children

Editorial

Viral Infections of the Oral Cavity in Children

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Various viral infections can affect the oral cavities of pediatric patients [1,2]. Some viral infections are more severe in children than they are in adults, and vice versa [1,2]. Children and adults respond differently to viral infections, as the maturity of specific immunity influences the clinical course of the disease [2]. Indeed, the specific immunity of neonates and children is inherently immature or can be modulated by tolerance induction in ways that impair it [1].

Viral infections of the oral cavity can be distinguished into those that do not result in visible damage or a disease in the oral cavity, but are transmitted orally or during dental procedures, and those associated with oral and perioral lesions [2,3]. However, some of them belong to both categories [2,4].

Primary infection with herpes simplex virus-1 is generally acquired during early childhood and is usually subclinical or underdiagnosed [5]. The primary infection manifests in the characteristic condition known as herpetic gingivostomatitis, which is characterized by painful, small vesicles bilaterally covering the gingival and oral mucosa [5]. Recurrent herpes simplex virus-1 infection is called herpes labialis or cold sores. It occurs unilaterally because the virus reactivates and latently infects some neurons in the trigeminal ganglion [6,7]. This is often triggered by a co-infection, sun exposure, or stress [7,8]. The symptomatic period can be shortened by the local administration of a paste containing aciclovir at the site of prodromal symptoms or immediately at the first sign of a blister [2]. There is no cure for herpes simplex virus-1, which can cause rare complications, such as facial paralysis, which is called Bell's palsy [9]. However, primary herpes simplex virus-1 infection can be treated with aciclovir, and recurrences can be treated with topical pastes containing aciclovir [2,5].

Human papillomaviruses (HPV) can cause benign and malignant diseases in various areas, such as the genital and oral mucosa or skin [10]. Infections with specific HPV genotypes have been associated with an increased risk of cervical cancer (HPV-16 and -18) and head and neck cancer (HPV-16) [11]. Vertical transmission via mothers is the most common route of HPV transmission in children younger than one year [2]. In children younger than 18 years, the most common HPV-related oral manifestations are, in descending order, focal epithelial hyperplasia, squamous cell papillomas, verrucae vulgaris, and condylomata acuminata [10]. Although the oncogenic role of HPV in oral squamous cell carcinoma in children is still unclear [10], vaccination is recommended at a younger age regardless of the patient's HPV status to improve its effectiveness [12].

SARS-CoV-2 infections occurred less frequently among children than they do among adults during the early phase of the pandemic, possibly because infected children were asymptomatic or had only mild symptoms [1]. However, some children with COVID-19 were later diagnosed with Kawasaki disease (KD), "Multisystem Inflammatory Syndrome in Children" (MIS-C), and other syndromes [1]. They are more likely to develop ulcerative/erosive, macular-petechial, especially erythematous oral mucosa lesions [1] than adults are, who are usually diagnosed with white plaques and erosive/ulcerative, maculopapular, or vesicular lesions [13]. COVID-19 vaccinations have been effective in protecting against the infection, even in pediatric subjects [14,15], and have been associated mainly with mild

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adverse effects, including local pain, swelling, and redness at the injection site, general weakness, joint or muscle pain, headache, chills, fever, nausea, and diarrhea [16]. A few adverse effects have been reported in children, including oral lesions with erosive-ulcerative phenotype, which is similar to adults [1]. In contrast, white lesions, such as lichenoid reactions and oral lichen planus, have been described only in adults [9].

Enteroviruses are RNA viruses that are usually fecally–orally transmitted [17]. They belong to the Picornaviridae family, have a single-stranded genome of about 9000 bases, and are acid-stable, allowing them to survive low pH in the stomach [17,18]. Among them, coxsackie A virus is the most common cause of hand, foot, and mouth disease, which is characterized by fever and blisters in the mouth and extremities [17]. However, Enteroviruses can also cause meningoencephalitis or severe pulmonary disease in children [17], and no antivirals are currently available [17].

Morbilli virus is a negative-stranded RNA virus that belongs to the paramyxovirus family. It is transmitted via direct contact and has an incubation period of less than one week [19]. Morbilli virus causes measles, which are characterized by a flu-like upper respiratory illness with a fever, followed by the onset of a red, blotchy exanthema that covers most of the body [19,20]. Measles can lead to severe complications such as subsclerosing panencephalitis, which can cause permanent brain damage [19,21]. The MMR vaccine is highly effective against measles, mumps, and rubella, and its use is strongly recommended [22]. It is also worth considering that the association between the MMR vaccination and autism has not been confirmed [22].

Mumps virus infection typically leads to inflammation and the swelling of the parotid gland, resulting in parotitis [23,24]. The infection heals spontaneously within 1–2 weeks, resulting in lifelong protection [23,24]. Infection with the mumps virus can lead to male infertility, again underlining the importance of the MMR vaccination [2].

Human immunodeficiency virus type 1 is most commonly transmitted vertically in children from an infected mother during childbirth, in utero, or through breastfeeding [25]; although, antiviral therapy administered to the mother before the child is born can effectively reduce the risk of transmission [26]. HIV-1 infection suppresses the host T cell response, leading to opportunistic infections similar to those seen in transplant patients or individuals with general immunosuppression [2]. Candida albicans causes most opportunistic infections in pediatric patients diagnosed with acquired immunodeficiency syndrome (AIDS) [2,27,28]. Effective antifungal therapies are available to treat Candida infections [29] that, combined with effective antiretroviral therapy, favor immune system recovery and opportunistic infection resolution [28]. However, there is a risk of developing a refractory HIV infection if the prescribed drug therapy is not strictly adhered to [2,30]. Combination therapies for viral infections have pioneered the treatment of HIV-1 infections, with at least three antiviral agents currently being used in therapy [26]. While the first HIV-1 inhibitor was developed in 1985, the therapy was revolutionized in 1995 with the introduction of protease inhibitors [26]. Future drugs for HIV infection will have a longer half-life and reduce the need for strict adherence to the drug therapy [31]. Existing preparations are also being reformulated to include multiple drugs in a single tablet and preparations with a longer half-life.

Vaccination programs have effectively prevented severe childhood infections, although viral infections remain a serious health problem in developing countries [14,25]. Emerging infections, such as human immunodeficiency virus (HIV), further contribute to the burden of viral infections during childhood [28]. Antiviral therapies will likely play a more significant role in treating childhood infections [5]. As new infections emerge, vaccines or antiviral agents promise to prevent or treat these infections and change the landscape of viral infections among children [5].

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