



## HFMD is a Common Viral Illness that Causes a Rash on the Hands, Foot, and Mouth

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### Abstract

The condition caused by a virus and referred to as "hand, foot, and mouth disease" (HFMD) mostly affects children less than 5 years old. Although the occurrence of this phenomenon is possible among adults, the probability of its manifestation is significantly diminished. Multiple enteroviruses have been suspected of playing a role in the development of HFMD in humans. Poliovirus is a family of viruses that includes poliovirus, coxsackieviruses, echoviruses, rhinoviruses, and other enteroviruses. Viruses belonging to this particular family have the potential to induce pathogenic conditions in human hosts.

Most cases of HFMD are brought on by enterovirus type A (HEV-A), in particular enterovirus 71 (EV-71), which is the virus responsible for the majority of HFMD cases across the globe. Other frequent causes include the enteroviruses coxsackievirus A16 (CVA16), coxsackievirus A6 (CVA6), coxsackievirus A5 (CVA5), and coxsackievirus A10 (CVA10). In the United States, HFMD is most often brought on by a CVA16. When a person has HFMD, they will often begin to feel better on their own within seven to ten days. Although they are uncommon, complications are not impossible to have. When coxsackieviruses are identified as the etiological agents of hand, foot, and mouth disease (HFMD), a significant proportion of patients are classified as having a moderate severity level. Conversely, infections attributed to EV-71 often lead to significant problems, and in some instances, fatality may occur.

Confusion sometimes arises between the Hand, Foot, and Mouth sickness and the Foot and Mouth (F&M) illness, also known as Hoof and Mouth disease, which is a prominent condition observed in cattle, sheep, and pigs. The Hand, Foot, and Mouth illness is more often known as HFM illness. However, it is essential to keep in mind that Foot and Mouth disease is brought on by separate virus strains, and there is presently no evidence to show that there is a direct association between the two conditions. The illness that affects animals and is known as Foot and Mouth disease (F&M) is not contagious to humans. On the other hand, the disease that affects humans and is known as Hand, Foot, and Mouth Disease (HFMD) is not contagious to animals.

Enteroviruses may often be isolated from infected patients' respiratory secretions, such as mucus, saliva, and sputum, as well as from the material that makes up their feces. Throughout the course of human history, the condition known as polio has been understood to be caused by an enterovirus. However, the introduction of global vaccination campaigns directed against the poliovirus has resulted in a significant drop in the number of cases of polio around the globe. Enteroviruses that do not cause polio have a high rate of mutation, which has led to the development of a diversified collection of more than 200 strains. These A variety of illnesses, including the common cold, flaccid paralysis, aseptic meningitis, myocarditis, conjunctivitis, and hand, foot, and mouth disease, are caused by non-polio enteroviruses. These enteroviruses may also cause polio.

Hand, Foot, and Mouth Disease (HFMD) is poorly tracked globally, although recurring outbreaks imply a high prevalence. Hand, Foot, and Mouth Disease (HFMD) may strike anybody at any age; however, it is more prevalent in children less than 5 years old.

**Keywords:** Epidemiological Characteristics; Risk Factors; Hand-foot-and-mouth Disease (HFMD); Children; Pathophysiology; Differential Diagnosis; Prevention; Conclusions

## Introduction

Hand, foot, and mouth disease (HFMD), a viral disorder of considerable prevalence, mostly impacts infants and young children, but it may sometimes manifest in adults. The sickness often affects the extremities such as the hands and feet, as well as the oral cavity, and perhaps the genitalia. Coxsackievirus A type 16 is the primary etiological agent responsible for the manifestation of hand, foot, and mouth disease. Nevertheless, it is worth noting that many other strains of coxsackievirus have also been identified as potential causative agents for this particular ailment. The western Pacific region has seen a correlation between the presence of enterovirus and the occurrence of hand, foot, and mouth disease. The coxsackievirus is a member of the Picornaviridae family, which comprises non-enveloped single-stranded RNA viruses [1,2].

## Etiology

Hand, foot, and mouth disease is an example of a viral exanthem that is most often caused by the coxsackievirus, which is a member of the family of enteroviruses. The enterovirus A71 and coxsackievirus A16 serotypes are the ones that are most often found to be the underlying cause of the disease [4]. The coxsackievirus A6 has emerged as a novel cause of HFMD in the United States as well as in other parts of the world. The Coxsackievirus A10 has been connected to a number of cases of severe disease. Coxsackieviruses A4 to A7, A9, B1 to B3, and B5 have also been associated with HFMD, but much less often [4].

## Epidemiology

This virus is not confined to a particular region; rather, it may be found in all parts of the world. Outbreaks are possible at day-care centers, summer camps, and even within families. This is due to the fact that children are more prone than adults to get infected with the virus, particularly those who are under the age of seven. According to the comprehensive monitoring that was carried out in China, more than ninety percent of the HFMD cases occurred in children less than five years old. It was determined that the mortality rate was around 0.03%, and that the late spring and early summer had a larger frequency of instances than other seasons. A study that was conducted in Vietnam found that there is a correlation between the incidence of HFMD and increasing average temperatures and relative humidities in the environment [5].

In 2021, the French monitoring system saw a notable escalation in the incidence of individuals diagnosed with Hand, Foot, and Mouth Disease (HFMD), with the reported cases surpassing 3,400. The association between Coxsackievirus A6 and A16 and atypical cases has been observed, whereas over 90% of the sequenced cases have been shown to be linked to Enterovirus. Coxsackievirus A6 continues to be the predominant etiological agent responsible for the occurrence of hand, foot, and mouth disease (HFMD) within the United States [6].

## Pathophysiology

The human enterovirus may be propagated by several means, including the oral ingestion of the virus shed from the gastrointestinal or upper respiratory tract of infected hosts, as well as transmission through fluid from vesicles or oral secretions. These different routes together contribute to the dissemination of the virus. It is during the first week of their illness, when the incubation period typically spans three to six days, that patients are most prone to transmitting the infection to others. Following the ingestion of the virus, it begins replication inside the lymphoid tissue located in the lower intestine and neck, subsequently progressing to the adjacent lymph nodes. This condition has the potential to disseminate to several organs, including the integumentary system, cardiovascular system, hepatic system, and the central nervous system [7].

## History and physical

The onset of hand, foot, and mouth disease is often characterized by a low-grade fever, diminished appetite, and a general sense of discomfort. The first manifestation often reported by those afflicted with hand, foot, and mouth illness is discomfort in the oral cavity or pharynx, resulting from the presence of enanthem. The presence of vesicles is characterized by a thin halo of erythema, which, if not addressed, might eventually rupture and result in superficial ulcers with a grayish-yellow base and an erythematous border. The exanthem may have a macular, popular, or vesicular morphology. The size of the lesions varies between about 2 mm and 6 mm, and they are not accompanied by pruritus or significant pain. The duration of these lesions is generally about ten days, with a propensity to rupture, resulting in painless, superficial ulcers that do not result in scarring. The exanthem has the capacity to affect several regions of the body, including the dorsum of the hand, foot, buttocks, legs, and arms. The most often seen oral lesions are ulcers found on the buccal mucosa and tongue. Nevertheless, it is worth noting that lesions on the soft palate may also occur.

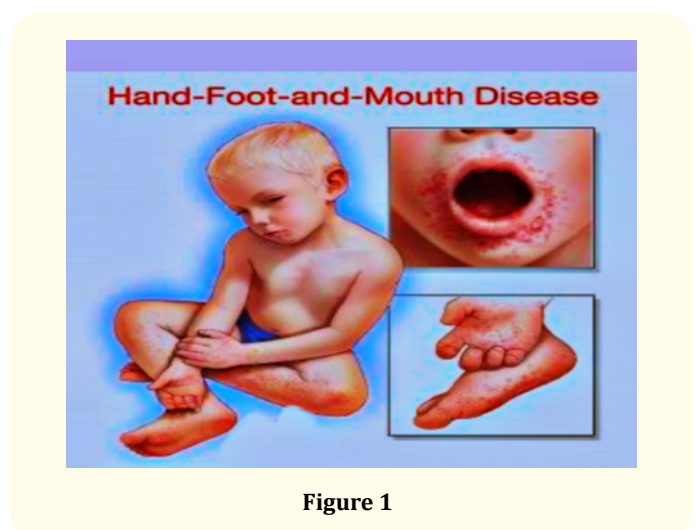


Figure 1

HFMD may sometimes manifest with atypical symptoms, including the simultaneous occurrence of aseptic meningitis. Enterovirus infections are well-documented for their impact on the central nervous system (CNS) and their association with several neurological conditions, including encephalitis, polio-like syndrome, acute transverse myelitis, Guillain-Barre syndrome, benign intracranial hypertension, and sudden cerebellar ataxia. Enterovirus infections are the underlying cause of hand, foot, and mouth disease [7].

### Evaluation

The use of clinical examination is often employed in order to establish a diagnosis of hand, foot, and mouth disease. The presence of the virus in the stool may typically be detected about six weeks post-infection. However, the duration for viral shedding from the oropharynx is often shorter, usually less than four weeks. Distinguishing between the herpes simplex virus and the varicella-zoster virus may be achieved by the use of light microscopy on biopsies or scrapings of vesicles. While serology may not possess high sensitivity in diagnosing Hand, Foot, and Mouth Disease (HFMD), it may still be used to monitor patients' recovery status by measuring IgG levels.

Serology is used by several medical institutions to differentiate between enterovirus 71 and coxsackievirus, since this differentiation has significance in terms of prognostic implications. Currently, a significant proportion of medical establishments possess readily available polymerase chain reaction (PCR) assays that may be used to validate the diagnosis of coxsackievirus. The use of real-time polymerase chain reaction (PCR) assays enables the assessment of viral infection in a lesion by analyzing a swab sample for the presence of coxsackievirus or enterovirus [8].

### Differential diagnosis

When considering the differential diagnosis for Hand, Foot, and Mouth Disease (HFMD), it is important to include other medical disorders that exhibit maculopapular or vesicular rashes, with or without oral lesions. The aforementioned circumstances encompass: Erythema multiforme is a dermatological condition characterized by the development of distinct skin lesions, often in response to an Herpangina is a viral infection that primarily affects children, characterized by the development of Herpes simplex is a viral infection caused by the herpes simplex virus (HSV).

Herpes zoster, also known as shingles, is a viral infection caused by the reactivation of the varicella-z. Kawasaki disease is a pediatric vasculitis that mostly affects children under the age of five.

Toxic epidermal necrolysis (TEN) is a severe and potentially life-threatening dermatological condition characterized by widespread skin detachment and necrosis.

Viral pharyngitis is a medical condition characterized by inflammation of the pharynx caused by viral pathogens.

Rocky Mountain spotted fever (RMSF) is a tick-borne infectious disease caused by the bacterium *Rickettsia rickettsii*. It is mostly transmitted to humans by the bite of infected.

Varicella zoster infection, often known as chickenpox, Steven-Johnson syndrome (SJS) is a severe and rare adverse drug reaction characterized by a combination of symptoms, including skin.

In the context of a current epidemic, it is crucial to acknowledge the challenge associated with effectively distinguishing between monkeypox and hand, foot, and mouth disease (HFMD) based on clinical presentation [9].

### Prognosis

Individuals who have received a diagnosis of hand, foot, and mouth illness might anticipate a favorable prognosis. A significant proportion of patients get complete restoration of health within a few weeks, without encountering any subsequent consequences. Acute illnesses often have a duration of around 10 to 14 days, with a low likelihood of recurrence or persistent infection. The hand, foot, and mouth disease has the potential to result in significant complications in some individuals. The aforementioned outcomes include the following effects:

- The prolonged duration of stomatitis has been associated with the emergence of distressing ulcers. There is a potential for the intensity of the discomfort to hinder one's ability to consume food, hence increasing the risk of dehydration, especially among younger individuals.
- The occurrence of aseptic meningitis is feasible; however, it is important to note that enterovirus 71 is far more probable as the causative agent for this particular illness. When comparing this particular virus to the coxsackie virus, it has been shown that the former is associated with a much higher prevalence of neurological complications. Possible results for the afflicted individual include acute cerebellar ataxia, a polio-like disorder, encephalitis, benign intracranial hypertension, and Guillain-Barre syndrome. The prevailing belief is that the virus is accountable for inducing harm to the gray matter, leading to motor dysfunction.
- Interstitial pneumonia, myocarditis, pancreatitis, and pulmonary edema are all illnesses that are brought on by coxsackievirus extremely seldom. Interstitial pneumonia is the most common of these.
- Several studies suggest a potential association between coxsackievirus infections and spontaneous abortions [10].

### Deterrence and patient education

The dissemination of knowledge to patients and parents plays a crucial role in the efforts to combat the transmission of hand, foot, and mouth disease (HFMD) within the pediatric population and between children and adults. Research has shown that adhering to a routine of frequent handwashing is a very efficacious strategy

in combating the transmission of Hand, Foot, and Mouth Disease (HFMD). A study including community intervention revealed that comprehensive education on appropriate hand hygiene practices resulted in enhanced personal hygiene among the participants, including their children. Consequently, there was a decrease in the incidence of Hand, Foot, and Mouth Disease (HFMD) seen among the study participants. Due to the potential risk of the child contracting a life-threatening illness, it is advisable for parents to exercise care by ensuring that the youngster avoids contact with others who have impaired immune systems [11,12].

### Laboratory testing

The diagnostic kits for pan-enterovirus, EV71, and Cox A16 that are now available on the market have been developed and manufactured following the established protocols provided by the Centers for Disease Control and Prevention (CDC).

### Treatment/Management

Hand, foot, and mouth illness is characterized by a relatively benign clinical condition and often exhibits a self-limiting course, with resolution occurring within a period of 7 to 10 days. The main approach to treatment is mostly based on providing assistance. The management of pain and fever may be achieved by the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen. Ensuring enough hydration of the patient is of paramount importance. Moreover, the combination of liquid ibuprofen and liquid diphenhydramine may be used as a gargling solution, serving to envelop the ulcers and alleviate discomfort. The use of steroids has been seen to elevate the likelihood of experiencing severe Hand, Foot, and Mouth Disease (HFMD) [13].

In response to the significant neurological implications linked to enterovirus 71-induced hand, foot, and mouth disease, researchers have devised specific pharmaceutical interventions throughout the last decade to manage this illness. As of the present, no medicinal intervention has received official authorization. Nevertheless, emerging substances, including molecular decoys, translation inhibitors, receptor antagonists, and replication inhibitors, have encouraging prospects as prospective therapeutic approaches. Pleconaril, an antiviral medicine with anti-picornaviral properties, shows promise as a therapeutic agent for the management of enterovirus 71 infection. Currently, there is a lack of licensed antiviral treatments for the management of Hand, Foot, and Mouth Disease (HFMD). Some anecdotal reports have shown a clinical response to acyclovir, however no large-scale investigations have yet confirmed this [14].

Various kinds of vaccine candidates targeting Hand, Foot, and Mouth Disease (HFMD) and enteroviruses have been developed. Currently, China has developed strain-specific inactivated whole-virus aluminum-adjuvant vaccines. These vaccinations have been authorized for widespread usage. In a clinical study including 10,077 participants, the EV71 C4a vaccine was administered in a three-dose regimen. The results showed that this vaccination

protocol conferred protection for a duration of almost two years. The overall efficiency of the vaccine was found to be 94.7%, with a 95% confidence range ranging from 87.8% to 97.6%. Vaccinations targeting virus-like particles (VLPs), DNA-based vaccinations, peptide-based vaccines, and subunit vaccines have all been developed and are now undergoing clinical evaluation at different stages [15].

### Preventive measures

Hand, foot, and mouth disease is mostly attributed to highly contagious viral pathogens. The transmission of the sickness may often occur prior to the host's conscious recognition of their own state of unwellness. By adhering to these principles pertaining to appropriate hygiene practices, individuals have the potential to either cease or substantially diminish the transmission of the disease.

It is advisable to use the practice of coughing and/or sneezing into the crook of your elbow.

It is advisable to engage in the practice of cleaning and disinfecting frequently touched objects, such as toys, countertops, and doorknobs.

It is advised to refrain from engaging in the practice of lending or borrowing items from others, including a range of objects such as eating utensils, beverages, towels, blankets, or garments.

It is advisable to implement measures that facilitate the physical segregation of ill children from those who are in good health to the greatest extent feasible.

It is important to engage in the regular maintenance of one's child's garments, bedding, and any other soiled items by means of thorough cleansing.

It is recommended to consistently use soap and water as the primary method for hand hygiene, ensuring a minimum duration of 20 seconds for thorough scrubbing on each instance [16].

### Conclusions

The prompt highlights the significance of understanding the temporal, geographical, and socio-demographic distribution of severe Hand, Foot, and Mouth Disease (HFMD) as well as other clinical risk factors in order to facilitate prompt diagnosis and treatment. In light of the clinical and epidemiological characteristics associated with severe Hand, Foot, and Mouth Disease (HFMD), it is imperative for public health and medical practitioners to implement targeted interventions for the pediatric population.

Many potential discoveries pertaining to hand, foot, and mouth disease (HFMD) might be inferred. Hand, Foot, and Mouth Disease (HFMD), a relatively benign viral infection, often afflicts young children, but it may also manifest in older persons.



Enteroviruses such as A16, 71, and A6132 are responsible for the onset of Hand, Foot, and Mouth Disease (HFMD). These viruses have the potential to manifest unique clinical signs and exhibit novel patterns of disease transmission.

Hand, Foot, and Mouth Disease (HFMD) is highly contagious and is transmitted by the exchange of body fluids or fecal matter. The potential consequences include the initiation of epidemics inside educational institutions and childcare facilities.

Symptoms such as fever, oral lesions, and cutaneous eruptions on the hands and feet are often seen in cases of Hand, Foot, and Mouth Disease (HFMD). In certain cases, individuals may get meningitis, encephalitis, paralysis, and nail loss.

Currently, there is a lack of available vaccines or therapeutic interventions for Hand, Foot, and Mouth Disease (HFMD). The majority of persons have spontaneous recovery during a period of 7 to 10 days without the need for medical intervention<sup>15</sup>. Hydrating oneself, refraining from consuming heated meals, and using analgesic medications may perhaps provide relief.

The most effective approach for preventing Hand, Foot, and Mouth Disease (HFMD) is frequent handwashing, avoidance of contact with those who are unwell, and regular disinfection of surfaces and objects.

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