Viral Infections of the Oral Mucosa and Perioral Region

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Abstract: **Viral infections of the oral mucosa and perioral region are commonly encountered in the practice of dentistry. The accurate and timely diagnosis of such infections, coupled with the institution of appropriate treatment, can often permit quick resolution of the condition with minimal discomfort and anxiety for the patient (and carers) and prevent the spread of infection to others, especially immunocompromised individuals. This article outlines the clinical presentation and appropriate management of common viral infections of the oral mucosa and perioral region.**

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Clinical Relevance: **The accurate diagnosis of viral infections of the oral mucosa and perioral region facilitates appropriate and early treatment, reducing the overall morbidity and potential complications.**

A number of viruses infect the oral mucosa and surrounding structures. The primary and reactivation manifestations of oral and perioral viral conditions are listed in Table 1. These lesions may increasingly be seen in the immunodeficiency states and dental professionals should be aware of the particular disease associations of individual viruses. This article identifies the aetiology, clinical presentation and management of the viral infections that are commonly encountered in the practice of dentistry.

CONDITIONS CAUSED BY HERPES GROUP VIRUSES

All the viruses in this group are morphologically identical, possess the property of latency (the virus can remain dormant, and become activated later) and are capable of reactivation.[1] Oral herpetic conditions can cause significant morbidity. The main disease processes and the associations with each virus type are described below.

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Primary Herpetic Gingivostomatitis

Primary herpetic gingivostomatitis (Figures 1 and 2) is the result of the primary infection of the oropharynx with herpes simplex virus (HSV) types 1 and 2. Although HSV-1 is predominately an oropharyngeal infection, HSV-2 (usually associated with genital lesions) may cause oral infections. The lesions caused by both virus types are indistinguishable. Concurrent oral and genital infection is a possibility, but is rare.

HSV is usually transmitted by contact with saliva: notably 5% of children and 10% of adults periodically shed infectious HSV in saliva, many carriers having no knowledge of their status.

On initial contact with either virus type, 20% of those infected develop symptoms, usually widespread oral and pharyngeal ulcers following vesicular eruptions. These can affect any area of the oral mucosa, most often the marginal and attached gingivae. Other features include pharyngitis, pyrexia, and cervicofacial lymphadenopathy. Generalized fever, malaise and nausea can precede the local lesions by a few days. Secondary infection of the ulcerated and erosive areas may occur. Occasional perioral manifestations are seen, such as skin rashes and crusts.

Most cases of primary herpetic gingivostomatitis are easily diagnosed

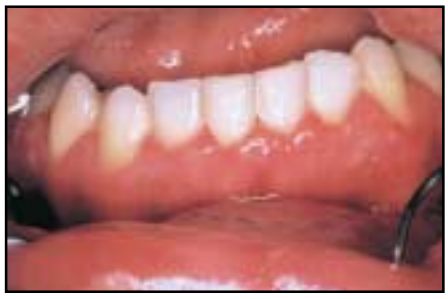

***Figure 1.** Full-width gingivitis in primary herpetic gingivostomatitis.*

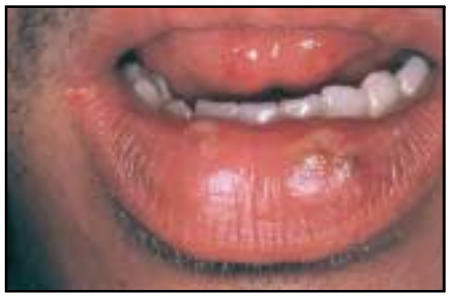

***Figure 2.** Ulcerated area and ruptured vesicles on the lips and tongue in primary herpetic gingivostomatitis in the patient shown in Figure 1.*

Virus type	Primary infection	Reactivation
Herpes simplex	Primary herpetic gingivostomatitis	Herpes labialis
Herpes zoster	Herpetic whitlow; chickenpox	Herpetic whitlow; shingles
Epstein–Barr, cytomegalovirus	Glandular fever	No
Coxsackie group	Herpangina; hand, foot and mouth disease	No
Human papillomavirus	Squamous cell papilloma Verruca vulgaris Condyloma accuminatum	Squamous cell papilloma Verruca vulgaris Condyloma accuminatum
Paramyxovirus	Mumps; measles	No

Table 1. *Viral conditions of the oral mucosa.*

from the patient's history and clinical examination; however, laboratory tests can be of use in immunocompromised individuals, who may present with an atypical pattern of disease.

The treatment for most sufferers of primary herpetic gingivostomatitis consists of supportive measures, as most patients present for medical treatment when the administration of antiviral drugs would be of little benefit. The relevant treatment modalities are outlined in Tables 2 and 3. Lesions generally resolve within 2 weeks of the appearance of symptoms. Antiviral drugs are indicated for immunocompromised patients, and where the complications are severe. Aciclovir (Zovirax) is the preferred drug for treating primary herpetic gingivostomatitis, used in the following regimen: 200 mg tablets or 5 ml sugar-free suspension five times daily for 5 days (for children under 2 years of age, 2.5 ml sugar-free suspension five times daily for 5 days). Intravenous administration is reserved for immunocompromised patients. As in most viral conditions this drug is of most benefit in the earliest stages of the disease.

It is important to note that in immunocompetent patients primary herpetic gingivostomatitis will occur only once, although a few cases of recurrent herpetic gingivostomatitis have been identified. If the lesions fail to resolve within 10 days, or a recurrence is suspected, the patient should be referred for exclusion of the acute leukaemias. Alternatively, the diagnosis of erythema multiforme should be considered.

Herpes Labialis

Herpes labialis is the condition caused by reactivation of the dormant HSV from its latent position in the trigeminal ganglion, spreading to the perioral skin and resulting in the formation of erythema and vesicles (Figure 3). These rapidly break down to form the characteristic crusted lesions or 'cold sores', which are usually preceded by a prodromal tingling sensation. The most commonly affected area is the mucocutaneous junction of the lip, but intraoral recurrences are not uncommon.

Most cases resolve within ten days, and heal without scar formation.

Recurrence rates for this virus vary between 16 and 45%. Triggers for the reactivation of the virus include trauma (possibly from dental extractions), immunosuppression, decompression of the trigeminal nerve, exposure to ultraviolet light, menstruation, fever and stress.

Dental extractions should be postponed in patients with active herpetic lesions, as in some patients this condition can produce severe pain, which mimics 'dry socket'.

Aciclovir is the drug of choice for active treatment, the appropriate administration being a 5% cream, which may shorten the clinical course (to approximately 5 days) or, in 45% of cases, abort the lesion. However, it must be applied in the prodromal phase to be of any significant benefit. Many patients can prevent reactivation of herpes labialis by the application of a high-factor sunscreen to their perioral skin in periods of exposure to strong sunlight.

Herpetic Whitlow

Herpetic whitlow occurs when HSV infects the subcutaneous tissues of the finger, producing an erythematous and vesicular eruption at that site analogous to a staphylococcal whitlow (Figure 4).

This is an extremely painful condition, which will prevent affected dental professionals from undertaking their normal duties for an extended period of time because of the potential for spreading the virus and because of the severe pain. The institution of adequate cross-infection control protocols (notably glove wearing) is effective in the prevention of herpetic whitlow. Importantly, previous experience with HSV (e.g. herpes labialis) does not appear to prevent the occurrence of this phenomenon.

Lesions often take 2–3 weeks to heal,

Condition	Local treatment	Systemic treatment
Herpetic gingivostomatitis	Supportive (Table 3)	(1) Aciclovir 200 mg five times daily for 5 days; (2) Supportive (Table 3)
Herpes labialis	(1)Aciclovir 5% cream; (2) Sunscreen	None
Herpetic whitlow	Prevent transmission	Aciclovir 200 mg five times daily for 5 days
Chickenpox	Supportive (Table 3)	Supportive (Table 3)
Shingles	Supportive (Table 3)	Aciclovir 800 mg five times daily for 5 days
Glandular fever	Supportive (Table 3)	Supportive (Table 3)

Table 2. *Management of oral herpetic conditions.*

1. Adequate intake of fluids
2. Antipyretic medication (e.g. paracetamol elixir)
3. Analgesics (e.g. paracetamol elixir)
4. Topical agents for the prevention of plaque build-up (e.g. 0.2% chlorhexidine mouthwash), which may also help in the prevention of secondary infection of the lesions
5. The patient (and carers) should be advised to avoid (if possible) contact with fingers, genitalia and eyes to prevent inoculation of these areas.

Table 3. *Supportive measures used in infections with herpes viruses.*

and the treatment available is aciclovir (200 mg tablets five times daily for 5 days). Importantly, aciclovir cannot prevent the recurrence of herpetic whitlow.

Chickenpox

Chickenpox (primary infection with varicella zoster virus: Figures 5 and 6) is contracted by close contact with other infected individuals. An incubation period of 14–21 days is followed by the characteristic rash, mainly affecting the face and trunk, appearing as papules. Vesicles then appear, becoming pustules and finally crusts. Other clinical features include oral ulceration, cervical lymphadenopathy, fever, malaise, irritability and temporary anorexia.

Rare complications include pneumonia and encephalitis, which necessitate immediate hospitalization. Subclinical infections may remain unnoticed.

The treatment is usually supportive as outlined in Table 3, and the immunocompromised are recommended to avoid infected or potentially infected individuals.

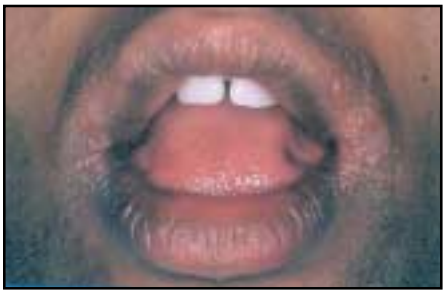

Figure 3. *Bilateral herpes labialis.*

Shingles

Reactivation of varicella zoster virus (Figures 7 and 8) from its dormant position in the dorsal root ganglion of spinal nerves (commonly thoracic region) or the trigeminal ganglion (30%) results in shingles (Zoster). The condition is associated with significant morbidity, and is known colloquially as 'a belt of roses from hell'. Clinical signs include a papular rash, which affects one dermatome, later forming vesicles and then crusts. Intraoral vesicles readily form ulcers and erosions, although the absence of skin lesions (with concomitant intraoral signs) is rare. Shingles usually occurs in the immunocompromised states; however, climatic change and old age may also be contributory causes. As pain is a constant feature – being present before, during and after the clinical course of the condition – shingles should be considered in the diagnosis for patients presenting with 'toothache-like' symptoms in the absence of objective signs.

The complications of Zoster are rare and include 'Ramsay-Hunt' syndrome, producing a facial nerve palsy (simulating a lower motor neurone lesion), and vesicles in the skin of the external auditory meatus, with or without ipsilateral soft palate ulceration.

Most patients recover without any ill effects. Often, however, elderly people and patients with ocular involvement will suffer post-herpetic neuralgia, post-herpetic pigmentation and post-herpetic scarring of the cornea. These symptoms can easily be prevented by the timely administration of aciclovir (800 mg tablets five times daily for 5 days: see Table 2). Symptomatic treatment for the intraoral component of this condition should be prescribed as in primary herpetic infections (Table 3).

The duration of the skin lesions of shingles may be shortened by the application of a 5% aciclovir ointment.[2] If ophthalmic shingles is suspected, an ophthalmological opinion should be sought.

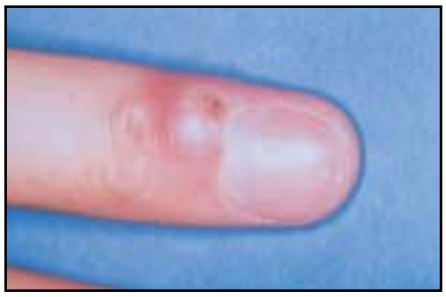

Figure 4. *Herpetic whitlow in the patient shown in Figure 1.*

In patients with Ramsay-Hunt syndrome, the timely prescription of a combination of high-dose steroids and aciclovir will often resolve the facial nerve palsy and prevent a significant proportion of these patients being left with a cosmetic defect.

Glandular Fever

The most common cause of glandular fever (infectious mononucleosis) is Epstein–Barr virus (EBV), although cytomegalovirus (CMV) can also be demonstrated in a number of patients.

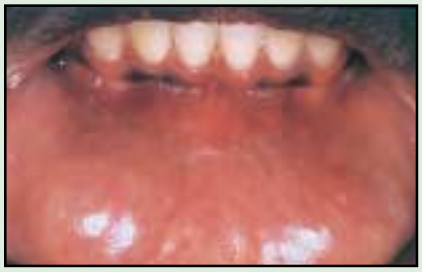

Figure 5. *An intraoral vesicle: the first presenting sign of chickenpox.*

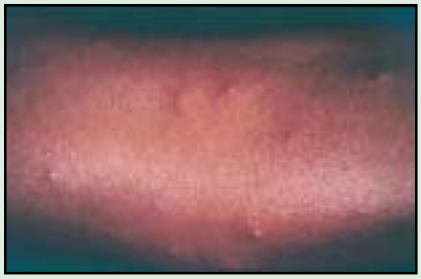

Figure 6. *Cutaneous lesions of chickenpox (same patient as Figure 5).*

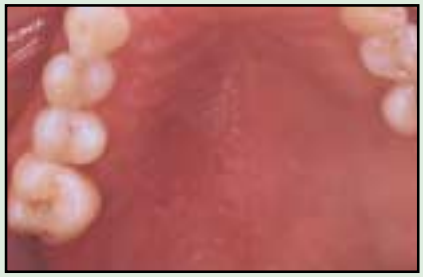

Figure 7. *Ipsilateral vesicles and rash characteristic of shingles affecting the maxillary nerve.*

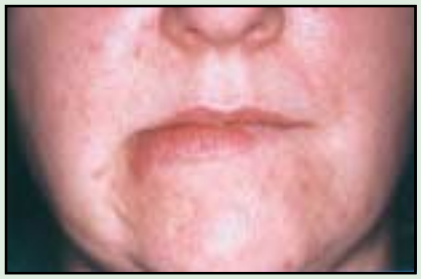

Figure 8. *Shingles affecting the right side of the lower lip (this is easily differentiated from angular cheilitis, which is usually bilateral).*

Glandular fever affects mainly adolescents and is transmitted through the saliva. Many infections are subclinical, the sufferer being unaware of his/her infective status, and by adulthood most people carry antibodies to the virus.

Glandular fever is characterized by obvious cervical lymphadenopathy, exudative facial swelling, soft palate petechiae, pharyngitis, tonsillitis and occasionally severe oral ulceration (Figure 9), fever, malaise and anorexia. Infrequently, the gingivitis that can also be present may be misdiagnosed as acute ulcerative gingivitis or pericoronitis.

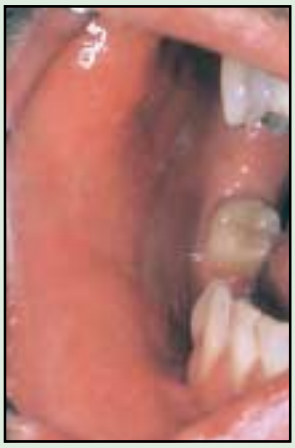

Figure 9. *Severe oral ulceration in glandular fever.*

The diagnosis of EBV-induced glandular fever relies on the demonstration of levels of IgM to EBV, a positive Paul-Bunnel or 'monospot' test for heterophil antibodies or the visualization of abnormal lymphocytes in peripheral blood. CMV-associated glandular fever will have a negative monospot test, although atypical lymphocytes are still seen in peripheral blood.

Treatment usually comprises the supportive measures shown in Table 3.

EBV often remains latent in oropharyngeal epithelium and reactivates in the immunocompromised individual to produce oral ulcers, non-Hodgkin's lymphomas (in the facial area) and hairy leukoplakia.

Cytomegalovirus

Cytomegalovirus, like HSV, is ubiquitous and infection is usually symptomless. Infections can result in mild febrile childhood illnesses, glandular fever, atypical oral ulcers, periodontal disease and cytomegalic inclusion disease.

Human Herpes Virus-8 (HHV-8)

HHV-8 has been identified only relatively recently, in connection with Kaposi's sarcoma and is now known as the Kaposi's sarcoma herpes virus or KSHV. The reader is referred to a specialist text for more information.

TREATMENT OF ORAL HERPETIC CONDITIONS

Tables 2 and 3 outline the appropriate methods of treatment of the various oral herpetic conditions; if any doubt exists as to the diagnosis or treatment of patients with these conditions, then referral to a Local Oral Medicine or Oral Surgery clinic is appropriate.

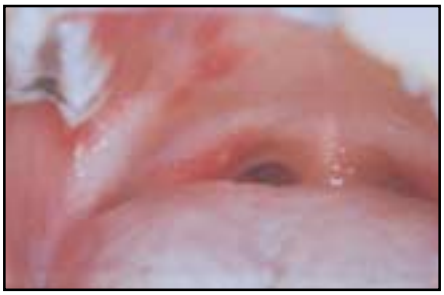

Figure 10. *Typical ulceration of the soft palate in herpangina.*

COXSACKIE GROUP VIRUSES

The results of infection by coxsackie group viruses probably represent the most common cause of oropharyngeal viral infections,[2] usually occurring in small epidemics due to the contagious nature of this virus group. The group is divided into coxsackie group A viruses and coxsackie group B viruses. The range of conditions caused by coxsackie viruses includes:

- oral ulceration;
- herpangina;
- hand, foot and mouth disease;
- mild febrile illnesses;
- encephalitis;
- meningitis.

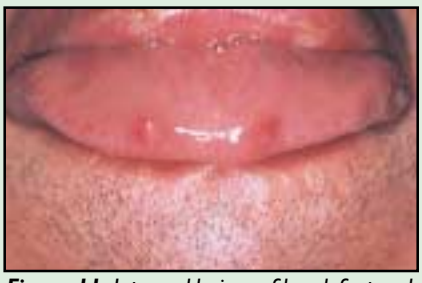

Figure 11. *Intraoral lesions of hand, foot and mouth disease.*

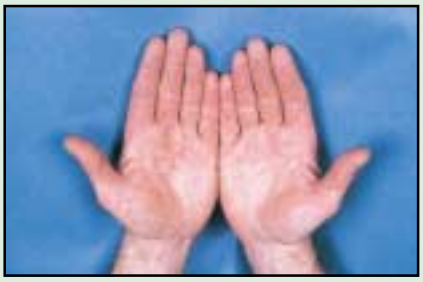

Figure 12. *Cutaneous lesions of hand, foot and mouth disease.*

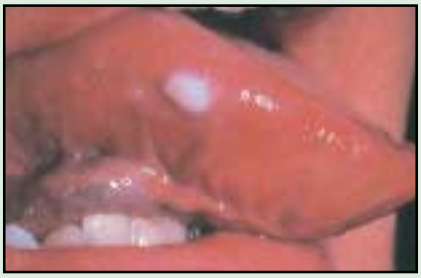

Figure 13. *Intraoral squamous cell papilloma.*

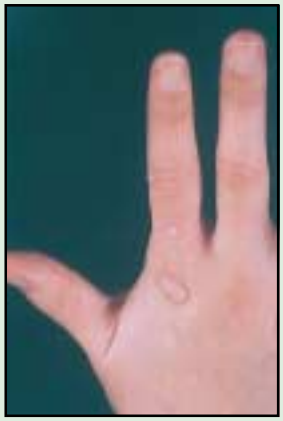

Figure 14. *Multiple cutaneous squamous cell papillomas.*

Herpangina (Figure 10) is caused by the coxsackie group of viruses (A7, A9, A16, B1, B2, B3, B4, B5); and echoviruses (9 or 17).[3] It is a characteristic self-limiting sore throat preceded by discrete vesicles on the soft palate, which may later form an area of ulceration. This usually resolves within 10 days.

Hand, foot and mouth disease (Figures 11 and 12) has an incubation period of 2–6 days and usually presents as a number of intraoral bullae, and a rash present on the hands and feet. Mild fever, malaise and anorexia may also be present. Many infections are subclinical. Coxsackie types A5, A10 and A16 are associated with this disease. Foot and mouth disease is caused by a highly contagious picorna virus, resulting in a severe infection in cloven-hoofed animals. Although humans can be infected, the last recorded human case in the UK was in 1966. Infection in humans is self-limiting and is characterized by an acute fever, followed by bullae on the oral mucous membrane and feet.

Because of the self-limiting and transient nature of herpangina and hand, foot and mouth disease, only clinical diagnosis of these infections is necessary.

As outlined in Table 3, the treatment for the lesions produced by infections of the coxsackie group is of a supportive nature.

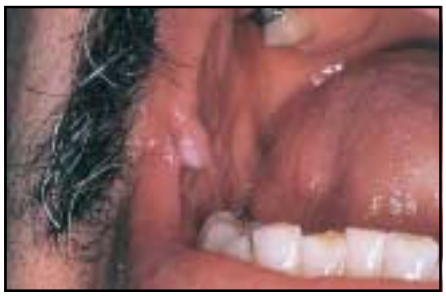

Figure 15. *Intraoral condylomata accuminatum.*

HUMAN PAPILLOMAVIRUS GROUP

Over 100 different human papillomavirus (HPV) types have now been identified, although only a few have specific disease associations. The most often recognized lesions are those of squamous cell papillomas or verruca vulgaris – known more commonly as simple warts (Figures 13 and 14). The intraoral lesions of squamous cell papilloma and verruca vulgaris are often indistinguishable and so will be described together.

The posterior aspect of the hard palate is the commonly affected site, along with the lips and tongue. The lesions have a 'cauliflower-like' appearance, and are often transmitted from another area of skin (usually the fingers) from the same individual. Lesions are diagnosed clinically and will not recur if excised along with their base. Ideally, the diagnosis should be confirmed histologically, but cryosurgery is often used successfully to remove these lesions (although failing to provide a specimen for pathological examination).

Owing to more extrovert sexual practices, venereal warts or condylomata accuminatum (Figure 15) are now often detected intraorally on the tongue and palate. Treatment is by simple excision.

Focal epithelial hyperplasia, also known as Heck's disease, is a rare intraoral manifestation of the HPV group. It presents as multiple raised plaques on the labial and buccal mucosa, and is an entirely benign condition. Patients can be reassured that no specific treatment is usually required.

The aetiology of HPV in leukoplakia and malignant oral conditions is still not resolved although koilocytosis is a clearly demonstrable cytopathic effect histologically in both groups of lesions.

PARAMYXOVIRUSES

Mumps

Mumps is characterized by bilateral swelling of the parotid salivary glands (Figure 16), although unilateral swelling is possible and the submandibular glands may be infected. Infection may be subclinical, mumps having an

Figure 16. *Bilateral parotitis as seen in mumps.*

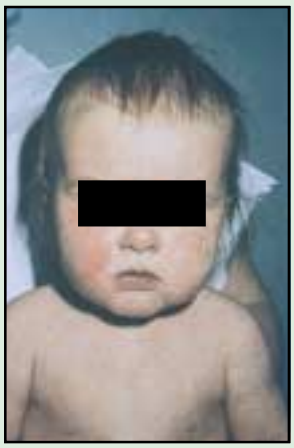

Figure 17. *Extensive skin rash in measles.*

incubation period of 14–21 days. Transmission is usually via infectious respiratory secretions. The clinical picture includes malaise, anorexia, fever and sialadenitis. Clinically, normal saliva is evident, but the salivary gland ducts are usually inflamed. This is an important diagnostic indicator. Patients report a dry mouth and trismus is clinically evident.

The complications of mumps are rare, and include pancreatitis, encephalitis, orchitis, oophoritis and deafness. Elderly individuals acquiring this infection are at a greater risk of complications.

The major causative organism of mumps is usually the mumps virus *per se*, although coxsackie virus, echovirus, EBV and HIV infections have all been associated with this condition.[3] Diagnosis can be confirmed by the demonstration of antibody to mumps virus.

The treatment is again of a supportive nature (Table 3), and the salivary gland swelling usually resolves within 2 weeks. Solid and long lasting immunity follows an attack; second attacks are rare. Mumps is now becoming much less common owing to the use of the combined measles, mumps and rubella (MMR) vaccine.

Measles

Measles (rubeola) is caused by the measles virus (morbillivirus), and has an incubation period of 7–14 days, many infections being subclinical. In the prodromal stages nasal discharge and suffusion from the eyes are obvious. The clinical features include Koplik's spots, a maculopapular rash (Figure 17), conjunctivitis, nasal exudate, cough, fever, malaise and anorexia.

As with many other viral conditions, serology is used to confirm the clinical diagnosis only if absolutely essential, such as in the immunocompromised individual.

Symptomatic treatment is all that is required (Table 3). The incidence of measles is decreasing in the UK owing to the MMR immunization programme. However, concern exists about long-term immunity to measles following MMR vaccination, in contrast to the life-long immunity following infection.

OTHER VIRUSES

Several other viruses have been reportedly associated with oral lesions in immunocompromised persons; new technologies will undoubtedly shed further light in this expanding field.[4]

Acknowledgements

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Further Reading

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