



## **Viral Diseases in Pediatric Dentistry: A Literature Review On Oral Manifestations and Management of Viral Diseases in Paediatric Patients other than HIV**

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### **1. Abstract**

Many children suffering of pain and discomfort regarding orofacial manifestations of viral infections. Pediatric dentists find it challenging to reach final diagnosis and provide appropriate management and care when facing lesions. A current literature review of these conditions is referred for more detail.

### **2. Introduction**

The effects of viral diseases in children are significantly different from the effects experienced by adults (Sällberg, 2009). Factors that predisposes the child to opportunistic infections are divided to systemic (HIV infection, autoimmune disease, endocrine disorders, organ transplants, malnutrition and diabetes mellitus) and local factors (changes in the quality or flow of the saliva for example in xerostomia) (Sällberg, 2009; Pinto & Hong, 2013). The most important factor is the host's immunity (Sällberg, 2009). Children, especially the neonate, naturally have immature immune systems which make the infection more sever in children than in adults (Sällberg, 2009).

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Currently, vaccination programmers successfully change the severity of viral infections or even prevent it in children (Sällberg, 2009).

Most of viral infections are diagnosed based on the clinical criteria (Saoji, 2008; Cameron & Widmer, 2008; Pinto & Hong, 2013; Stoopler & Balasubramaniam, 2013). Quick and early confirmation of diagnosis of the viral infections can be done by exfoliative cytology and polymerase chain reaction (Cameron & Widmer, 2008). In general, due to the oral lesions the child may complain from discomfort, sore throat and difficulty of swallowing with excessive salivation, which may lead to dehydration (Thomas, 2007; Cameron & Widmer, 2008; Chen et al, 2007; Dias & Dias, 2012). Although the viral oral lesions lead to pain, discomfort, and difficulty of swallowing among of children which has a subsequent effect on the children growth and development, researchers continue to search for various methods to alleviate the pain and prevent the virus transmission. The dentists are the first to detect the oral viral diseases it puts extra pressure on the dentists as proper infection control in the dental office is needed to prevent viral transmission. The present overview aims to educate pediatric dentists concerning newer information and summarize it.



### 3. Viruses affecting the oral cavity in children

#### 3.1. Herpes simplex virus (HSV) type 1 and 2

Infection with herpes simplex virus type 1 (HSV-1) is common worldwide with prevalence of 70–80% (Thomas, 2007). HSV-1 is usually associated with infections of the skin and oral mucosa, while HSV type 2 associated with genital infections (Thomas, 2007; Pinto & Hong, 2013). However, oral infections may also be caused by HSV type 2 when this virus is transmitted by genito-oral contact (Birek, 2000). HSV is transmitted through direct contact with the lesions or by oral secretions and have an incubation period of 1–26 days (Thomas, 2007; Dias & Dias 2012; Pinto & Hong, 2013).

##### 3.1.1. Primary herpetic gingivostomatitis (PHGS)

Primary herpetic gingivostomatitis (PHGS) is the most common cause of infectious lesions in the oral cavity in the children caused by HSV-1 (Thomas, 2007; Cameron & Widmer, 2008; Pinto & Hong, 2013). And also it is the most common clinical manifestation of HSV infections which occur in 25–30% of infected children with HSV (Thomas, 2007; Sällberg, 2009; Pinto & Hong, 2013). PHGS is seen most often in children, aged between 6 months and 5 years while the majority of this infection is subclinical (Thomas, 2007; Sällberg, 2009; Pinto & Hong, 2013; Stoopler & Balasubramaniam, 2013).

##### 3.1.1.1. Clinical manifestations of PHGS

PHGS initially started with sudden onset of fever, headache, malaise, pharyngitis, anorexia, nausea, irritability and submandibular/cervical lymphadenopathy followed by appearance of the oral lesions (Thomas, 2007; Pinto & Hong, 2013). The oral lesions present as numerous bilateral vesicles that rapidly rupture to become ulcers these



ulcers often coalesce to form irregular shaped painful ulcers with an erythematous margin covered by a yellow-grey pseudomembrane (Thomas, 2007; Cameron & Widmer, 2008; Pinto & Hong, 2013). These ulcers affect a variety of intraoral surfaces both keratinized and nonkeratinized tissues and can also appear extra orally on the lips and perioral skin (Thomas, 2007; Pinto & Hong, 2013; Stoopler & Balasubramaniam, 2013). Complication may occur is labial epithelisation as a result of adherent the lip ulcers after the healing which leads to limiting mouth opening and creating social embarrassment (Thomas, 2007). In healthy individuals the recurrent intraoral lesions are rare and are limited to the keratinized mucosa (Birek, 2000; Pinto & Hong, 2013). The differential diagnosis of PHGS includes lesions associated with varicella zoster virus and coxsackie virus, aphthous ulcer, necrotizing gingivitis and erythema multiforme (Pinto & Hong, 2013).

### 3.1.2. Recurrent herpes labialis (RHL)

Recurrent herpes labialis (RHL) is the most common form of the recurrent HSV infections in the healthy individuals (Stoopler & Balasubramaniam, 2013). RHL is also called cold sore or fever blister, which is caused by reactivation of the latent HSV-1 in the trigeminal ganglion (Arduino & Porter, 2006; Sällberg, 2009; Stoopler & Balasubramaniam, 2013). The recurrence of the lesions can be stimulated by factors such as stress, environmental triggers (exposure to sunlight), surgical trauma, dental extraction, hormonal changes, illness (influenza) and radiotherapy of the head and neck (Birek, 2000;



Sällberg, 2009; Stoopler & Balasubramaniam, 2013). Most of the patients experienced prodromal symptoms prior to the occurrence of the lesion, which often include pain or discomfort, tingling and/or burning sensation in the area of the recurrence (Birek, 2000; Sällberg, 2009; Stoopler & Balasubramaniam, 2013). RHL is characterized by painful blisters surrounded by erythema at the mucocutaneous junction of the lips which are usually unilateral (Birek, 2000; Sällberg, 2009; Stoopler & Balasubramaniam, 2013). These blisters tend to certainly recur at the same site for each individual (Pinto & Hong, 2013). The blisters usually heal within 3–5 days (Sällberg, 2009).

### 3.2. Varicella–zoster virus (VZV)

Varicella zoster virus (VZV) causes two types of infection, primary infection (varicella) and recurrent infection due to reactivation of the latent virus called zoster (Cameron & Widmer, 2008; Pinto & Hong, 2013). VZV infection causes chicken pox when occurs in an individual who has no varicella–zoster antibody (Cameron & Widmer, 2008; Pinto & Hong, 2013). This virus is highly infectious and the mode of transmission is mainly respiratory (Birek, 2000; Pinto & Hong, 2013). Chicken pox in general is a mild to moderately severe, self-limiting disease in children however, it may be severe or even fatal when occurs in newborn infants or adults (Cameron & Widmer, 2008; Pinto & Hong, 2013).

#### 3.2.1. Clinical manifestations of chicken pox

Chicken pox is characterized by fever and malaise for a day followed by a pruritic skin rash all over the body but more predominately on the head and the trunk (Birek, 2000; Cameron & Widmer, 2008; Saoji, 2008; Sällberg, 2009; Pinto & Hong, 2013).



The rash progresses through five stages: erythema, papules, vesicles, drying vesicles and scabs (Cameron & Widmer, 2008; Pinto & Hong, 2013). Oral lesions associated with this infection are relatively common and often involve the lips, palate and buccal mucosa (Saoji, 2008; Sällberg, 2009; Pinto & Hong, 2013). Oral lesions are characterized by presence of small white opaque vesicles which are easy to rupture to form aphthous like ulcers (Birek, 2000). Complications may occur are central nervous systemic involvement, pneumonia and recurrent zoster (Sällberg, 2009; Pinto & Hong, 2013). The differential diagnosis of VZV oral ulcers are trauma and other viral disease (Pinto & Hong, 2013).

### 3.3. Epstein-Barr virus (EBV)

Epstein-Barr virus (EBV) infection causes infectious mononucleosis (Sällberg, 2009; Pinto & Hong, 2013). Most of the primary infection of EBV in children is subclinical and the most affected group is with average age 5.2 years old (Cameron & Widmer, 2008; Sällberg, 2009; Saldaña et al, 2012; Pinto & Hong, 2013). This virus is highly infectious and is mainly transmitted through saliva which is also called the “kissing disease” (Cameron & Widmer, 2008; Saldaña et al, 2012; Pinto & Hong, 2013). Infectious mononucleosis is characterized by low-grade fever, malaise, headache, lymphadenopathy, and progresses to the development of tonsillitis with or without pharyngitis (Cameron & Widmer, 2008; Sällberg, 2009; Hug et al, 2010; Pinto & Hong, 2013). The oral lesions in the children presents as ulcers, petechiae in the soft palate and posterior pharynx, with gingival



ulcerations (Cameron & Widmer, 2008; Pinto & Hong, 2013). Complications may occur are anemia, conjunctivitis, edema thrombocytopenia, arthritis, jaundice, exanthema, hepatomegaly and splenomegaly (Saldaña et al, 2012). The differential diagnosis of oral lesions of EBV includes trauma, reactive gingival lesions, hematologic disorders and malignancy (Pinto & Hong, 2013).

### 3.4. Cytomegalovirus (CMV)

Cytomegalovirus (CMV) is a herpesvirus and is found in all bodily secretions of infected individuals (Pinto & Hong, 2013). CMV infection is very rare and in newborn infant associates with significant morbidity and mortality (Pinto & Hong, 2013). In children with a history of congenital CMV infection developmental dental defects, such as hypomaturation and enamel hypoplasia (generalized and localized) have been reported (Pinto & Hong, 2013). The differential diagnosis of oral lesions in CMV disease includes HSV associated infection, aphthous ulcer and Coxsackie related ulcers (Pinto & Hong, 2013; Zaheer K, et al, 2022).

### 3.5. Enteroviruses

Enteroviruses cause Hand Foot Mouth Disease (HFMD) and herpangina which affects mostly children (Sällberg, 2009; Dias & Dias 2012; Pinto & Hong, 2013). Coxsackie group A (4, 5, 6, 7, 9, 10, 16, 24) viruses which is the most common cause of HFMD as well as herpangina in children (Yamashita et al, 2005; Chen et al, 2007; Saoji, 2008; Cameron & Widmer, 2008; Sällberg, 2009). The most predominant serotype is A16 (Chen et al, 2007; Saoji, 2008; Sällberg, 2009). HFMD can also be caused by coxsackie B viruses (2 to 5), enterovirus 71, echovirus 18 or polio virus (Chen et al, 2007;



Sällberg, 2009; Pinto &Hong, 2013). Enteroviruses have incubation period of 5 to 7 days and can stay in the body of the infected individual for few weeks even after recovery (Dias &Dias, 2012). The most important preventive strategies are good general hygienic programs as enteroviruses are transmitted through the feco-oral route and multiply in the gastrointestinal tract (Saoji, 2008). The development of a vaccine is recommended to prevent enteroviruses 71 infection (Chen et al, 2007).

### 2.5.1. Clinical manifestations of HFMD and herpangina

HFMD begins with a fever followed by oral and skin lesions (Saoji, 2008). Oral lesions initially appear as vesicles, and then become ulcerated producing multiple small superficial aphthous-like ulcers with erythematous halos (Chen et al, 2007; Saoji, 2008; Cameron & Widmer, 2008; Dias & Dias, 2012; Pinto &Hong, 2013). The ulcers are usually seen on buccal mucosa, tongue, palate, lips and gingiva (Saoji, 2008; Dias & Dias, 2012; Pinto &Hong, 2013). Skin lesions appear as vesicles surrounded by erythematous halos similar to that in the oral cavity which commonly appears on the hands and feet (Saoji, 2008; Sällberg, 2009; Pinto &Hong, 2013). These lesions are similar to that with varicella but are more accentuated and oval (Cameron &Widmer, 2008; Saoji, 2008). Complications may occur in association with HFMD include aseptic meningitis, meningioencephalitis, polio-like paralysis, severe pulmonary disease or myocarditis especially if the cause of the infection is enterovirus 71 (Chang et al, 2002; Chen et al, 2007; Saoji, 2008; Sällberg, 2009;





Pinto &Hong, 2013). Enterovirus 71 might lead to disability or even death (Chang et al, 2002; Chen et al, 2007). Herpangina initially started with an acute onset of fever, sore throat and dysphagia followed by the appearance of oral vesicles which is similar to that with HFMD but more extensive involving the posterior areas of the mouth (the posterior part of buccal mucosa, soft palate, the tonsils and pharyngeal mucosa) (Yamashita et al, 2005; Cameron &Widmer, 2008; Pinto &Hong, 2013). The vesicles quickly rupture to form small ulcers (2-4 mm) (Pinto &Hong, 2013). Unlike HFMD, herpangina has no skin lesions and few oral vesicles (Cameron &Widmer, 2008; Saoji, 2008). The differential diagnosis of HFMD and herpangina includes other viral ulcers such as HSV, CMV and EBV (Pinto &Hong, 2013).

### 3.6. Human papillomavirus (HPV)

There are about a hundred serological types of human papillomaviruses (HPVs), all of which may cause lesions in different areas of the body (e.g., oral cavity, larynx, esophagus or genitalia) (Syrjanen, 2010). HPV diseases affecting the oral cavity in children are relatively rare (Pinto &Hong, 2013). Oral HPVs might appear in very young children as a result of vertical transmission of the virus from the mother to the child during vaginal delivery (Sällberg, 2009; Syrjanen, 2010). However, sexual transmission of the virus due to sexual abuse occurs especially in older children (Pinto &Hong, 2013). The clinical manifestations of oral HPV infections include squamous papilloma, verruca vulgaris, condyloma acuminatum and focal epithelial hyperplasia (Pinto &Hong, 2013). The majority of HPV diseases are



asymptomatic (Pinto &Hong, 2013). Malignant transformation or the recurrence of the HPV lesions is very rare (Pinto &Hong, 2013).

Verruca vulgaris (common wart) is most common presentation of HPV infection in children (Syrjanen, 2010) which appears as a painless white nodule with a rough surface (Pinto &Hong, 2013). This nodule is benign and usually found on the labial mucosa, tongue and vermilion border (Pinto &Hong, 2013). Squamous papilloma is a painless, benign, exophytic nodule which has a cauliflower appearance because of numerous finger-like surface projections on its surface (Pinto &Hong, 2013). This nodule can be pink or white and usually found on the soft palate, tongue and lips (Pinto &Hong, 2013). Condyloma acuminatum is caused mostly by HPV (6-11) which is similar to the squamous papilloma but tends to be larger (1-1.5 cm) and clustered (Sällberg, 2009; Pinto &Hong, 2013). Focal epithelial hyperplasia (Heck's disease) is common in children and caused by HPV (13-32) which is characterized by multiple, popular normal-colored lesions (Pinto &Hong, 2013). These benign lesions can be seen on oral mucosa or gingiva (Pinto &Hong, 2013). The differential diagnosis of HPV associated oral lesions includes other viral lesions such as molluscum contagiosum and verruciform xanthoma (Pinto &Hong, 2013). To prevent HPV infection, two vaccines (Gardasil, Cervarix) have been developed and are recommended for individuals who have not been infected with HPV (Pinto &Hong, 2013).



### 3.7. Morbilli-virus

Measles is an acute highly infectious disease caused by morbilli-virus which belongs to the paramyxovirus family (Sällberg, 2009; Pinto & Hong, 2013). This virus is transmitted by direct contact and has an incubation period of less than one week (Sällberg, 2009). The initial symptoms of measles are an influenza-like upper respiratory disease with fever followed by skin rash (Tierney & Wang, 2006; Lefebvre et al, 2010). This rash is characterized by the eruption of a red spotty exanthema all over the body (Tierney & Wang, 2006; Lefebvre et al, 2010). Oral lesions are characterized by Koplik's spots which is white papules spots on the buccal mucosa opposite the second molars (Tierney & Wang, 2006; Lefebvre et al, 2010). Complications may occur in case of absence of vaccination, such as subsclerosing pan-encephalitis which leads to permanent brain damage (Tierney & Wang, 2006; Sällberg, 2009). The trivalent measles, mumps, rubella (MMR) vaccine has decreased the prevalence of measles (Sällberg, 2009; Pinto & Hong, 2013).

### 4. Management of the above mentioned viruses

Before the treatment of viral infections, you must know if the viruses have vaccine or not, the table below show the available vaccine and the summary of main route of the transmission.

The majority of viral infections are self-limiting and healing occurs without scar formation and usually within a few days (Sällberg, 2009; Cameron & Widmer, 2008; Dias & Dias, 2012; Sällberg, 2009; Stoopler & Balasubramaniam, 2013; Pinto & Hong, 2013). Several agents can be used for treatment of viral infections to decrease general and local symptoms associated with the lesions and accelerate the



healing (Arduino &Porter, 2006; Thomas, 2007; Cameron &Widmer, 2008; Sällberg, 2009; Pinto &Hong, 2013). In most cases supportive care and symptomatic treatment with antipyretics, hydration and adequate pain control is necessary (Stoopler &Balasubramaniam, 2013). Local antiseptics such as chlorhexidine as a mouthwash can be used in older children with severe ulceration whereas in young children a cotton pellet soaked in chlorhexidine can be swabbed over the affected areas (Cameron & Widmer, 2008). Lip cream as a barrier can be used to avoid adherence of the lips as a result of healing of PHGS lesions (Thomas, 2007). In case of HFMD and chicken pox; antihistamines and calamine lotion for itching are also prescribed (Birek, 2000; Dias &Dias, 2012; Saoji, 2008). Topical use of 2% viscous lidocaine or lidocaine spray (Xylocaine) is used to control the pain and improves the infected child's food intake (Arduino & Porter, 2006; Cameron & Widmer, 2008). The use of lidocaine should be avoided in children younger than two years of age to prevent possible systemic overdose and due to side effects such as methemoglobinemia (Arduino & Porter, 2006; Pinto & Hong, 2013). Recently a long term randomized control trial by Hopper *et al* in 2014 showed that viscous lidocaine is not superior to a flavored gel placebo in increasing children's oral intake and other oral topical agents alone without viscous lidocaine can improve oral intake.

Systemic and/or topical antiviral therapy:

Systemic oral acyclovir suspension is prescribed at a concentration of 15 mg/kg five times per day, especially if the child is suffering from



extreme pain and unable to drink 72 to 96 hours of the disease onset (Pinto & Hong, 2013). The maximum single dose is 200 mg for healthy children (older than 2 years of age) to treat and for prophylaxis purpose of primary as well as recurrent HSV infections and chicken pox, (Naesens & De Clercq, 2001; Arduino & Porter, 2006; Sällberg, 2009; Pinto & Hong, 2013). The right time to give antiviral agents is within 72 hours after the appearance of the rash in the healthy individuals (Birek, 2000). Ganciclovir is indicated for CMV infection in newborn infant (Pinto & Hong, 2013). Topical use of 5% acyclovir ointment in case PHGS applied every hour at the onset of symptoms is useful to reduce the pain and extent of viral shedding (Birek, 2000; Arduino & Porter, 2006; Sällberg, 2009; Pinto & Hong, 2013). Whereas in RHL applied at the site of the prodromal symptoms or immediately at appearance of a blister will particularly decrease the symptomatic period and reduce it by 1 or 2 days (Arduino & Porter, 2006; Sällberg, 2009). The use of penciclovir 1% cream has also been successful with RHL (Arduino & Porter, 2006).

Surgical excision is the treatment of all of the following verruca vulgaris, squamous papilloma and condyloma acuminatum (Pinto & Hong, 2013). While the focal epithelial hyperplasia can spontaneously resolve, conservative excision of lesions have performed for diagnostic or esthetic purposes (Pinto & Hong, 2013).



In this table a summary of main route of the transmission and the available vaccine (Pinto & Hong, 2013; Charlotte Guillouet, et al, 2022).

Virus	Vaccine	Main route of the transmission
Herpes simplex virus	No vaccine	Direct contact with the lesions or infected oral secretions Has an incubation period of 1-26 days
Varicella-zoster virus	Vaccine is available	Is highly infectious Mainly respiratory spread & direct contact with the lesions
Epstein-Barr virus	No vaccine	Is highly infectious, the virus has been found in saliva and blood The virus transmitted mainly through saliva "kissing disease"
Enteroviruses	No vaccine	Feco-oral route and the virus has been found in throat secretions, saliva, vesicle fluid and stool of the infected individual Enteroviruses can stay in the body of the infected individual for few weeks even after recovery
Human papillomavirus	Vaccine is available	Sexual transmission especially in older children (sexual abuse) Vertical transmission of the virus from the mother to the child during vaginal delivery (very young children)
Morbilli-virus (paramyxovirus)	Triple vaccine mumps, measles and rubella (MMR)	Mainly respiratory spread Direct contact Have an incubation period of less than one week

## 5. Conclusion

Various forms of viral infections are sometimes presented to the dentist in the oral cavity. The dentist therefore needs to be aware of such diseases, to quickly detect and identify the infection and proper



differential diagnosis. Effective treatment strategies are required to prevent virus transmission to others and also to avoid its complications. Therefore, the patients may need to be referred to other dental and medical professionals. Although the dentists may be the first to detect the oral viral diseases it puts extra pressure on the dentists as proper infection control in the dental office is needed to prevent viral transmission.

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## المظاهر الفموية وعلاج الأمراض الفيروسية لدى الأطفال المرضى باستثناء فيروس نقص المناعة المكتسبة الايدز

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### الملخص:

العديد من الأطفال يعانون من الألم وعدم الراحة فيما يتعلق بالأعراض الفموية والوجهية الناتجة عن الأمراض الفيروسية. أطباء الأسنان كخط أول في اكتشاف المرض يجدون بعض الصعوبة في الوصول إلى التشخيص النهائي والعلاج المناسب لمثل هذه الحالات. في هذا البحث سوف نتطرق لهذا الموضوع بتفاصيل أكثر من حيث التشخيص والعلاج.

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