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Coxsackievirus: Practical Recognition of Hand, Foot, and Mouth Disease Syndrome in Children

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Abstract

The hand-foot-and-mouth syndrome represents a significant clinical and epidemiological challenge in pediatric practice due to its high contagiousness, rapid spread in organized children's groups, and the absence of specific antiviral treatment. This study provides a comprehensive analysis of the clinical characteristics, diagnosis, and management of hand-foot-and-mouth syndrome in outpatient settings. The primary etiological agents of this disease are enteroviruses, primarily Coxsackievirus A16 and Enterovirus 71, which demonstrate a strong affinity for epithelial tissues of the skin and mucous membranes. The article details the pathogenesis, where viral replication initially occurs in the mucosa of the oropharynx and gastrointestinal tract, followed by systemic dissemination through viremia. Clinically, the syndrome manifests with a triad of fever, painful enanthema in the oral cavity, and a characteristic vesicular or maculopapular rash on the palms, soles, and occasionally on the buttocks or genital area. The study encompassed two hundred fifty pediatric patients aged from six months to eighteen years, with eighty-four diagnosed cases of hand-foot-and-mouth syndrome, constituting thirty-three point six percent of the total sample. The analysis highlights that the highest incidence was observed in children under five years old, particularly those attending childcare institutions. Diagnosis was primarily clinical, based on typical presentation, as laboratory confirmation was not always accessible or required. The study thoroughly describes differential diagnostic approaches, distinguishing hand-foot-and-mouth syndrome from other pediatric conditions such as herpetic stomatitis, varicella, scarlet fever, measles, and allergic dermatitis. A clear set of clinical criteria for diagnosis is proposed, emphasizing the relevance of a syndromic approach in the absence of virological confirmation. The article reviews therapeutic tactics, including the use of antipyretics, oral antiseptics, local analgesics, and hydration therapy. In the overwhelming majority of cases, symptomatic treatment was effective, and the disease had a benign and self-limited course, with resolution typically occurring within seven days. No severe complications or hospitalizations were recorded. The study also addresses epidemiological aspects, describing several outbreaks in preschool institutions and underlining the role of early recognition and isolation of cases to prevent widespread transmission. Practical recommendations are provided for pediatricians and family doctors, aimed at improving outpatient care and enhancing clinical vigilance. Furthermore, the article identifies gaps in current diagnostic and treatment protocols and calls for the development of standardized clinical guidelines tailored to resource-limited settings. The findings underscore the importance of medical education, parental awareness, and timely intervention as critical components of effective disease control. In conclusion, the research contributes to the optimization of diagnostic strategies, supports evidence-based symptomatic management, and reinforces the need for coordinated public health measures in the context of pediatric infectious diseases.

Keywords: Hand, Foot, And Mouth Disease (Hfmd), Coxsackievirus A16, Enterovirus A71, Clinical Diagnosis, Symptomatic Treatment, Diagnostic Criteria, Complications, Etiological Agents, Viral Infections, Pediatric Population, Epidemiological Outbreaks.

Introduction

Hand, Foot, and Mouth Disease (HFMD) is a viral illness that typically affects children under the age of five and is characterized by hallmark symptoms such as oral lesions and rashes on the hands and feet. Coxsackievirus A16 (CV-A16) and Enterovirus A71 (EV-A71) are the main etiological agents of this disease. [1-24].

The most common etiological factor of HFMD is Coxsackievirus A16, which has a tropism for epithelial cells of the skin and mucous membranes. The pathogenetic mechanism of syndrome development includes primary viral replication in the mucosa of the oropharynx and gastrointestinal tract, followed by viremia, which is accompanied by damage to the epithelial lining of the skin and mucous membranes, resulting in characteristic vesicles, and also poses a risk of generalized infection affecting the nervous system or myocardium.

The disease is highly contagious and is mainly transmitted via the fecal-oral and airborne droplet routes. [2] HFMD becomes particularly epidemiologically significant during the summer-autumn period in regions with warm and humid climates, leading to annual outbreaks in organized children's groups [2].

The relevance of studying the Hand, Foot, and Mouth syndrome lies in its wide prevalence among the pediatric population and the high frequency of outbreaks reported in kindergartens and schools, contributing to the rapid spread of infection in organized groups. A notable clinical feature of the disease is its polymorphism, which significantly complicates differential diagnosis with other infectious and allergic pathologies such as herpes infection, scarlet fever, chickenpox, and allergic dermatoses. This variability in the clinical presentation often results in diagnostic errors at the initial stage [4].

An additional complicating factor is the absence of specific etiological treatment and preventive vaccines for most serotypes of the causative agents, limiting the effectiveness of both treatment and prevention of the disease. Particular attention is drawn to the potential for developing severe complications, including aseptic meningitis, encephalitis and myocarditis, which are especially characteristic of infections caused by Enterovirus 71. “Coxsackievirus can rarely cause interstitial pneumonia, pancreatitis, and pulmonary edema.” Considering this, and the growing role of outpatient care, there is an urgent need to improve clinical algorithms for early detection, diagnosis, timely isolation of patients, and organization of supportive therapy [5-7].

Timely identification and accurate diagnosis of Hand, Foot, and Mouth syndrome are key factors in preventing complications in patients and in curbing further spread of the infection among children. The absence of specific therapy underscores the importance of early identification of cases, continuous monitoring of their condition, as well as implementation of preventive and anti-epidemic measures in child care institutions. This makes the study of the clinical course of this disease extremely relevant for modern pediatrics and pediatric infectious medicine.

Research Objective

A comprehensive analysis of the clinical manifestations, frequency, and features of the course of Hand, Foot, and Mouth syndrome in children in outpatient settings, as well as the improvement of diagnostic criteria, evaluation of therapeutic approaches, identification of the infectious activity of the pathogen, and development of recommendations for early detection and management of patients in order to prevent the development of complications and limit the spread of enteroviral infection.

Materials and Methods

The study was conducted in outpatient settings from January to May 2025. It included 250 children aged from 6 months to 18 years. Among the 250 patients (100%), 84 (33.6%) were diagnosed with enteroviral infection. 166 patients who did not meet the conditions of this study were excluded. The diagnosis was based on the clinical manifestations of the disease, specifically the characteristic rashes (macular rash), most often localized on the skin of the hands, feet, and in the oral cavity. To confirm the diagnosis of Hand, Foot, and Mouth syndrome, the presence of characteristic rash elements in at least one of the typical localizations (palms, soles, or oral mucosa) in combination with the corresponding clinical picture was sufficient, allowing for diagnosis without the need for additional laboratory methods.

To analyze current approaches to the diagnosis and treatment of Hand, Foot, and Mouth syndrome, as well as to clarify the clinical aspects of this disease, a systematic review of scientific literature sources was conducted. The review was carried out through searches in international scientific databases such as PubMed, Google Scholar, and ResearchGate. Search queries included the following key phrases: "Coxsackievirus hand foot mouth syndrome children", "Enterovirus infection diagnosis", "Hand-foot-mouth disease management", and "Coxsackie A16 clinical features". This search made it possible to collect a wide range of peer-reviewed articles, clinical guidelines, and review papers published over the past 5 years. In the process of selecting sources, preference was given to articles with up-to-date data on the clinical manifestations of the syndrome, diagnostic methods, pathogenesis, and therapeutic approaches. The collected information was used to improve diagnostic criteria, clarify treatment methods, and develop recommendations for early detection and management of patients with Hand, Foot, and Mouth syndrome in outpatient settings.

Results

The conducted study included 84 children aged from 6 months to 18 years, who were diagnosed with Hand, Foot, and Mouth syndrome based on clinical examination and specific symptoms. The sample accounted for 33.6% of the total number of initially examined patients (250 children) who visited the outpatient department during the period from January to May 2025, as shown in Table 1. The remaining 166 children (66.4%) were excluded from observation due to the absence of clinical manifestations characteristic of this pathology, such as macular rash localized on the palms, soles, and oral mucous membranes.

Regarding the gender composition of the sample, male children predominated among the examined group: the number of boys was 46 (54.8%), while girls accounted for 38 (45.2%). The boy-to-girl ratio was approximately 1.2:1, indicating a slight predominance of the disease among boys. A similar gender imbalance in the distribution of Hand, Foot, and Mouth syndrome cases is also confirmed by the study of Wang, Y., Zhang, Y., Zhang, X., et

al. (2013) and is likely due to physiological and immunological characteristics of the child's body depending on gender, as well as behavioral activity differences in children [8].

The analysis of the age structure of the examined patients was carried out according to the classification of periods of postembryonic human development. The group of infants (from 1 month to 1 year) included 12 children (14.3%), indicating a significant susceptibility of infants to this infection due to the immaturity of the immune system. The early childhood group (1-3 years) included 30 children (35.7%), which indicates the highest vulnerability during this period, when active social interaction among children and the formation of primary immune defense occur. The preschool age group (3-7 years) consisted of 26 children (31.0%), which is also a significant proportion, considering the high level of contact among children in this age category. The younger school-age group (7–11 years) was represented by 12 children (14.3%), while the adolescent group (12–18 years) included only 4 children (4.7%), confirming the trend of decreasing incidence with age, likely due to developed immunity.

Table 1: Age and Gender Distribution of Children with Hand-Foot-and-Mouth Syndrome (n = 84)

Age Group	Age Range	Gender	Number of Children	Percentage (%)
Infants	6–12 months	Boys – 7	12	14.30%
		Girls – 5		
Toddlers	1–3 years	Boys – 18	30	35.70%
		Girls – 12		
Preschoolers	3–7 years	Boys – 13	26	31.00%
		Girls – 13		
School-age Children	7–11 years	Boys – 6	12	14.30%
		Girls – 6		
Adolescents	12–18 years	Boys – 2	4	4.70%
		Girls – 2		

Between January and May 2025, 250 children aged 6 months to 18 years with suspected infectious diseases were examined in outpatient settings. Based on clinical analysis, it was established that in 84 children (33.6% of the total examined), the clinical picture corresponded to the diagnosis of hand-foot-mouth syndrome. The remaining 166 children (66.4%) were excluded from further analysis due to the absence of typical clinical manifestations of this disease.

The diagnosis was established based on the clinical picture: the presence of characteristic macular rashes on the skin of the palms, soles, and oral area, and the corresponding course of the disease, which is pathognomonic for this infection.

An analysis of the age structure of children with enteroviral etiology showed that the largest proportion consisted of early childhood patients (1-3 years old) - 12 children (42.9%) and preschool age (3-7 years old) -10 children (35.7%). Infants (1 month to 1 year) accounted for 7.1% of cases (2 children), younger school age (7-11 years) — 14.3% (4 children), while among adolescents (12-18 years), no cases were registered. Thus, the highest incidence was observed among younger children, which corresponds to the literature data on the increased susceptibility of this age group to enteroviral infections.

In terms of gender distribution among the examined children, boys predominated: 46 patients (54.8%) compared to 38 girls (45.2%). The male-to-female ratio was approximately 1.2:1, indicating a slight predominance of incidence among males, consistent with the study by Wang, Y., Zhang, Y., Zhang, X., et al. (2013) [8].

During epidemiological observation, three localized outbreaks of hand-foot-mouth syndrome were identified in children's collectives -two preschools and one elementary school. These outbreaks were characterized by high contagiousness, rapid infectious spread among younger children, and active involvement of contacts, as determined anamnesticly.

Within the framework of the study, identification of specific etiological agents was not conducted, as laboratory verification of the pathogen was unavailable in outpatient settings. For clinical purposes, a syndromic diagnostic approach was used, based on the characteristic clinical picture of hand-foot-mouth syndrome. It is worth noting that, according to literature, cases with mild and moderate courses are most often associated with Coxsackievirus A16, while more severe forms with pronounced intoxication, persistent febrile fever, and signs of neuroinfection are more commonly associated with Enterovirus type 71. However, without laboratory confirmation in our study, we cannot reliably assert the specific serotype of the pathogen in each case. [1-22]

In the clinical study involving 84 children, a number of characteristic symptoms were identified that allow for a high probability of diagnosis based on physical examination alone. The most pathognomonic sign was macular or maculopapular rashes, which in 100% of cases were localized on the palms and soles, as also noted in the work of Bondarenko Y, Kulyk D, Pustova N, Bilovol A, Makieieva N. These lesions often had well-defined borders, were accompanied by erythema (in 91.7% of patients), and could progress to vesicle or superficial erosion formation. However, it should be noted that enteroviral infection can also manifest as macular rashes on the torso, as shown in photo 1 [1-22].

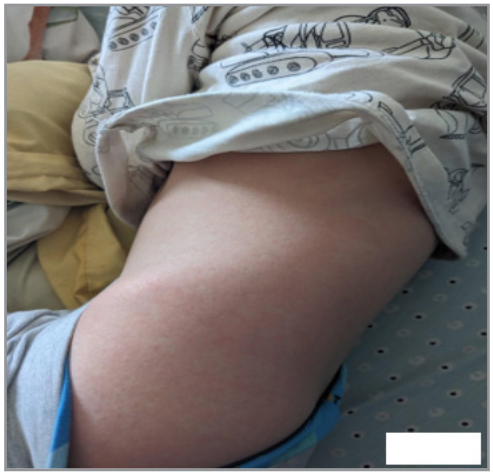

Figure 1: Enteroviral Exanthem on the Torso

Alongside skin lesions, significant changes in the oral mucosa were observed - in 94% of cases, signs of aphthous stomatitis were detected. Erosions were located on the mucosa of the cheeks, lips, tongue, and palate, accompanied by pain that limited food intake, especially in children under 5 years old (reduced appetite was recorded in 78.6%). In 15.5% of children, vesicles were additionally observed, which later ruptured, forming superficial erosions with a whitish coating.

Among general symptoms, fever up to 38–39 °C prevailed (in 85.7% of cases), along with lethargy, irritability, weakness, sore throat, and discomfort during swallowing. The fever usually lasted from 2 to 4 days and was accompanied by moderate intoxication. The general condition in most children was assessed as moderate (72.6%), and in 8.3% — severe, which required active outpatient monitoring [19-22].

An important diagnostic sign was the symmetrical localization of rashes on the palms and soles in combination with erosive changes in the mouth — this clinical tandem is typical for hand-foot-mouth syndrome and allows for its differentiation without the use of complex laboratory methods. At the same time, skin itching was either absent or minimal, which is also a characteristic distinction from other dermatoses [22].

Table 2: Clinical Symptoms of Hand, Foot, and Mouth Disease (HFM) Based on Age and Severity

Age Group	Main Symptoms	Severity	Notes
0–3 years	Refusal to eat, increased salivation, oral enanthema, fever, irritability	Moderate	Children at this age cannot clearly express pain, often only behavioral symptoms noted Rash on palms and soles (vesicles), ulcers in the mouth
3–6 years	Mouth pain, sore throat, fever, rash on palms and soles, oral ulcers	Moderate to Severe	Children can describe pain (e.g., mouth pain), making diagnosis easier
	Refusal to eat due to oral pain		
6–10 years	Sore throat, headache, general weakness, skin rash	Mild to Moderate	Less common age group for HFM; symptoms often milder
All age groups	Rash on palms/soles – 100% Oral ulcers – 94% Fever – 86%	—	Based on retrospective analysis of 84 children
	Refusal to eat – 78,6% Increased salivation – 40% Irritability – 36%		

For the purpose of differential diagnosis, it is important to consider the features of the course of other diseases. For example, primary herpes infection is accompanied by a vesicular rash mainly on the facial skin and lips, and more pronounced intoxication. In scarlet fever — a characteristic “strawberry tongue,” symmetrical rash on the trunk, cheek hyperemia with pallor of the nasolabial triangle are typical. Chickenpox is characterized by polymorphic rashes (spots, papules, vesicles, crusts) on various parts of the body, including the scalp. Allergic dermatoses are usually not accompanied by fever and do not involve lesions of the oral mucosa [22-23].

Within the framework of the conducted study, an analysis of treatment methods for children with hand-foot-mouth syndrome in outpatient settings was carried out, with a focus on symptomatic therapy, its effectiveness, and cases of complications.

The main direction of treatment was a symptomatic approach aimed at alleviating the main clinical manifestations of the disease, such as fever, oral pain, and prevention of dehydration. The use of antipyretics was necessary in 64 cases (76.2% of patients). Ibuprofen in age-appropriate dosages was most commonly used, which effectively reduced body temperature and simultaneously

alleviated pain. In cases of intolerance or contraindications to ibuprofen, paracetamol was used [22,24].

To relieve local pain syndrome caused by lesions of the oral mucosa, local anesthetics in the form of gels and sprays based on lidocaine or benzocaine were used in 41 children (48.8%). This reduced discomfort during eating and drinking, which in turn reduced the risk of dehydration, as also noted in the works of Bondarenko Y, Kulyk D, Pustova N, Bilovol A, Makieieva N., Robert Koch-Institut. (2025) and the visual analog scale VAS ≤5.

Rehydration therapy was indicated in 22 children (26.2%) who, due to pain and general weakness, tended to reduce fluid intake. The main method of rehydration was the prescription of oral saline solutions, which helped restore the water-electrolyte balance without the need for hospitalization [22,24].

The evaluation of the effectiveness of supportive therapy showed that in 77 patients (91.7%), a significant improvement in clinical condition was observed within the first 2-3 days from the start of treatment. Fever reduction, decreased oral pain, improved appetite, and general well-being made it possible to complete treatment in outpatient settings without complications. The average duration of the clinical course of the disease was 5-7 days. No complications were observed within the framework of this study.

Conclusion

As a result of the study, it was established that hand-foot-mouth syndrome, caused by Coxsackie A group viruses (mainly A16 and A6), holds an important place in the structure of enteroviral infections, particularly in the pediatric population. The disease is characterized by a high level of contagiousness, rapid spread in groups, and seasonal activity, which determines its epidemiological significance. The analysis of the available scientific literature made it possible to generalize current views on the pathogenesis, transmission routes, viral activity characteristics, and clinical typology of the infection. It was found that the most vulnerable category is children aged 6 months to 5 years, which is associated with physiological immaturity of the immune system and high contact rates in everyday conditions.

The clinical analysis of the syndrome's course showed the presence of a specific symptom complex that in most cases allows the disease to be recognized already at the primary stage of consultation. The pathognomonic signs included fever, painful vesicles in the oral cavity, and symmetrical rashes on the palms and soles, which may later spread to other areas of the skin. At the same time, variable clinical manifestations are observed, including mild or atypical forms, which complicate differential diagnosis with such diseases as herpetic stomatitis, chickenpox, allergic dermatitis, and enteroviral exanthema. Therefore, clinical reasoning by the physician, based on the analysis of symptom dynamics and epidemiological history, plays a key role.

It is important to emphasize that in conditions of limited access to specific laboratory confirmation methods (e.g., PCR or serology), especially at the primary healthcare level, clinical diagnosis plays a leading role. Its accuracy affects the timeliness of diagnosis, the effectiveness of therapeutic measures, and the prevention of complications, including neurological or cardiac ones that may occur in severe cases of the disease. This work systematizes the main diagnostic guidelines that are of practical value for clinicians in daily practice.

The study also confirmed that an urgent issue remains the insufficient awareness of this infection both among primary care physicians and parents. This situation leads to frequent cases of self-treatment or late medical consultation, which in turn contributes to the spread of infection among the child population. The paper summarizes clinical markers that should be clearly identified during the patient's examination to improve diagnostic accuracy and avoid errors in management tactics.

In summary, it can be stated that an objective understanding of the clinical picture of hand-foot-mouth syndrome, thorough knowledge of its course variants, careful history-taking, and focus on typical signs enable the physician to timely establish a preliminary diagnosis and initiate appropriate symptomatic treatment. This, in turn, helps reduce the risk of complications, minimize the spread of infection in organized children's groups, and lessen the burden of morbidity in the early childhood population.

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Conflict of Interests

The authors declare no conflict of interest related to this study.

References

1. Khajuria, A., Saini, D., Gupta, R. K., Sharma, A., & Babber, S. (2024). Epidemiological and Clinical Profile of Hand, Foot, and Mouth Disease in Children in a Tertiary Care Center in Jammu. Cureus, 16(4), e58704. https://doi.org/10.7759/cureus.58704
2. Huang, Z., Wang, M., Qiu, L., Wang, N., Zhao, Z., Rui, J., Wang, Y., Liu, X., Hannah, M. N., Zhao, B., Su, Y., Zhao, B., & Chen, T. (2019). Seasonality of the transmissibility of hand, foot and mouth disease: a modelling study in Xiamen City, China. Epidemiology and infection, 147, e327. https://doi.org/10.1017/S0950268819002139
3. Xia, M., Zhu, Y., Liao, J., Zhang, S., Yang, D., Gong, P., Zhang, S., Jiang, G., Cheng, Y., Meng, J., Chen, Z., Liao, Y., Li, X., Zeng, Y., Zhang, C., & Long, L. (2024). Clinical, aetiological, and epidemiological studies of outpatient cases of hand, foot, and mouth disease in Chengdu, China, from 2019 to 2022: a retrospective study. BMC public health, 24(1), 3427. https://doi.org/10.1186/s12889-024-20909-8
4. Wang, J., Zhou, J., Xie, G., Zheng, S., Lou, B., Chen, Y., & Wu, Y. (2020). The Epidemiological and Clinical Characteristics of Hand, Foot, and Mouth Disease in Hangzhou, China, 2016 to 2018. Clinical pediatrics, 59(7), 656–662. https://doi.org/10.1177/0009922820910822
5. Lee, J. Y., Son, M., Kang, J. H., & Choi, U. Y. (2018). Serum interleukin-6 levels as an indicator of aseptic meningitis among children with enterovirus 71-induced hand, foot and mouth disease. Postgraduate medicine, 130(2), 258–263. https://doi.org/10.1080/00325481.2018.1416257
6. Chen, Y. F., Hu, L., Xu, F., Liu, C. J., & Li, J. (2019). A case report of a teenager with severe hand, foot, and mouth disease with brainstem encephalitis caused by enterovirus 71. BMC pediatrics, 19(1), 59. https://doi.org/10.1186/s12887-019-1428-4

7. Guerra AM, Orille E, Waseem M. Hand, Foot, and Mouth Disease. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Updated 2023 Mar 4. Available from: https://www.ncbi.nlm.nih.gov/books/NBK431082/
8. Wang, Y. R., Sun, L. L., Xiao, W. L., Chen, L. Y., Wang, X. F., & Pan, D. M. (2013). Epidemiology and clinical characteristics of hand foot, and mouth disease in a Shenzhen sentinel hospital from 2009 to 2011. BMC infectious diseases, 13, 539. https://doi.org/10.1186/1471-2334-13-539
9. Thammasonthijarern, N., Kosoltanapiwat, N., Nuprasert, W., Sittikul, P., Sriburin, P., Pan-Ngum, W., Maneekan, P., Hataiyusuk, S., Hattasingh, W., Thaipadungpanit, J., & Chatchen, S. (2021). Molecular Epidemiological Study of Hand, Foot, and Mouth Disease in a Kindergarten-Based Setting in Bangkok, Thailand. Pathogens (Basel, Switzerland), 10(5), 576. https://doi.org/10.3390/pathogens10050576
10. Zeng, H., Zeng, B., Yi, L., Qu, L., Cao, J., Yang, F., Yang, H., Xie, C., Yan, Y., Deng, W., Li, S., Zhang, Y., Li, B., Lu, J., & Zeng, H. (2025). The Emergence of Coxsackievirus A16 Subgenotype B1c: A Key Driver of the Hand, Foot, and Mouth Disease Epidemic in Guangdong, China. Viruses, 17(2), 219. https://doi.org/10.3390/v17020219
11. Dumaidi, K., Al-Jawabreh, A., Zraiqi, A., Fashafsha, A., & Dumaidi, A. (2025). First Report of Hand, Foot, and Mouth Disease (HFMD) Outbreak in the West Bank, Palestine: Molecular Characterization of Coxsackievirus A16 (CV-A16). The Canadian journal of infectious diseases & medical microbiology = Journal canadien des maladies infectieuses et de la microbiologie medicale, 2025, 9133821. https://doi.org/10.1155/cjid/9133821
12. Wang, J., Jiang, L., Zhang, C., He, W., Tan, Y., & Ning, C. (2021). The changes in the epidemiology of hand, foot, and mouth disease after the introduction of the EV-A71 vaccine. Vaccine, 39(25), 3319–3323. https://doi.org/10.1016/j.vaccine.2021.05.009
13. Mao, Q., Wang, Y., Yao, X., Bian, L., Wu, X., Xu, M., & Liang, Z. (2014). Coxsackievirus A16: epidemiology, diagnosis, and vaccine. Human vaccines & immunotherapeutics, 10(2), 360–367. https://doi.org/10.4161/hv.27
14. Zhu, P., Ji, W., Li, D., Li, Z., Chen, Y., Dai, B., Han, S., Chen, S., Jin, Y., & Duan, G. (2023). Current status of hand-foot-and-mouth disease. Journal of biomedical science, 30(1), 15. https://doi.org/10.1186/s12929-023-00908-4
15. Ciccarese, G., Broccolo, F., Serviddio, G., & Drago, F. (2023). Clinical, diagnostic features and complications of hand, foot, and mouth disease caused by coxsackievirus A6 in children and adults. Journal of medical virology, 95(1), e28405. https://doi.org/10.1002/jmv.28405
16. Chen, Y., Dai, B., Han, S., Duan, G., Yang, H., Chen, S., Ji, W., & Jin, Y. (2023). Arising Concerns of Atypical Manifestations in Patients with Hand, Foot, and Mouth Disease. Vaccines, 11(2), 405. https://doi.org/10.3390/vaccines11020405
17. Liu, B., Luo, L., Yan, S., Wen, T., Bai, W., Li, H., Zhang, G., Lu, X., Liu, Y., & He, L. (2015). Clinical Features for Mild Hand, Foot and Mouth Disease in China. PloS one, 10(8), e0135503. https://doi.org/10.1371/journal.pone.0135503
18. Starkey, S. Y., Mar, K., Khaslavsky, S., Seeburruth, D., Khalid, B., Virmani, D., Lam, J. M., & Mukovozov, I. (2024). Atypical cutaneous findings of hand-foot-mouth disease in children: A systematic review. Pediatric dermatology, 41(1), 23–27. https://doi.org/10.1111/pde.15461
19. Li, M., Li, Y., Du, J., Zhang, Y., Xi, M., Yan, K., Liu, R., Wang, X., Xu, P., Yuan, J., & Deng, H. (2024). Clinical features of hand, foot and mouth disease caused by Coxsackievirus A6 in Xi'an, China, 2013-2019: A multicenter observational study. Acta tropica, 257, 107310. https://doi.org/10.1016/j.actatropica.2024.107310
20. Duan, X., Chen, Z., Li, X., Yuan, P., & Long, L. (2021). Virus Shedding in Patients With Hand, Foot and Mouth Disease Induced by EV71, CA16 or CA6: Systematic Review and Meta-analysis. The Pediatric infectious disease journal, 40(4), 289–294. https://doi.org/10.1097/INF.0000000000002985
21. Li, X., Wang, Q., Chen, Z., Duan, X., Han, Y., Luan, R., & Long, L. (2020). Viral shedding in patients with hand, foot and mouth disease induced by EV71, CA16, or CA6: A protocol for systematic review and meta analysis. Medicine, 99(29), e21258. https://doi.org/10.1097/MD.0000000000021258
22. Bondarenko, Y., Kulyk, D., Pustova, N., Bilovol, A., & Makieieva, N. (2025). VIRAL EXANTHEMS IN CHILDREN: ETIOPATHOGENESIS, CLINICAL FEATURES, PATIENT MANAGEMENT IN OUTPATIENT PRACTICE. Grail of Science, (51), 888–906. https://doi.org/10.36074/grail-of-science.18.04.2025.119
23. Riley L. E. (1998). Herpes simplex virus. Seminars in perinatology, 22(4), 284–292. https://doi.org/10.1016/s0146-0005(98)80017-7
24. Robert Koch-Institut. RKI-Ratgeber: Hand-Fuß-Mund-Krankheit (HFMK). Epidemiologisches Bulletin. 2025;11:13–9. Available from: https://edoc.rki.de/bitstream/handle/176904/12438/EB-11-2025_10-25646-13064.pdf?sequence=1&isAllowed=y