

# Dermatologic Manifestations of Hand-Foot-and-Mouth Disease

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## Background

Hand-foot-and-mouth disease (HFMD) is a viral illness with a distinct clinical presentation of oral and characteristic distal extremity lesions. Most commonly, the etiologic agents are coxsackieviruses, members of the Picornaviridae family.

## Pathophysiology

Epidemic hand-foot-and-mouth disease (HFMD) viral infections are usually caused by members of the Enterovirus genus, most commonly, coxsackievirus A16, A6, or enterovirus 71. In addition, sporadic cases with coxsackievirus types A4-A7, A9, A10, B1-B3, and B5 have been reported. Infections usually occur as isolated events, but epidemics occur regularly. An outbreak of HFMD in China during 2003 was caused by echovirus 19.<sup>[1]</sup> More widespread involvement resembling eczema herpeticum, systemic involvement, and late-stage onychomadesis are characteristic of the A6 strain.

Large outbreaks of HFMD in China in recent years have shown that increasing numbers of outbreaks are caused predominantly by enterovirus 71 (86.5%), and in part by coxsackievirus A16 (6.9%). The high incidence of mixed infections with enterovirus 71 and coxsackievirus 16 (17.6% of the total coxsackievirus 16–infected cases) has never before been observed in China. A high incidence of mixed infections with enterovirus 71 and coxsackievirus 16 was also observed.<sup>[2]</sup>

The incubation period averages 3–6 days. Coxsackievirus infection is highly contagious. During epidemics, the virus is spread by horizontal transmission from child to child and from mother to fetus. Transmission occurs by means of direct contact with nasal and/or oral secretions, fecal material, or aerosolized droplets in a fecal-oral or oral-oral route. Initial viral implantation in the buccal and ileal mucosa is followed by spread to lymph nodes within 24 hours. Viremia rapidly ensues, with spread to the oral mucosa and skin. By day 7, neutralizing antibody levels increase and the virus is eliminated.

However, a study from China in 2011 showed that the neutralizing antibody response was not correlated with disease severity, suggesting that cellular immune response, besides neutralizing antibodies, could play a critical role in controlling the outcome of enterovirus 71 infection in humans.<sup>[3]</sup>

## Epidemiology

### Frequency

#### *United States*

Hand-foot-and-mouth disease (HFMD) epidemics tend to occur every 3 years in the United States.

#### *International*

Worldwide HFMD occurrences are reported. A seasonal pattern is present in temperate climates, with a peak incidence in late summer and early fall.

### Race

No racial predilection is recognized for hand-foot-and-mouth disease.

### Sex

The male-to-female ratio for hand-foot-and-mouth disease is 1:1. Recent large outbreaks of HFMD in China have shown a male-to-female ratio closer to 1.5:1.<sup>[4]</sup>

### Age

Most cases of hand-foot-and-mouth disease affect children younger than 10 years, although cases in adults are reported. Recent large outbreaks of HFMD in China have shown that 95% on infections occur in children younger than 5 years.<sup>[4]</sup>

### Clinical Presentation

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