

Enterovirus infections: main types related to clinical syndromes

Infecções por enterovírus: principais tipos relacionados às síndromes clínicas

Fabrício Caldeira Reis^{1*} , Alex Domingos Reis² , Bráulio Caetano Machado³ , Rita de Cássia Compagnoli Carmona³ 

¹ Secretaria Municipal de Meio Ambiente de Avaré, Avaré, SP, Brasil.

² Laboratório de Sequenciamento em Larga Escala, Faculdade de Medicina da Universidade de São Paulo, São Paulo, SP, Brasil. 

³ Núcleo de Doenças Entéricas, Centro de Virologia, Instituto Adolfo Lutz, São Paulo, SP, Brasil. 

*Corresponding author/Autor de correspondência: fabricao.aldeira@avare.sp.gov.br

Received/Recebido: 15.04.2026

Accepted/Aceito: 04.09.2026

Publication/Publicação: 16.10.2026

Editor-in-chief/Editor Chefe: Adriana Bugno

ABSTRACT

This narrative review highlights recent advances in the understanding of enterovirus infections and the main enterovirus types associated with clinical syndromes, synthesizing current knowledge of type-specific manifestations. We searched PubMed®, Scientific Electronic Library Online (SciELO), and Virtual Health Library (VHL) for articles published between 2010 and 2025. The search used descriptors and/or keywords in Portuguese and English: “enterovirus infection disease”, “enterovirus infection genotypes”, “enterovirus infection pathogenic”, and “enterovirus clinical syndromes”, focusing on recent studies addressing enterovirus infections and the types most commonly associated with clinical syndromes. A total of 78 articles were selected for analysis. The review examined the distribution of enteroviruses by species, recommended clinical specimen types for diagnosis according to clinical presentation, and the major enterovirus types and their associated clinical syndromes. Numerous studies have demonstrated the epidemic potential and genetic diversity of enteroviruses, revealing patterns of endemic circulation. However, the mechanisms underlying the ability of a wide variety of enterovirus types to infect the same tissue remain poorly understood.

Keywords. Enterovirus Infections, Syndrome, Serotype.

RESUMO

Este artigo apresenta uma revisão narrativa destacando os avanços recentes na compreensão das infecções por enterovírus e os principais tipos associados às síndromes clínicas, auxiliando na consolidação do conhecimento atual sobre manifestações específicas de cada tipo. Foi realizada uma busca bibliográfica por artigos publicados entre 2010 e 2025 nas seguintes bases de dados *online*: PubMed®, Scientific Electronic Library Online (SciELO) e Virtual Health Library (VHL). Utilizaram-se descritores e/ou palavras-chave em português e inglês: “doença por infecção por enterovírus”, “genótipos de infecção por enterovírus”, “patogenicidade da infecção por enterovírus” e “síndromes clínicas por enterovírus”, com foco em estudos recentes que abordam infecções por enterovírus e os tipos mais comumente associados a síndromes clínicas. Um total de 78 artigos foi selecionado para análise. Esta revisão examinou a distribuição de enterovírus por espécie, os tipos de amostras clínicas recomendadas para o diagnóstico de infecções por enterovírus com base na apresentação clínica e caracterizou os principais enterovírus, seus genótipos e as síndromes clínicas associadas. Numerosos estudos demonstraram o potencial epidêmico e a diversidade genética dos enterovírus, revelando padrões de circulação endêmica. No entanto, os mecanismos subjacentes à grande variedade de tipos que podem infectar o mesmo tecido ainda são pouco compreendidos.

Palavras-chave. Infecções por Enterovírus, Síndrome, Sorotipo.

INTRODUCTION

Enteroviruses (EVs) are associated with a wide spectrum of clinical diseases in humans and affect various organs (**Figure 1**). Clinical manifestations range from nonspecific febrile illness to severe diseases such as acute flaccid paralysis, encephalitis, aseptic meningitis, perinatal-disseminated enteroviral disease, myocarditis, pericarditis, pleurodynia, respiratory illnesses, exanthemas, enanthems, conjunctivitis, uveitis, gastroenteritis, hepatitis, arthritis, pancreatitis, and chronic infections in immunocompromised hosts¹. This diversity is particularly evident among coxsackieviruses, which comprise 27 identified genotypes and exhibit considerable phenotypic overlap, underscoring the complex relationship between viral genetic variability and disease manifestation².

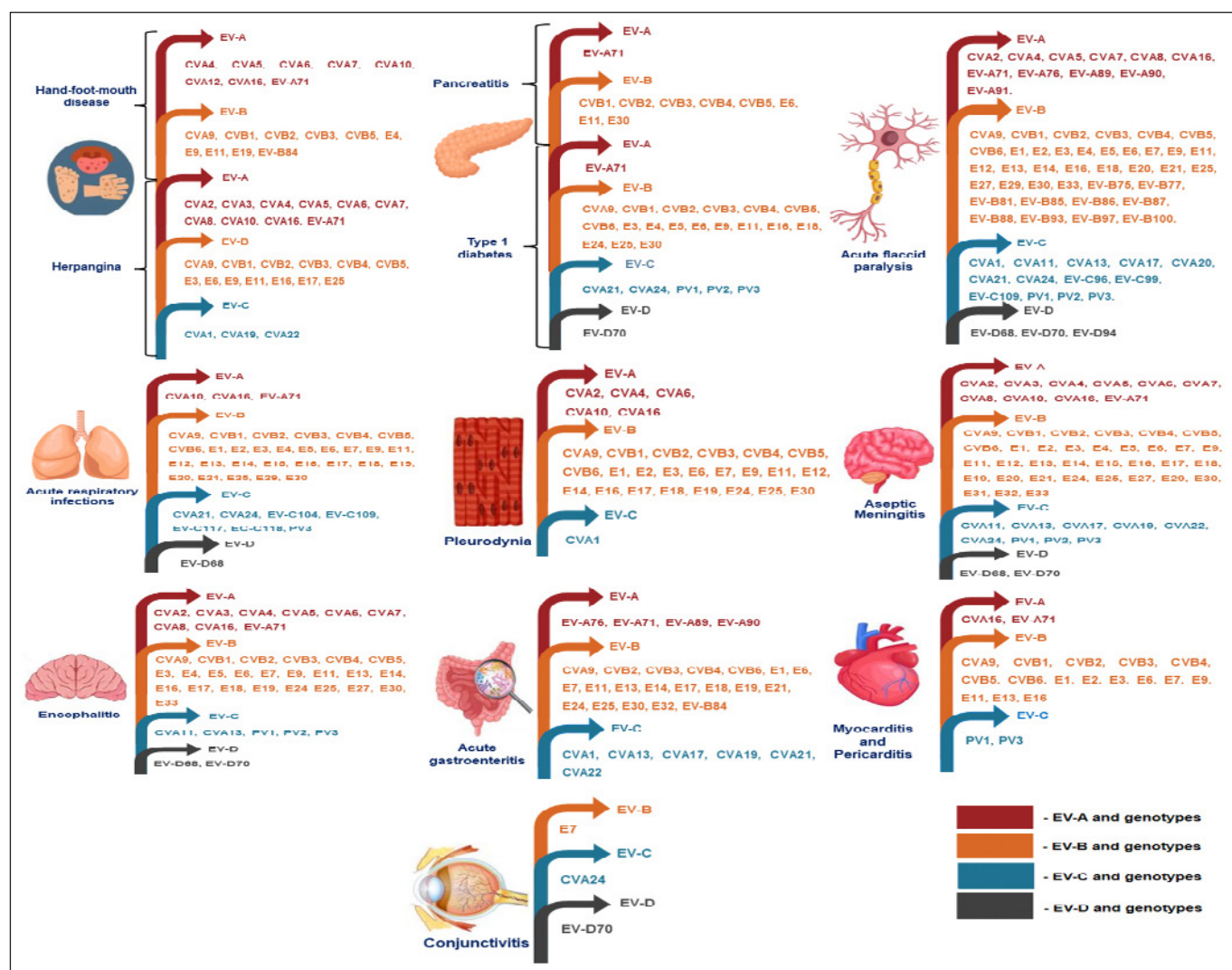


Figure 1. Main enterovirus genotypes and clinical syndromes. CV – Coxsackievirus; E – Echovirus; EV – Enterovirus; PV – poliovirus

Adapted from Picornavirus Home³

The license terms of illustrations can be found at <https://br.freepik.com/>

EVs are a group of non-enveloped, positive-sense, single-stranded RNA (ssRNA) viruses and belong to the order *Picornavirales*, family *Picornaviridae*, genus *Enterovirus*. The genus *Enterovirus* has been divided into 15 species based on genetic characteristics; major members include poliovirus (PV), coxsackievirus (CV), echovirus (E), enterovirus (EV), and rhinovirus (RV). Over 100 EV types have been associated with several human diseases. Of these, 45 have been discovered in the past 10 years, all of which are classified into four species: *Enterovirus alphacoxsackie* (formerly *Enterovirus A—EV-A*), *Enterovirus betacoxsackie* (formerly *Enterovirus B—EV-B*), *Enterovirus coxsackiepol* (formerly *Enterovirus C—EV-C*)⁴. EV-A consists of 25 types; EV-B consists of 63 types; EV-C consists of 23 types; and EV-D consists of five types⁵. Following enterovirus exposure, viral replication occurs in the oropharynx and the intestinal tract. Viremia follows, which may result in infection of central nervous system cells. After focusing on polioviruses, recent studies have examined virion structures, receptor-host interactions, decapsulation, and other characteristics of non-polio enteroviruses (NPEVs)⁶. The World Health Organization (WHO) recommends surveillance of EVs as part of the global action plan for poliovirus elimination, including data on NPEVs such as detection, outbreak response, and monitoring of EVs associated with serious illnesses⁵.

EVs are excreted in the feces of infected individuals. They are generally detectable in sewage, water resources, treated drinking-water supplies, and some foods. Age is associated with clinical presentation occurring most frequently in children under 10 years old⁷.

The five most prevalent NPEV types globally are CVA6, EV-A71, CVA16, EV-D68, and E-30, though their distribution varies by region. Data from established surveillance systems in the USA, Europe, and Asia support this distribution, showing co-circulation of EV-A, EV-B, and EV-D species with varying degrees of prevalence⁸. The COVID-19 pandemic interrupted NPEV circulation in 2020, followed by a rebound with diminished genotype diversity⁹.

MATERIAL AND METHODS

Narrative reviews synthesize qualitative research findings and summarize quantitative results derived from studies employing diverse methodologies or theoretical concepts¹⁰. This review was conducted using keywords and descriptors defined by the Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH): “enterovirus infection disease”, “enterovirus infection genotypes”, “enterovirus infection pathogenic”, and “enterovirus clinical syndromes”, in both Portuguese and English. We focused on recent studies on enterovirus infections and the main types associated with clinical syndromes.

We searched in PubMed®, Scientific Electronic Library Online (SciELO), and Virtual Health Library (VHL) for articles published between 2010 and 2025. Duplicate articles were excluded. We initially screened titles, abstracts, and keywords to exclude irrelevant studies. We then reviewed full-text articles and excluded those that did not meet the inclusion criteria. We also removed unavailable articles.

We categorized the remaining articles by clinical syndromes and topics of interest, including: pathogenic features of enteroviruses; infections of the central nervous system, heart, eyes, skin, and mucous membranes; skeletal muscle infections; other clinical manifestations; diagnostic approaches; therapeutic strategies; and vaccines targeting enteroviruses.

This review provides an overview of enterovirus infections and the primary types associated with various clinical syndromes. Because circulating enteroviruses are increasingly diverse and associated

with severe and emerging clinical syndromes, this review aims to consolidate current knowledge on type-specific manifestations. Understanding these correlations is essential for improving surveillance, diagnosis, and public health response strategies.

RESULTS AND DISCUSSION

The search using the specified descriptors identified 7,013 articles. Of these, 2,105 were duplicates across one database, leaving 4,908 articles for initial screening. After title and abstract review, 4,510 articles were excluded because they did not meet the inclusion criteria. We sought the remaining 398 articles for retrieval. However, five articles were not available for retrieval. From the 393 full-text articles assessed for eligibility, 315 were excluded. After the full-text assessment, 78 studies remained and were included in this review (Figure 2).

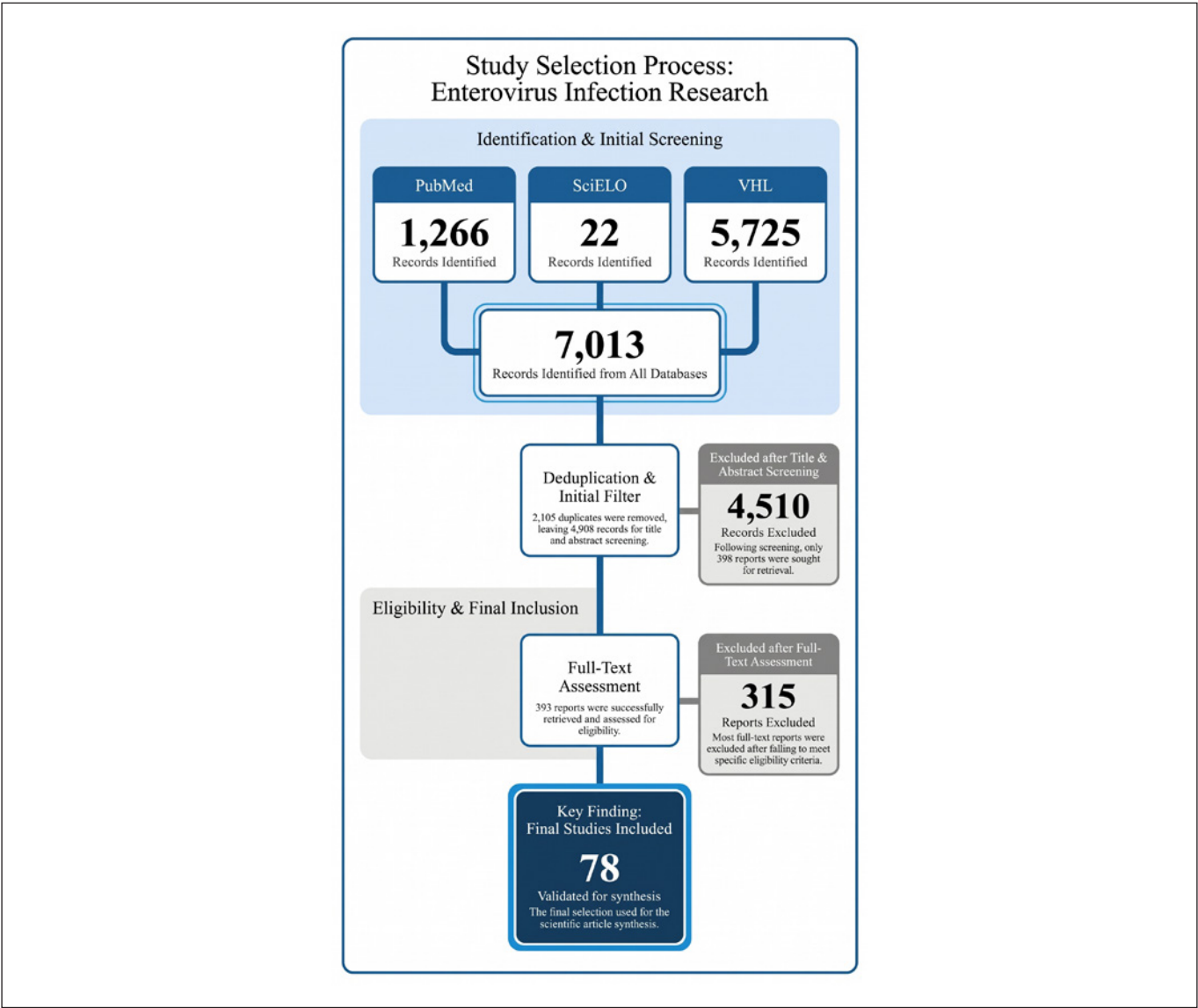


Figure 2. Flowchart summarizing the identification, screening, and inclusion of studies. VHL – Virtual Health Library Portal

Pathogenic feature of enterovirus

EVs are transmitted through fecal-oral and transplacental routes and via respiratory droplets spread¹¹. EVs enter the cell through receptor-mediated endocytosis. The host factor phospholipase A2 group XVI was identified as a universal EVs host factor that facilitates the displacement of viral genomes from virus-containing endocytic vesicles¹². After binding to its cognate receptor and entering the cell, the virus uncoats, releasing the positive-sense RNA genome into the cell cytoplasm. Host ribosomes translate the viral RNA into a single polyprotein, which is then catalytically cleaved. Capsid proteins assemble, and the virus packages newly synthesized positive-sense viral RNA into the virion. Enteroviruses (EVs) primarily replicate in the epithelial cells of the oropharyngeal and intestinal mucosa. Although they exhibit characteristic tissue tropisms and can infect various target cells such as neurons and cardiomyocytes, replication in enterocytes can trigger a viremia. This viremia leads to a second stage of replication in reticuloendothelial tissues (lymph nodes and spleen), subsequently enabling the virus to disseminate to the organs for which it has specific tropism¹³. Autophagy has been described as an important factor for the replication and survival of some EVs. The rapid expansion and regeneration of the tissue, along with low levels of autophagy in neural progenitor cells (NPCs), may explain their susceptibility to EV infection, as CVB has been shown to replicate preferentially in cells undergoing active proliferation¹⁴. Some studies indicate that apoptosis is a major pathogenic feature of EV infection, resulting in host cell death and tissue damage, and Enteroviral proteases cleave host factors and then lead to cellular or tissue malfunctions, such as apoptosis, translation shutdown, and cytokine suppression, causing pathogenesis¹⁵.

Central nervous system infections

Aseptic meningitis (AM): meningitis is an inflammatory process in the layers of the brain and spinal cord meninges. The infection affects the arachnoid layer, pia mater, and the cerebrospinal fluid. The inflammatory process extends along the subarachnoid space of the spinal cord and brain, involving the ventricles, characterizing a clinical condition of neurological alteration¹⁶. EVs cause more than 90% of cases, and clinical manifestations change from a benign course to severe manifestations, depending on the patient's age, immune status, and etiologic agent¹⁷. Polioviruses, echoviruses, and coxsackieviruses A and B1, B2, and B5 are key etiologic agents¹⁸. Among these types, the most common are CVB, CVA9, E4, 6, 9, 11, 13, 18, and 30¹⁹⁻²¹.

Encephalitis: encephalitis is an inflammatory process in the brain, usually due to infection, and rash and diarrhea are important clinical features that help to distinguish enteroviral encephalitis from other forms²². The most commonly described symptoms are headache, drowsiness, altered level of consciousness, seizures, focal deficits, papilledema, behavioral changes, sensorium, flaccid muscle weakness, focal neurological findings, mental status changes, and coma²³. Some enteroviruses can cause a persistent infection in the CNS and lead to neurodegenerative diseases. Evidence suggests a correlation between the development of the neuroimmune system and enteroviral neuroinvasion²⁴. Encephalitis has been described in infections with EV-A71, EV-B75, EV-A76, EV-A89, CVA2, CVA9, CVA10, CVB1, CVB5 and echoviruses E4, E5, E6, E9, E11, E19, E17, E21 and E30^{25,26}. Recently, a systematic review of observational studies evaluated the global epidemiology of EV types causing CNS infections, and EV-A71 was the most common associated with encephalitis, followed by E30 and E18^{27,28}.

Acute flaccid paralysis/Acute flaccid myelitis: acute flaccid paralysis (AFP)/acute flaccid myelitis (AFM) is a serious neurological disease that causes weakness or paralysis of the limbs, affecting mainly children, similar to poliomyelitis caused by PV types 1, 2, and 3²⁹. Despite the severity of his condition, only 0.1-1% of PV infections result in AFP of the limbs, meaning many wild poliovirus infections occur silently³⁰. Poliomyelitis is being eradicated through measures implemented worldwide to strengthen epidemiological and laboratory surveillance actions and intensive vaccination campaigns³¹.

In this scenario, NPEVs have assumed an increasingly important role in cases of paralytic illnesses, mainly emerging enteroviruses EV-D68 and EV-A7³²⁻³⁴. Other types considered common have also been frequently detected, such as CVA2, CVA4, CVA13, CVB3, CVB5, E6, E7, E11, E13, E30, and E18. This disease has also been associated with the more recently identified emerging types CVA12, CVA11, EV-A90, EV-C99, EV-C105, and EV-C109^{27,33,35,36}. Notably, a novel recombinant form of Echovirus 11 (E11) detected in Spain in 2022 was associated with a case of acute flaccid paralysis (AFP), expanding the spectrum of enterovirus types linked to paralytic disease³⁷.

Heart infections

Myocarditis and pericarditis: myocarditis results from an external inflammatory trigger that induces the host's immune response, ranging from a minimally transient response to a cellular infiltration. If the immune system does not eliminate the infectious pathogen early, a chronic infection develops with or without an accompanying inflammatory process. In fulminant cases of myocarditis, resulting in myocyte necrosis, there may be significant loss of contractile tissue, accompanied by rapid development of heart failure and early host death³⁸. One of the most prevalent and most intensely studied myocarditis-causing viruses is CVB3³⁹. Pericarditis is characterized by the expansion and inflammation of the pericardium, the membrane that surrounds the heart. The most common cause of myocarditis and pericarditis in adults is CVB viruses, which have been identified in up to 50% of viral cardiac cases⁴⁰.

Eye infection

Acute hemorrhagic conjunctivitis (AHC): AHC is a highly contagious enterovirus infection of the conjunctiva and cornea⁴¹. Symptoms include abrupt-onset of red eye, pain, photophobia, eyelid edema, foreign body sensation or irritation, excessive tearing and eye discharge, follicular reaction, and subconjunctival hemorrhage. EV-D70 and CVA24 cause most cases and outbreaks of AHC^{41,42}. The disease is transmitted person-to-person or through sharing of contaminated personal care items. Outbreaks of AHC due to CVA24 may recur in the same location after a considerable period, and public health precautions are necessary to control the epidemic. Many countries have reported extensive outbreaks of AHC due to CVA24⁴³. In 2023, metagenomic sequencing confirmed the re-emergence of the Coxsackievirus A24 variant (CV-A24v) genotype IV as the causative agent, with the strains showing high genetic similarity to contemporaneous strains circulating in China and carrying novel mutations in the VP1 protein⁴⁴. Similarly, Bhutan reported more than 10,000 AHC cases in 2023, with CV-A24v genotype IV forming a new genetic lineage distinct from prior strains (2002-2017), confirming the regional re-emergence of this variant across South and Southeast Asia⁴⁵.

Skin and mucous membrane infections

Pharyngeal syndromes: EVs classically cause an undifferentiated febrile illness but are also recognized as a cause of pharyngitis and upper respiratory tract infections. NPEVs have been identified in 8% to 29% of cases of pharyngitis in children⁴⁶. Pharyngeal inflammation is associated with CVB4 infection. A 2014 study in Taiwan found pharyngeal and pharyngeal tonsil involvement in 27.5% of children with CVB4 infection treated at Chang Gung Memorial Hospital⁴⁷.

Hand, foot, and mouth disease (HFMD) and herpangina: HFMD and herpangina are rash conditions caused by enteroviruses. HFMD is highly contagious and has led to significant morbidity and mortality worldwide. EV-A71, CVA6, CVA10, and CVA16 are major causative agents⁴⁸. Herpangina, characterized by fever and painful vesicular lesions in the posterior oropharynx, is also commonly associated with Coxsackievirus A4 (CVA4)⁴⁹ and Coxsackievirus A2 (CVA2)⁵⁰. A herpangina outbreak in Eastern China identified CVA2 as the dominant type, with patients exhibiting high fever and hematological changes⁵¹.

Additionally, EV-A71 surveillance in Qingdao, China (2023-2024) revealed an unexpected co-circulation of genotypes C4 and B5⁵². It is a self-limited disease with mild symptoms or asymptomatic. Still, in some cases, there are reports of serious manifestations of the CNS such as encephalitis, meningitis, AFP, pulmonary edema, and myocarditis, and classic clinical characteristics are fever, oral ulcers, and rashes on the hands, feet, and buttocks, affecting mainly children under five years old⁵³. Few studies have demonstrated the presence of some EV types in HFMD, such as E25, CVA2, EVD-68, RV-56, and EV-B74 (an unusual strain), mainly CVA6 and A16⁵⁴⁻⁵⁶. CVA6 has also been confirmed as a major pathogen in other specialized populations, such as pediatric oncology patients in the United States, where it was one of the most frequently detected types⁵⁷.

Skeletal muscle infection

Pleurodynia (Bornholm disease): Bornholm disease (epidemic myalgia) is characterized by severe chest pain, muscle aches, fever, and spasms. Pain is typically unilateral and accompanied by localized hyperesthesia and edema. Laboratory findings may include elevated creatine phosphokinase and leukopenia. The clinical condition is often preceded by prodromal symptoms such as fever, sore throat, headache, and myalgia for one to two days. Symptoms usually resolve within two to four days but can recur or persist for several weeks. While coxsackievirus B (CVB) is the most commonly associated etiologic agent, other types – including echovirus genotypes 1, 6, 8, 9, 10, and 19, as well as coxsackievirus A4 (CVA4) – have also been less frequently implicated⁵⁸.

Other clinical manifestations of infection

Pancreatitis/Type 1 diabetes (T1D): pancreatitis is a gastroenterological disease characterized by inflammation and damage to the exocrine pancreas. It is generally self-limiting, but in some cases severe clinical complications develop, resulting in severe acute pancreatitis. CVB and EV-A71 have been reported in cases of pancreatitis¹.

Classically, T1D is a chronic autoimmune disease characterized by the loss of insulin-producing beta cells in the pancreas. Studies are currently seeking to understand the role of EVs in infecting beta cells and the host's autoimmune response, which can result in beta-cell death, but this relationship has yet to be elucidated⁵⁹. Infection with CVB4 causes a considerable decrease in insulin production in vitro cultures of beta cells⁶⁰. A systematic review of enterovirus infections and T1D presented highlighted a significant association between enterovirus infection, detected with molecular methods, and autoimmunity/T1D⁶¹.

Acute gastroenteritis: acute gastroenteritis (AGE) is one of the most common diseases and a major cause of morbidity and mortality among infants and young children around the world. Viruses such as rotavirus, norovirus, astrovirus, and adenovirus are among the most common causes of childhood diarrhea. Currently, EV types have been detected in patients with AGE, indicating their likely etiological role¹. However, their role in acute gastroenteritis remains poorly understood⁶². Therefore, more studies are needed to clarify the role of EVs in acute gastroenteritis.

Acute respiratory infections: respiratory infections are one of the most important causes of mortality and morbidity worldwide, affecting mainly children, but they can also affect adults⁶³. Recently, outbreaks caused by emerging EV-D68 types have been reported, increasing cases worldwide in recent years, possibly due to viral genome variation, causing diseases in the upper and lower respiratory tract and, in some cases, neurological development problems. EV-D68 has advanced from a rarely detected respiratory virus to a pathogen responsible for increasing rates of severe respiratory disease⁶⁴. Its acid lability and lower optimum growth temperature suggest that EV-D68 is similar to human rhinoviruses (HRVs)⁶⁵. Different EV-D68 types have been reported in the United States, Canada, Europe, Thailand, China, New Zealand, Brazil, and several African countries⁶⁶⁻⁶⁹. Rare enterovirus C types (EV-C104, EV-C105, EV-C109) have been detected in respiratory samples, with EV-C105 infections occurring primarily in children, in one case, and associated with neurological complications (cerebellitis). Prolonged infections with EV-C104 and EV-C109 in immunocompromised adults have also been documented, showing evidence of intra-host viral evolution over several months⁷⁰. EV-C105 strains from Spain formed a novel clade (C1) with unique antigenic epitope mutations, possibly explaining its recent expansion in Europe⁷¹. Menegolla⁷² recommends that health care professionals consider EV-D68 as a possible cause of unexplained acute severe respiratory disease, even without fever, and consider laboratory testing of respiratory samples for enterovirus when the cause of respiratory infection in critically ill patients is not clear. EV-D68 is emerging as a pathogen. Its transmission potential indicates the need for better forms of surveillance⁷³.

Diagnosis of enterovirus infections

EV detection and typing: the wide variability of enterovirus (EV) clinical manifestations complicates diagnosis, as the same type can cause different syndromes and different types can produce similar symptoms. Guide sample collection for laboratory diagnosis by clinical presentation, and collect it as early as possible after symptom onset. Appropriate specimen types include stool, cerebrospinal fluid (CSF), nasopharyngeal aspirates/swabs, vesicular fluid, bronchoalveolar lavage (BAL), blood, conjunctival swabs, and biopsy tissues (including nail tissue) (**Figure 3**). Historically, EV diagnosis

relied on virus isolation in cell culture followed by serotype identification via neutralization assays – a laborious, time-consuming, and technically demanding process. Currently, molecular methods such as RT-qPCR are considered the gold standard⁷⁴. Although molecular assays have become the primary tool for routine diagnostics because of their high sensitivity, specificity, and rapid turnaround, viral isolation still plays a crucial role in reference laboratory settings. It remains the WHO-recommended method for poliomyelitis surveillance. Cell culture can be used in several situations: for confirmation of PCR-negative specimens in case of a suspected new variant, for detection of more than one viral strain in a specimen, for typing by neutralization, for microneutralization assays to measure serum neutralizing antibodies, for assessment of effects of antivirals as well as for quality control purposes. Many EVs can be isolated from mammalian cell line cultures⁷⁵.

The EVs can evolve through mutation and recombination. They circulate in human and animal hosts, and viruses from the same species can recombine to produce other viable hybrid viruses. Molecular typing approaches to enteroviruses targeting the VP1 region of the enteroviral genome, which encodes type-specific neutralization epitopes, are successfully applied during enteroviral outbreak investigations in many countries worldwide⁷⁴. EV typing compares sequences encoding the viral protein one (VP1) capsid protein. Viruses of different types have < 75% nucleotide identity and < 85% amino acid identity⁷⁶.

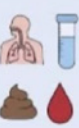
Diseases	Recommended Specimen Types		Diagnostic Observations/Notes
Meningitis/Encephalitis	CSF, feces, respiratory specimen, blood (possible)		EV RNA is detectable in CSF in most cases of meningitis by PCR, but inconsistently in encephalitis. EV excretion in throat and stool specimens is prolonged, but detection does not automatically establish an etiological link
Acute Flaccid Paralysis (AFP)/Myelitis	Respiratory route, CSF, feces, blood		CSF specimens should be tested for enteroviruses. In many cases of EV-D68 and EV-A71, the virus was only detectable in the respiratory tract and/or feces. Respiratory tract tests are necessary in cases of CNS/paralysis/myelitis. In classic AFP (without myelitis), consider polio and obtain a stool specimen
Myocarditis/Pericarditis	Feces, respiratory route, blood and/or cardiac biopsy		Typing can be useful; CVBs associated with myocarditis. Tissue biopsy can confirm the diagnosis
Viral Hemorrhagic Conjunctivitis	Ocular swab		Viral hemorrhagic conjunctivitis by enterovirus is highly infectious
Hand-Foot-Mouth/Herpangina	Vesicle fluid, respiratory route, and/or feces		Generally high viral loads in vesicle fluid. CVA6 associated with onychomadesis; virus recovered from nails
Respiratory Disease	Respiratory specimen, possibly feces		Nasopharyngeal aspirates or swabs are generally recommended. Consider HRV and EV, and PCR cross-reactivity

Figure 3. Recommended clinical sample types for EV diagnosis in different clinical manifestations
Adapted from Harvala et al⁷⁴

Serological tests: the large number of enterovirus types hampers serological diagnosis. In the past, neutralization (IgG) and ELISA (IgG and IgM) specific tests were used to confirm acute EV infection in the laboratory. Still, their clinical utility is limited because of antigen cross-reactivity between different types⁷⁴. In some situations, when direct EV detection is impossible, antibody detection can be useful for diagnosis, for example, suspected cardiac infections (myocarditis, pericarditis, and cardiomyopathy). Neutralization assays are necessarily type-specific; testing for several EV antibodies is time-consuming and laboratory-intensive for different EV types. On the other hand, they are considered very useful for seroprevalence studies to assess population immunity or for individual serological examination of paired serum samples (two-week interval between acute and convalescent serum samples). A 4-fold increase in EV-specific antibody concentrations between the acute and convalescent sera is diagnostic of recent infection, and a 1:8 titer in a neutralization test would indicate protective antibody levels⁷⁴.

Therapeutic approach and vaccines against enteroviruses

Poliomyelitis was successfully controlled worldwide using the formalin-inactivated Salk polio vaccine and the Sabin oral polio vaccine⁷⁷. Currently, China NMPA (National Medical Products Administration) has licensed three inactivated EV-A71 vaccines against HFMD. In addition to EV-A71, CVA6, CVA10, and CVA16 are major HFMD causative agents. However, the inactivated EV-A71 whole-virus vaccine failed to cross-protect against infections by other HFMD-causing enteroviruses⁴⁸. Treatment of NPEV infections includes primarily supportive care for the infected individual⁷⁸. Viral meningitis, HFMD, conjunctivitis, pharyngitis, pancreatitis, and other enterovirus-related diseases have no specific treatment^{22,23,79}. Intensive care therapies may be required for severely ill patients, and Immune globulin is sometimes employed for treatment of severe cases⁷⁹. Advances in antiviral therapy aim to understand the mechanisms of viral replication and the components with antiviral activities. Developing a pan-enterovirus vaccine and antiviral drugs is an important and achievable goal in the future⁸⁰.

CONCLUSION

Enterovirus infections remain a major public health concern due to their wide range of clinical manifestations, from mild illness to severe conditions such as sepsis. Early recognition, rapid diagnosis, and timely control measures are essential to limit viral spread. Although outbreaks worldwide highlight the diversity of circulating enterovirus types, non-polio enteroviruses (NPEVs) are still not included in the World Health Organization's global surveillance guidelines. The lack of systematic national surveillance limits knowledge of their prevalence and true burden on human health. Integrating NPEVs into surveillance systems would improve case detection and outbreak preparedness. Despite recent advances, it remains unclear why so many enterovirus types can infect the same tissues. Further investigation into their epidemiological, evolutionary, genetic, and virulence characteristics is therefore needed to improve prevention, diagnosis, and control strategies.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding this manuscript.

FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

AUTHOR'S CONTRIBUTIONS

Fabício Caldeira Reis: responsible for drafting the manuscript, as well as for the analysis and revision of its content. Alex Domingos Reis: participated in drafting and revising the manuscript. Braulio Caetano Machado: contributed to the critical revision of the work and added important perspectives to the text. Rita de Cássia Compagnoli Carmona: was involved in all stages of the study, including the conception and design of the research, the data analysis and interpretation, and the drafting and critical revision of the manuscript. All the authors have read and agreed to the published version of the manuscript.

USE OF ARTIFICIAL INTELLIGENCE

The authors declare that the figures included in this manuscript were reviewed and enhanced using Scidraw. ai. No other artificial intelligence tools were used in the preparation, writing, or revision of this manuscript.

ACKNOWLEDGMENTS

The authors wish to thank their colleagues at the Enteric Diseases Laboratory, Virology Center (NDE/CV) for their collaborative efforts. We are particularly grateful to Dr. Maria do Carmo Sampaio Timenetsky, Director of the CV, for her invaluable support and leadership. We also thank the Adolfo Lutz Institute for its institutional support.

REFERENCES

1. Tapparel C, Siegrist F, Petty TJ, Kaiser L. Picornavirus and enterovirus diversity with associated human diseases. Infect Gent Evol. 2013;14:282-93.
<https://doi.org/10.1016/j.meegid.2012.10.016>
2. Machado RS, Tavares FN, Sousa Jr IP. Global landscape of coxsackieviruses in human health. Virus Res. 2024;344:199367.
<https://doi.org/10.1016/j.virusres.2024.199367>
3. Picornavirus home. Enterovirus. [cited 2023 Nov 23]. Available from:
<https://www.picornaviridae.com/ensavirinae/enterovirus/enterovirus.htm>
4. International Committee on Taxonomy of Viruses – ICTV. Family: *Picornaviridae*. Genus: *Enterovirus*. London: ICTV; 2023 [cited 2024 Nov 23]. Available from:
<https://ictv.global/report/chapter/picornaviridae/picornaviridae/enterovirus>

5. Harvala H, Jasir A, Penttinen P, Celentano LP, Greco D, Broberg E. Surveillance and laboratory detection for non-polio enteroviruses in the European Union/European Economic Area, 2016. Euro Surveill. 2017;22(45):16-00807.
<https://doi.org/10.2807/1560-7917.ES.2017.22.45.16-00807>
6. Baggen J, Thibaut HJ, Strating JRPM, van Kuppeveld FJM. The life cycle of non-polio enteroviruses and how to target it. Nat Rev Microbiol. 2018;16(6):368-81.
<https://doi.org/10.1038/s41579-018-0005-4>
7. World Health Organization – WHO. Guidelines for drinking-water quality. Fourth Edition Incorporating the First Addendum. Geneva, Switzerland. 2017; ISBN 978-92-4-154995-0.
8. Xie Z, Khamrin P, Maneekarn N, Kumthip K. Epidemiology of enterovirus genotypes in association with human diseases. Viruses. 2024;16(7):1165.
<https://doi.org/10.3390/v16071165>
9. Vlok M, Majer A. Global prevalence of non-polio enteroviruses pre- and post-COVID-19 pandemic. Microorganisms. 2025;13(8):1801.
<https://doi.org/10.3390/microorganisms13081801>
10. Siddaway AP, Wood AM, Hedges LV. How to do a systematic review: a best practice guide for conducting and reporting narrative reviews, meta-analyses, and meta-syntheses. Annu Rev Psychol. 2019;70:747-70.
<https://doi.org/10.1146/annurev-psych-010418-102803>
11. Crom SCM, Rossen JWA, van Furth AM, Obihara CC. Enterovirus and parechovirus infection in children: a brief overview. Eur J Pediatr. 2016;175(8):1023-9.
<https://doi.org/10.1007/s00431-016-2725-7>
12. Staring J, von Castelmuur E, Blomen VA, van den Hengel LG, Brockmann M, Baggen J et al. PLA2G16 represents a switch between entry and clearance of *Picornaviridae*. Nature. 2017;19;541(7637):412-6.
<https://doi.org/10.1038/nature21032>
13. Muehlenbachs A, Bhatnagar J, Zaki SR. Tissue tropism, pathology and pathogenesis of enterovirus infection. J Pathol. 2015;235(2):217-28.
<https://doi.org/10.1002/path.4438>
14. Sin J, Mangale V, Thienphrapa W, Gottlieb RA, Feuer R. Recent progress in understanding coxsackievirus replication, dissemination, and pathogenesis. Virology. 2015;484:288-304.
<https://doi.org/10.1016/j.virol.2015.06.006>

15. Ho BC, Yang PC, Yu SL. MicroRNA and pathogenesis of enterovirus infection. *Viruses*. 2016;6;8(1):11. <https://doi.org/10.3390/v8010011>
16. Zueter ARM, Zaiter A. Infectious meningitis. *Clin Microbiol News*. 2015;37(6):43-51. <https://doi.org/10.1016/j.clinmicnews.2015.02.004>
17. Cordey S, Schibler M, L'Huillier AG, Wagner N, Gonçalves AR, Ambrosioni J et al. Comparative analysis of viral shedding in pediatric and adult subjects with central nervous system-associated enterovirus infections from 2013 to 2015 in Switzerland. *J Clin Virol*. 2017;89:22-9. <https://doi.org/10.1016/j.jcv.2017.01.008>
18. van der Linden L, Wolthers KC, van Kuppeveld FJM. Replication and inhibitors of enteroviruses and parechoviruses. *Viruses*. 2015;10;7(8):4529-62. <https://doi.org/10.3390/v7082832>
19. Carmona RCC, Machado BC, Sousa CA, Vieira HR, Alves MRM, Souza KAF et al. Distribution of species in patients with central nervous system infections in São Paulo State, Brazil. *J Med Virol*. 2020;92:3849-56. <https://doi.org/10.1002/jmv.26131>
20. Castillo F, Turón-Viñas E, Armendariz L, Carbonell E, Rabella N, del Cuerpo M et al. Characteristics of enterovirus infection-associated neurologic disease associated in a pediatric population in Spain. *Enferm Infecc Microbiol Clin*. 2024;42(3):242-50. <https://doi.org/10.1016/j.eimc.2023.02.002>
21. Li Z, Yang X, Bai R, Li P, Qin Y, Luo M. Circulated echovirus 18 strains in Guangdong Province and worldwide: a novel perspective on genetic diversity and recombination patterns. *Virulence*. 2025;16(1):2534519. <https://doi.org/10.1080/21505594.2025.2534519>
22. Jain S, Patel B, Bhatt GC. Enteroviral encephalitis in children: clinical features, pathophysiology, and treatment advances. *Pathog Glob Health*. 2014;108(5):216-22. <https://doi.org/10.1179/2047773214Y.00000000145>
23. Costa BK, Sato DK. Viral encephalitis: a practical review on diagnostic approach and treatment. *J Pediatr (Rio J)*. 2020;96(S1):12-9. <https://doi.org/10.1016/j.jped.2019.07.006>
24. Chen BS, Lee HC, Lee KM, Gong YN, Shih SR. Enterovirus and encephalitis. *Front Microbiol*. 2020;20;11:261. <https://doi.org/10.3389/fmicb.2020.00261>

25. Rudolph H, Schrotten H, Tenenbaum T. Enterovirus infections of the central nervous system in children: an update. *Pediatr Infect Dis J*. 2016;35(5):567-9.
<https://doi.org/10.1097/INF.0000000000001090>
26. van Rensburg MJ, Mans J, Mafuyeka RT, Strydom KA, Myburgh M, van Zyl WB. Diversity of enteroviruses in cerebrospinal fluid specimens of patients hospitalized with meningitis and encephalitis in South Africa. *J Med Virol*. 2024;96(3):e29514.
<https://doi.org/10.1002/jmv.29514>
27. Suresh S, Rawlinson WD, Andrews PI, Stelzer-Braid S. Global epidemiology of nonpolio enteroviruses causing severe neurological complications: a systematic review and meta-analysis. *Rev Med Virol*. 2020;30(1):e2082.
<https://doi.org/10.1002/rmv.2082>
28. Berginc N, Lunar MM, Šramel N, Poljak M. Molecular epidemiology and characterization of enteroviruses detected in cerebrospinal fluid and respiratory samples in Slovenia, 2014-2023. *J Med Virol*. 2024;96(7):e29827.
<https://doi.org/10.1002/jmv.29827>
29. Bao J, Thorley B, Isaacs D, Dinsmore N, Elliott EJ, McIntyre P et al. Polio – the old foe and new challenges: an update for clinicians. *J Paediatr Child Health*. 2020;56(10):1527-32.
<https://doi.org/10.1111/jpc.15140>
30. Böttcher S, Neubauer K, Baillot A, Rieder G, Adam M, Diedrich S. Stool screening of Syrian refugees and asylum seekers in Germany, 2013/2014: identification of Sabin like polioviruses. *Int J Med Microbiol*. 2015;305(7):601-6.
<https://doi.org/10.1016/j.ijmm.2015.08.008>
31. Waldman EA. Poliomielite e seu controle pela imunização. In: João Baptista Risi Junior. (Org.). *Poliomielite no Brasil: do reconhecimento da doença ao fim da transmissão*. 1a. ed. Rio de Janeiro: Editora Fiocruz, 2019, v. 1, p. 19-46.
<https://doi.org/10.7476/9786557080627>
32. Suresh S, Forgie S, Robinson J. Non-polio *Enterovirus* detection with acute flaccid paralysis: a systematic review. *J Med Virol*. 2018;90(1):3-7.
<https://doi.org/10.1002/jmv.24933>
33. Fischer TK, Simmonds P, Harvala H. The importance of enterovirus surveillance in a post-polio world. *Lancet Infect Dis*. 2022;22(1):e35-e40.
[https://doi.org/10.1016/S1473-3099\(20\)30852-5](https://doi.org/10.1016/S1473-3099(20)30852-5)

34. Carmona RCC, Reis FC, Cilli A, Dias JMM, Machado BC, Morais DR et al. Beyond poliomyelitis: a 21-year study of non-polio enterovirus genotyping and its relevance in acute flaccid paralysis in São Paulo, Brazil. *Viruses*. 2024;16(12):1875.
<https://doi.org/10.3390/v16121875>
35. Sousa Jr IP, Oliveira MLA, Burlandy FM, Machado RS, Oliveira SS, Tavares FN et al. Molecular characterization and epidemiological aspects of non-polio enteroviruses isolated from acute flaccid paralysis in Brazil: a historical series (2005-2017). *Emerg Microbes Infect*. 2020;9(1):2536-46.
<https://doi.org/10.1080/22221751.2020.1850181>
36. Cong R, Xiao J, Ji T, Sun Q, Lu H, Yang D et al. Genetic characterization and molecular epidemiological analysis of enterovirus C99 in China. *J Med Virol*. 2024;96(2):e29449.
<https://doi.org/10.1002/jmv.29449>
37. Fernandez-Garcia MD, Garcia-Ibañez N, Camacho J, Gutierrez A, Garcia LS, Calvo C et al. Enhanced echovirus 11 genomic surveillance in neonatal infections in Spain following a European alert reveals new recombinant forms linked to severe cases, 2019 to 2023. *Euro Surveill*. 2024;29(44):2400221.
<https://doi.org/10.2807/1560-7917.ES.2024.29.44.2400221>
38. Schultheiss HP, Kühl U, Cooper LT. The management of myocarditis. *Eur Heart J*. 2011;32(21):2616-25.
<https://doi.org/10.1093/eurheartj/ehr165>
39. Sinnecker D, Laugwitz KL, Moretti A. Extending human induced pluripotent stem cell technology to infectious diseases: new model for viral myocarditis. *Circ Res*. 2014;29;115(6):537-9.
<https://doi.org/10.1161/CIRCRESAHA.114.304786>
40. Persichino J, Garrison R, Krishnan R, Sutjita M. Effusive-constrictive pericarditis, hepatitis, and pancreatitis in a patient with possible coxsackievirus B infection: a case report. *BMC Infect Dis*. 2016;8;16:375.
<https://doi.org/10.1186/s12879-016-1752-3>
41. Medina NH, Haro-Muñoz E, Pellini AC, Machado BC, Russo DH, Timenetsky MD et al. Acute hemorrhagic conjunctivitis epidemic in São Paulo State, Brazil, 2011. *Rev Panam Salud Publica*. 2016;39(2):137-41. Available from:
<https://www.scielosp.org/article/rpsp/2016.v39n2/137-141/>
42. Zhang L, Zhao N, Huang X, Jin X, Geng X, Chan TC et al. Molecular epidemiology of acute hemorrhagic conjunctivitis caused by coxsackie A type 24 variant in China, 2004-2014. *Sci Rep*. 2017;23;7:45202.
<https://doi.org/10.1038/srep45202>

43. Chen L, Yang H, Zhang HL, Shi XL, Peng B, Meng J. Pathogen surveillance of acute conjunctivitis reveals recent emergence of coxsackievirus A24 variants and high genotypic diversity of human adenoviruses in Shenzhen, China, 2018-2024. J Clin Virol. 2025;180:105852.
<https://doi.org/10.1016/j.jcv.2025.105852>
44. Haider SA, Jamal Z, Ammar M, Hakim R, Afrough B, Kreku A et al. Genomic characterization of the Coxsackievirus A24 variant in the acute hemorrhagic conjunctivitis outbreak (2023) in Islamabad, Pakistan through metagenomic next generation sequencing. J Virol Methods. 2025;338:115213.
<https://doi.org/10.1016/j.jviromet.2025.115213>
45. Gyeltshen S, Dorji T, Dorji K, Wangchuk S, Tshering D, Poolpanichupatam Y et al. Coxsackievirus A24 variant associated with acute hemorrhagic conjunctivitis outbreak in Bhutan, 2023. Sci Rep. 2025;15(1):14864.
<https://doi.org/10.1038/s41598-025-94776-7>
46. Hosoya M, Ishiko H, Shimada Y, Honzumi K, Suzuki S, Kato K et al. Diagnosis of group A coxsackieviral infection using polymerase chain reaction. Arch Dis Child. 2002;87(4):316-9.
<https://doi.org/10.1136/adc.87.4.316>
47. Lee CJ, Huang YC, Yang S, Tsao KC, Chen CJ, Hsieh YC et al. Clinical features of coxsackievirus A4, B3 and B4 infections in children. PLoS One. 2014;9(2):e87391.
<https://doi.org/10.1371/journal.pone.0087391>
48. Li ML, Shih SR, Tolbert BS, Brewer G. Enterovirus A71 vaccines. Vaccines. 2021;9(3):199.
<https://doi.org/10.3390/vaccines9030199>
49. Lv T, Li Y, Yu P, Chen X, Li H, Zhang N et al. Genome analysis of coxsackievirus A4 identified from herpangina children in Northern China. Curr Microbiol. 2025;82(2):81.
<https://doi.org/10.1007/s00284-025-04075-7>
50. Itani TM, Chalapa VI, Slautin VN, Imangaliev BS, Kungurtseva MS, Patrusheva AK et al. Circulation of non-polio enteroviruses in the Ural Federal District and Western Siberia in 2023: the return of an old foe? Arch Virol. 2025;170(5):110.
<https://doi.org/10.1007/s00705-025-06284-8>
51. Xing B, Hu L, Hu X, Sun Y, Liang Z, Fu J et al. Epidemiological, clinical, and molecular characteristics of coxsackievirus A2 infections during a herpangina outbreak in children on an Island in Eastern China in 2024: a surveillance-based study. Gut Pathog. 2025;17(1):85.
<https://doi.org/10.1186/s13099-025-00762-9>

52. Gong J, Liu S, Liu S, Sun R, Xiao S, Su Z et al. Genetic characterization of human enterovirus A71 genotypes C4 and B5 circulating in Qingdao City, Shandong province, China, from 2023 to 2024. Front Cell Infect Microbiol. 2025;15:1684067.
<https://doi.org/10.3389/fcimb.2025.1684067>
53. Chang YK, Chen KH, Chen KT. Hand, foot and mouth disease and herpangina caused by enterovirus A71 infections: a review of enterovirus A71 molecular epidemiology, pathogenesis, and current vaccine development. Rev Inst Med Trop São Paulo. 2018;60:e70.
<https://doi.org/10.1590/S1678-9946201860070>
54. Sousa Jr IP, Burlandy FM, Tavares FN, Silva EE. Enterovirus B74 associated with hand, foot and mouth disease. Infect Genet Evol. 2018;65:15-7.
<https://doi.org/10.1016/j.meegid.2018.07.011>
55. Carmona RCC, Machado BC, Reis FC, Jorge AMV, Cilli A, Dias AMN et al. Hand, foot, and mouth disease outbreak by Coxsackievirus A6 during COVID-19 pandemic in 2021, São Paulo, Brazil. J Clin Virol. 2022;154:105245.
<https://doi.org/10.1016/j.jcv.2022.105245>
56. Rueca M, Vairo F, Spaziante M, Fabeni L, Forbici F, Berno G et al. Molecular genotyping of circulating enterovirus in the Lazio Region from 2012 to 2023. Viruses. 2024;16(7):1013.
<https://doi.org/10.3390/v16071013>
57. Asowata OE, McMillen T, Jani K, Clark B, Morjaria S, Kamboj M et al. Prevalence and epidemiology of enterovirus species in a pediatric oncology patient population. J Clin Virol. 2025;178:105881.
<https://doi.org/10.1016/j.jcv.2025.105881>
58. Lal A, Akhtar J, Isaac S, Mishra AK, Khan MS, Noreldin M et al. Unusual cause of chest pain, Bornholm disease, a forgotten entity; case report and review of literature. Respir Med Case Rep. 2018;25:270-3.
<https://doi.org/10.1016/j.rmcr.2018.10.005>
59. Rodriguez-Calvo T. Enterovirus infection and type 1 diabetes: unraveling the crime scene. Clin Exp Immunol. 2019;195(1):15-24.
<https://doi.org/10.1111/cei.13223>
60. Nyalwidhe JO, Gallagher GR, Glenn LM, Morris MA, Vangala P, Jurczyk A et al. Coxsackievirus-induced proteomic alterations in primary human islets provide insights for the etiology of diabetes. J Endocr Soc. 2017;1(10):1272-86.
<https://doi.org/10.1210/js.2017-00278>
61. Yeung WCG, Rawlinson WD, Craig ME. Enterovirus infection and type 1 diabetes mellitus: systematic review and meta-analysis of observational molecular studies. BMJ. 2011;342:d35.
<https://doi.org/10.1136/bmj.d35>

62. Gosert R, Heininger U, Hirsch HH. Enterovirus detection in patients with acute gastroenteritis in Switzerland. J Med Virol. 2018;90(4):685-91.
<https://doi.org/10.1002/jmv.25005>
63. Canela LNP, Magalhães-Barbosa MC, Raymundo CE, Carney S, Siqueira MM, Prata-Barbosa A et al. Viral detection profile in children with severe acute respiratory infection. Braz J Infect Dis. 2018;22(5):402-11.
<https://doi.org/10.1016/j.bjid.2018.09.001>
64. Elrick MJ, Pekosz A, Duggal P. Enterovirus D68 molecular and cellular biology and pathogenesis. J Biol Chem. 2021;296:100317.
<https://doi.org/10.1016/j.jbc.2021.100317>
65. Piralla A, Principi N, Ruggiero L, Girello A, Giardina F, Sando E et al. Enterovirus-D68 (EV-D68) in pediatric patients with respiratory infection: The circulation of a new B3 clade in Italy. J Clin Virol. 2018;99-100:91-6.
<https://doi.org/10.1016/j.jcv.2018.01.005>
66. Holm-Hansen CC, Midgley SE, Fischer TK. Global emergence of enterovirus D68: a systematic review. Lancet Infect Dis. 2016;16(5):e64-e75.
[https://doi.org/10.1016/S1473-3099\(15\)00543-5](https://doi.org/10.1016/S1473-3099(15)00543-5)
67. Raboni SM, Giamberardino HI, Debur MC, Santos JS. Enterovirus D68-associated respiratory infection in southern Brazil, 2018 – A population-based laboratory surveillance. J Clin Virol. 2020;129:104503.
<https://doi.org/10.1016/j.jcv.2020.104503>
68. Ikuse T, Aizawa Y, Kachikawa R, Kamata K, Osada H, Win SMK et al. Detection of enterovirus D68 among children with severe acute respiratory infection in Myanmar. J Microbiol Immunol Infect. 2024;57(2):123-30.
<https://doi.org/10.1016/j.jmii.2024.01.001>
69. Lima ARJ, Santos HO, Pereira JS, Leite AB, Nascimento JPM, Souza JVC et al. Enterovirus D68 subgenotype B3 circulation in Children with acute respiratory illness in the State of Alagoas, Brazil. Viruses. 2025;17(2):242.
<https://doi.org/10.3390/v17020242>
70. Fall A, Zhuang TX, Dodge A, Abdullah O, Norton JM, Villafuerte D et al. Molecular characterization of emerging and uncommon enteroviruses C104, C105, and C109 in respiratory samples from Maryland, USA, 2018-2024. Viruses. 2025;17(9):1183.
<https://doi.org/10.3390/v17091183>

71. Fernandez-Garcia MD, Camacho J, Diez-Fuertes F, Pedro ER, Garcia-Ibañez N, Navascués A et al. Detections of rare enterovirus C105 linked to an emerging novel clade, Spain, 2019 to 2024. Euro Surveill. 2025;30(6):2500073.
<https://doi.org/10.2807/1560-7917.ES.2025.30.6.2500073>
72. Menegolla IA, Martins LG, Patzer JD, Calderaro PC, Peres CCMC, Fay VS et al. Enterovirose no Rio Grande do Sul: uma vigilância a ser estruturada? Bol Epidemiológico. 2016;18(3):1-3.
73. Qiu X, Cao F, Cheng S, Li J. Molecular epidemiology, coinfection, and diversity of enteroviruses detected in respiratory samples collected from patients with influenza-like illness in Hangzhou, China, in 2023. Virol J. 2025;22:227.
<https://doi.org/10.1186/s12985-025-02862-z>
74. Harvala H, Broberg E, Benschop K, Berginc N, Ladhani S, Susi P et al. Recommendations for enterovirus diagnostics and characterisation within and beyond Europe. J Clin Virol. 2018;101:11-7.
<https://doi.org/10.1016/j.jcv.2018.01.00>
75. World Health Organization – WHO. Polio laboratory manual 4th edition. Geneva 27, Switzerland: Department of Immunization, Vaccines and Biologicals CH-1211. 2004. pp. 1-167. Available from:
<https://iris.who.int/server/api/core/bitstreams/4f3de082-d394-45ed-81f5-ea1f001991f1/content>
76. Nix WA, Oberste MS, Pallansch MA. Sensitive, seminested PCR amplification of VP1 sequences for direct identification of all enterovirus serotypes from original clinical specimens. J Clin Microbiol. 2006;44(8):2698-704.
<https://doi.org/10.1128/JCM.00542-06>
77. Baicus A. History of polio vaccination. World J Virol. 2012;1(4):108-14.
<https://doi.org/10.5501/wjv.v1.i4.108>
78. Jubelt B, Lipton HL. Chapter 18 – Enterovirus/picornavirus infections. Handb Clin Neurol. 2014; 123:379-416.
<https://doi.org/10.1016/B978-0-444-53488-0.00018-3>
79. Abzug MJ. The enteroviruses: problems in need of treatments. J Infect. 2014;68(1):S108-S14.
<https://doi.org/10.1016/j.jinf.2013.09.020>
80. Lin JY, Kung YA, Shih SR. Antivirals and vaccines for Enterovirus A71. J Biomed Sci. 2019;26:65.
<https://doi.org/10.1186/s12929-019-0560-7>