

Coxsackievirus infection (Hand, foot and mouth disease)

What is a Coxsackievirus?

The Coxsackieviruses are common pathogens causing a number of diseases, of which the most common is hand, foot and mouth disease (HFMD).

Virology

The Coxsackieviruses are RNA viruses of the *Picornaviridae* family, *Enterovirus* genus which includes echoviruses and polioviruses. Infections are often asymptomatic. They are divided into groups A and B:

- Coxsackievirus A:
 - Usually affects skin and mucous membranes.
 - Causes herpangina and HFMD.
 - There are a number of different viruses within the group. The most common causes of HFMD are Coxsackievirus A16 (CA16) along with the closely related enterovirus 71 (EV71).
- Coxsackievirus B:
 - Usually affects the heart, lungs, pancreas and liver.
 - Causes Bornholm disease, hepatitis, myocarditis and pericarditis.

Coxsackieviruses of both types are a leading cause of aseptic meningitis. They may also cause nonspecific febrile and upper respiratory tract illnesses.

Spread is usually from the faeco-oral route or oral-oral route, with an incubation period of 2-6 days.

The virus is named after the town of Coxsackie in New York State.

Epidemiology^[1] ^[2]

Infection with this group of enteroviruses is very common. In temperate climates, it is most frequent in summer and autumn and, in the tropics, all year round.

Enterovirus disease, particularly HFMD tends to affect those aged under 10 but children of any age and adults can also be affected. It occurs worldwide, both on a sporadic basis and in epidemics. There have been a number of serious outbreaks of HFMD in the Western Pacific region. China has led the quest for vaccines, following a major outbreak with fatalities.

In the UK outbreaks occur regularly in nurseries, schools and childcare centres. Most adults have developed immunity.

Coxsackievirus symptoms

Hand, foot and mouth disease^[1]

- Most often caused by CA16 and the closely related EV71. Subtypes A 6 and 10 can also cause it but it can result from infection with other group A or B viruses^[3] ^[4] .
- Usually a mild illness with a prodromal phase, followed by tender oral ulcerative lesions and then usually maculopapular lesions on the hands and feet.
- Rarely there are neurological or other complications which can be very severe.
- See the separate article [Hand Foot and Mouth Disease](#) for more information.

Herpangina^[5]

- Incubation period of about four days.

- Affects mainly children up to the age of 10.
- Mild pyrexia, headache, sore throat, dysphagia, loss of appetite and sometimes vomiting and abdominal pain occurring.
- Red spots appear on the uvula, soft palate and tonsils which develop into tiny grey-white papulovesicles, about 1 mm or 2 mm in diameter .
- There is an erythematous halo, which progresses to a shallow ulcer.
- It is caused mainly by CA16 but can involve other Coxsackievirus A serotypes and occasionally Coxsackievirus B (serotypes 1-5).
- It resolves uneventfully in 5-10 days.

Bornholm disease

- Usually caused by Coxsackievirus B.
- Pain on inspiration is similar to pleuritic pain and pulmonary embolism may be suspected. The muscles are locally tender.
- Fever, headache or nonspecific abdominal pain – either as prodromal symptoms or with the onset of chest pain. May be myalgia elsewhere.
- Duration is normally a few days, but may be ≤ 3 weeks; it can recur/relapse.

See the separate article [Bornholm Disease](#).

Myocarditis

- Coxsackievirus B is one of the more common causes of myocarditis, with potential to progress to dilated cardiomyopathy^[6] .
- Viral myocarditis may be asymptomatic, or may present with symptoms of heart failure and left ventricular dysfunction.

See the separate article [Myocarditis](#) for more information.

Pericarditis

- Coxsackievirus B is one of the more common causes of pericarditis.

- The cardinal presenting symptom is [chest pain](#).

Aseptic meningitis^[7]

- Coxsackieviruses are one of the most common causes of aseptic (viral) meningitis.
- In particular A and B viruses are involved.
- There is a peak in summer months.

See the separate article [Meningitis](#) for more information.

Other clinical conditions

- Coxsackie A viruses can cause a [haemorrhagic conjunctivitis](#).
- Coxsackievirus B5 causes pustular stomatitis with [erythema multiforme](#).
- Coxsackievirus A4 causes a widespread vesicular eruption.
- There has been some investigation into Coxsackievirus B4 as a possible part of the aetiology of [type 1 diabetes mellitus](#). There are also possible associations of Coxsackieviruses with postviral fatigue syndromes, [Reye's syndrome](#) and [pancreatitis](#).
- Coxsackievirus B1 has been reported as causing severe infection and death in neonates in America in 2007–2008^[8].

Investigations^[1]

Usually diagnosis is clinical but some laboratory tests are available.

- The virus can be isolated from throat, vesicle or rectal swabs (placed in viral transport medium) or from faecal culture. Viral shedding in faeces can be intermittent so more than one specimen may be required.
- IgM with enzyme-linked immunosorbent assay (ELISA) can aid diagnosis. Blood samples are required in the acute phase because IgM disappears rapidly.

- Polymerase chain reaction (PCR) has made enteroviral subtyping possible and is increasingly the test of choice in specialist centres, although rarely used in routine clinical practice.

Coxsackievirus treatment^[1]

- There is no known treatment for Coxsackievirus infections, so management is supportive
- For HFMD/herpangina:
 - Reassurance, and encourage adequate fluid intake.
 - Antipyretic analgesics such as paracetamol and ibuprofen are the main treatment.
 - Topical oral analgesic options are available although there is no evidence of efficacy and some cannot be used by children. Examples are lidocaine oral gel, benzydamine oral rinse or spray, choline salicylate oral gel, warm salty mouthwashes.
- For other conditions:
 - Antiviral agents are not indicated. One research study found that interferon- β may be useful in the management of Coxsackie B myocarditis^[9].

Advice for pregnant women^[1]

- There are no known adverse consequences for the fetus if a pregnant woman is in contact with HFMD.
- Seek specialist advice if a woman develops HFMD within three weeks of expected delivery, as there may be a risk of passing the infection to the newborn. In rare cases this can lead to severe infection in the neonate, although usually illness is mild.
- Coxsackievirus B may cause an increase in early spontaneous abortions, stillbirths and (rarely) fetal myocarditis^[10] ^[11].

Coxsackievirus prognosis^[1]

These diseases tend to be self-limiting, although there are occasional case reports of adult fatalities.

The prognosis of HFMD is excellent, with the vast majority resolving spontaneously in 5–10 days. Those cases caused by Coxsackieviruses have less risk of developing neurological complications than those caused by EV71, although they can do very occasionally.

Aseptic meningitis usually resolves without sequelae but encephalitis is more likely to have adverse outcomes.

Although prognosis for those with Coxsackie B myocarditis or pericarditis is generally good, there are risks of complications such as dilated cardiomyopathy, dysrhythmias, cardiac failure and sudden cardiac death.

Coxsackievirus prevention

Good hygiene measures reduce spread of Coxsackieviruses within the family. Advise careful handwashing and drying after using the toilet. Advise against sharing cups, eating utensils, towels and clothing. Advise covering of the mouth and nose when coughing and sneezing, and hygienic disposal of tissues used.

China has led the way with development of, and clinical trials for, a vaccine to protect against HFMD and Coxsackieviruses. Plans for an immunisation strategy against EV71 are underway in China but a vaccine for Coxsackievirus A16 has not yet been successful^{[12] [13] [14]}.

Further reading

- [Zhang M, Wang H, Tang J, et al](#); Clinical characteristics of severe neonatal enterovirus infection: a systematic review. *BMC Pediatr.* 2021 Mar 15;21(1):127. doi: 10.1186/s12887-021-02599-y.

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