycare center (a total of 4,540 children <14 years of age). Children with fever and vesicular rash on the palms and/or soles and in the mouth were considered HFMD patients. Pharyngeal and/or dermal exudate and/or feces were collected for virologic confirmation from 37 representative HFMD patients (17 with multiple specimens) selected by sentinel pediatricians in outpatient clinics. Viral RNA was extracted directly from specimens (NucliSENS Easy-Mag, Bio-Mèrieux, Marcy-l'Étoile, France) and was used in the amplification methods. Enterovirus RNA was detected by an in-house real-time PCR that amplified a fragment within the 5′ untranslated region by using described primers (*2*). For genotyping, the viral

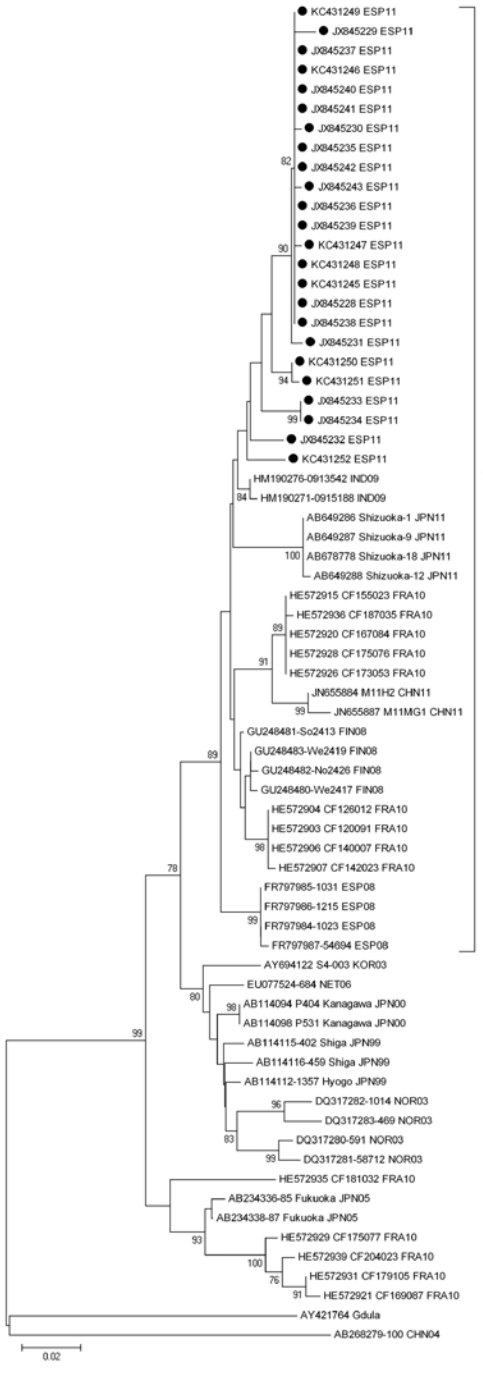


Figure. Phylogenetic analysis of the partial viral protein 1 gene sequence (positions 2929–3348, based on strain Shizuoka-18, GenBank accession no. AB678778) of coxsackievirus A6 isolated from distinct patients with hand, foot, and mouth disease detected in Irun, Spain, April–September 2011, compared with the Gdula prototype strain and other representative strains. Black dots indicate the strains in this study (GenBank accession nos. JX845228–JX845243 and KC431245–431253). The tree was constructed by using the neighbor-joining method with 1,000 bootstrap replications and shows bootstrap values >75%. Genetic distances are based on pairwise analysis by using the Kimura 2-parameter method in MEGA5.1 software (www.megasoftware.net). Bracket indicates strains showing nucleotide identity >94% and detected in outbreaks during 2008–2011. Scale bar indicates the number of substitutions per nucleotide position.

protein 1 gene was amplified by using described methods (*3*), followed by partial sequencing of the obtained amplicons by using the 3130XL Genetic Analyzer (Applied Biosystems, Foster City, CA, USA). Control measures recommended were frequent and careful handwashing with soap and running water by children and staff and increasing the cleaning of surfaces and objects in daycare centers and nursery schools.

During April–September 2011, a total of 99 cases of HFMD were notified; 53 patients were boys. Twenty-five cases occurred in the daycare center, all before May 13 (attack rate 55.6%), and 74 were community acquired, occurring mainly after that date. All cases occurred in children <4 years of age (median age 1.8 years; incidence 77 cases/1,000 inhabitants). The highest incidence occurred in children 12–36 months of age (122.4 cases/1,000 inhabitants). In addition to a papulovesicular rash on the palms, soles, and/or buttocks, 89 (90%) HFMD patients showed a perioral papulovesicular rash that did not extend to the rest of the face. None of the children were hospitalized.

Enterovirus was detected in 49 samples (28 pharyngeal, 2 dermal, 19 fecal) from 33 HFMD patients. For 30 of these patients, the samples were sufficient for genotyping. CVA6 was detected in 27 (90%) patients and CVA10 in 2 (7%) patients; for 1 patient, no genotype was obtained. Seven (7%) of the 99 children with HFMD were brought for medical assistance for onychomadesis during the 9–67 days after the HFMD episode. In 2 of them, HFMD had been virologically confirmed as being caused by CVA6.

Our results suggest that CVA6 can cause HFMD outbreaks that develop rapidly and reach a high incidence in children. Despite the mildness of the disease, the high attack rate in the daycare center alarmed families and staff. HFMD is not subject to epidemiologic surveillance in Spain, and thus its real incidence cannot be identified.

Although CVA6 has long been known to cause HFMD (*1*), it has not usually been considered to play a major role in this disease. Except in a few countries, CVA6 has been infrequently detected until recent years. However, since 2008, this virus has caused major outbreaks of HFMD in some countries of eastern Asia and Europe and, more recently, in the United States (*4*–*9*); the CVA6 strains in this outbreak shared >97% of nucleotide identities in the viral protein 1 gene and showed sequence similarity >94% with the strains that caused these outbreaks. These strains segregated in a phylogenetic tree (Figure), supporting the recent international spread of emerging CVA6 genetic variants (*4*). In Taiwan and Japan, the emergence of these strains has been associated with a change in the predominant clinical expression of the infections produced by CVA6, from herpangina before 2009 to HFMD in 2010–2011 (*7*,*8*). The development of a perioral rash has also been associated to HFMD caused by CVA6 (*10*).

Although the course of HFMD is usually self-limiting, illness and death rates vary among outbreaks. Severe illness is more frequent in outbreaks caused by HEV71 (*1*); in outbreaks caused by CVA6 in Taiwan and the United States, the illness affected a broader spectrum of skin sites and was associated with more severe and extensive rash than was HFMD caused by other coxsackieviruses (*7*,*9*).

In conclusion, reports of HFMD outbreaks associated with CVA6 are increasing. Improved HFMD surveillance is required, with virus genotyping as a key element.

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## Rabies Update for Latin America and the Caribbean

**To the Editor:** Rabies incidence in Latin America and the Caribbean has decreased and several countries (Uruguay, Chile, Costa Rica, Mexico, and Panama) and areas of Peru, Brazil, and Argentina are free of human rabies transmitted by dogs, although there are certain areas to which this disease is still endemic (*1*). Coordinated actions for regional elimination of human rabies transmitted by dogs began in 1983 in Latin America and the Caribbean with the assistance of the Pan American Health Organization (PAHO). This effort has led to an ≈90% reduction of human and canine rabies (*2*). In this region, rabies is associated with poverty and considered a neglected disease (*3*). Resolution 19 of the 49th Directing Council of PAHO in 2009 regarding neglected diseases and other infections related to poverty set a target for eliminating human rabies transmitted by dogs by 2015. PAHO is currently developing strategies to assist countries during this period (*4*).

Since 2010, a total of 111 human rabies cases transmitted by bats, dogs, and other animal species were reported from Latin America and the Caribbean: 40 transmitted by dogs and 63 by bats (Table). Although a major reduction in human rabies transmitted by dogs was observed in 2010 (only 6 cases), the total number of cases increased to 24 in 2011; most were confirmed by laboratory testing.

The higher risk areas for human rabies transmitted by dogs, for which more collaboration and financial support are urgently needed, are Haiti, Bolivia, Guatemala, Dominican Republic, and parts of Brazil (Maranhão State) and Peru (Puno Region). Unfavorable conditions in which persons in these areas are living limit control strategies and maintain rabies transmission (*3*).

According to the PAHO Epidemiologic Surveillance System for Rabies, during 2010–2012, Bolivia and Haiti had the highest incidence of human rabies transmitted by dogs in the Western Hemisphere: 15% (6/40) and 40% (16/40) of all cases, respectively (*5*). Many factors, including national disasters and social, cultural, and economic factors, have interfered with canine rabies control programs in these countries.

Bolivia has a population of 10 million, and 60.0% of the population is considered below the national poverty line. This country has poor suburbs on the outskirts of large cities, with large populations of unowned dogs and limited resources to implement dog mass vaccination campaigns and animal birth control programs. Haiti has a population of >10 million, and 77% of the population is considered below the national poverty line. In 2010, Haiti was devastated by a major earthquake that affected all sectors, including laboratory diagnosis for rabies (*6*). After the earthquake, the country was struck by a cholera epidemic. Financial resources have been diverted to control such priorities and to provide humanitarian aid. Haiti and Bolivia heavily depend on technical cooperation and donations from other governments or institutions, and are a high priority for elimination of human rabies transmitted by dogs (*7*).

Another challenge for Latin America and the Caribbean is development of a common strategy for preventing human rabies transmitted by bats, especially in remote areas in the Amazon region (Peru, Ecuador, and Brazil) and Mexico (*7*), from which 97% of human rabies cases were reported during this period. Since 2000, vampire bats have been the leading cause of human rabies in Latin America and the Caribbean (*8*). Comparison of data for 2010–2012 with data for the previous 3 years shows a 5.2% increase in bat-transmitted human rabies, especially during 2011, which accounted for ≈53% of reports during the past 3 years (*5*).

Bats have been identified as a reservoir for many *Lyssavirus* spp. genotypes, and the geographic distribution of variants has been associated with climate changes and ecologic imbalances. Spread of bats has been facilitated by human-made shelters near human dwellings (*9*).

Although rabies control in Latin America and the Caribbean has been successful, certain approaches currently used, such as mass vaccination campaigns for dogs, postexposure prophylaxis, and epidemiologic surveillance, require improvement in some countries. In addition, allocation of resources is needed to enhance national programs