Herpes simplex virus: an occupational hazard in dentistry

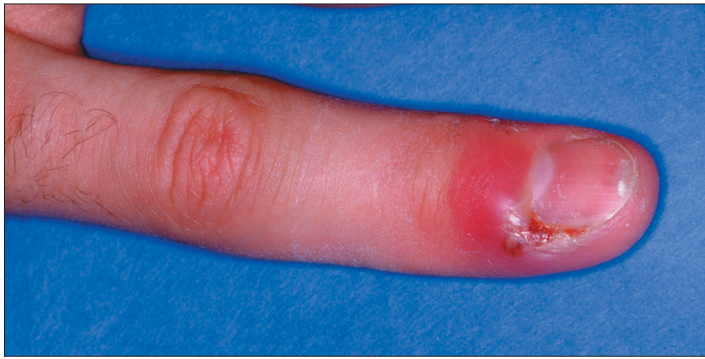**M.A.O. Lewis**
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Approximately 70% of the population in the western world become infected with the herpes simplex virus type 1 (HSV-1) by the second decade of life. This review discusses the role of the HSV-1 as a potential occupational hazard for dental workers, focusing on herpes labialis, herpetic whitlow and keratitis. The risks associated with the dental treatment of patients with HSV-1, both from the perspective of the clinician and the patient are presented. Procedures for minimising the impact of HSV-1 within the dental practice, in particular infection control, delivery of treatment and patient education, are addressed. The management options for recurrent herpes labialis are also reviewed.

Key words: Herpes simplex virus, herpes labialis, herpetic whitlow, keratitis, infection, antiviral therapy, education, dental
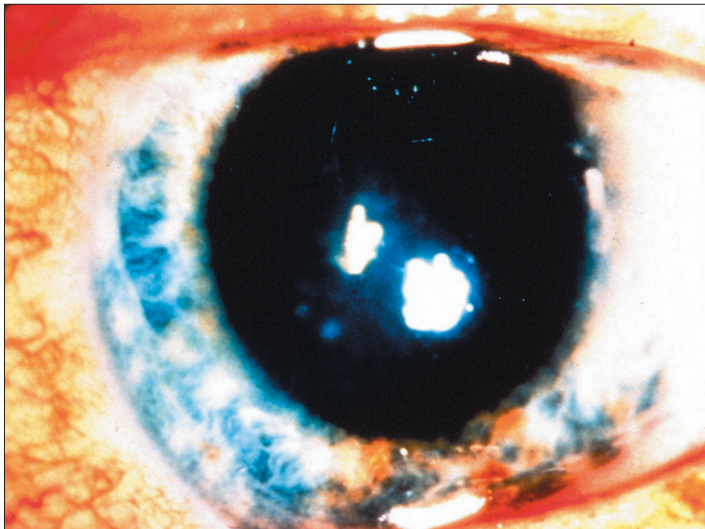
Infection with herpes simplex virus type 1 (HSV-1) is widespread and 40% of children in the UK have detectable antibodies to HSV-1 by the age of 12 years. The incidence of these markers for infection with HSV–1 infection increases to 90% of the population by the age of 60 years[1]. Given the large number of infected individuals and the high incidence of recurrent infection, it is not surprising that HSV-1 is the most frequent virus encountered in the orofacial tissues of humans[2].

Primary HSV-1 infection

Initial infection with HSV-1 characteristically occurs by viral inoculation of the oral mucosa during the first few years of life and results in primary herpetic gingivostomatitis[3]. The symptoms of primary HSV-1 infection are variable and may occasionally either go unrecognised or be misinterpreted as an episode of teething in a child. It has been estimated that only about 5% of individuals develop significant signs that may include multiple oral ulcers, gingivitis, fever and cervical lymphadenopathy[1,4]. Regardless of the severity of initial symptoms, primary infection in an otherwise healthy individual completely resolves within 10–14 days. However, HSV-1 is not eradicated from the host despite the development of specific immunity and the virus remains latent in the orofacial tissues, particularly within the trigeminal nerve[2,5].

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Figure 1. Herpetic whitlow on the finger of a dentist

Figure 2. Herpetic infection affecting the eye

Whilst the vast majority of cases of primary HSV-1 infection present as gingivostomatitis, the virus can also cause a primary infection in the fingers (herpetic whitlow) (*Figure 1*) and eyes (ocular herpes, keratitis) (*Figure 2*) both of which have special relevance in dentistry. These two conditions are described in more detail below.

Recurrent HSV-1 infection

Latent HSV-1 reactivates to cause secondary infections in approximately a third of infected individuals[1]. In most cases, the reactivated virus causes herpes labialis, more commonly known as cold sores or fever blisters, at the mucocutaneous junction of the lower or upper lip[1] (*Figures 3 and 4*). However, reactivated HSV-1 can also produce similar lesions at other sites on the face, nose or chin[3] (*Figures 5 and 6*). Reactivation of HSV-1 can also cause episodes of recurrent oral ulceration, particularly in the hard palate (*Figure 7*). In addition, there is increasing evidence that many individuals, particularly children, periodically shed HSV-1 in their saliva without the development of any clinical signs or symptoms. Various triggers may be responsible for the reactivation of latent HSV-1 within susceptible individuals, the most frequently implicated being emotional stress, illness, sunlight, menstruation and physical trauma[1].

The herpes labialis cycle

Herpes labialis is the most frequent manifestation of reactivation of HSV-1. The frequency of recurrent herpes labialis is highly variable, occurring as rarely as once every 5–10 years in some sufferers to being present as often as monthly in others[3]. An episode of herpes labialis progresses through a number of distinct stages over a period of about ten days (*Figure 8*)[3]. An attack characteristically starts with the prodromal stage, during which the patient experiences pain, burning or itching at the site of lesion development. These symptoms are not always present but between 46–60% of sufferers usually experience the prodrome symptoms, often referred to as the 'tingle' stage[3]. An area of erythema and swelling subsequently develops at the affected site before the appearance of multiple painful, fluid-filled intra-epithelial vesicles. After about 24 hours, the vesicles rupture to produce a painful area of ulceration. At this stage the exudate from the lesion is highly infectious and contains up to 1 million viral particles per ml. After a further 24 hours, the ulcer dries to leave a 'scab' or 'crust'. Levels of shedding of HSV-1 decline rapidly once the lesion has crusted[3]. Finally, the tissues heal as an area of pink-red skin that gradually fades.

Risk of HSV-1 transmission in the dental practice

The presence of HSV-1 within the orofacial tissues represents a potential hazard for clinical staff during the provision of routine dental care[6]. As described above, HSV-1 is shed in high numbers from active herpes labialis particularly during the blister and ulcer stages[7]. The risk of a dental worker acquiring an HSV-1 based infection from a patient is greatest at these times although transmission of the virus is also possible at the crust stage[2]. In addition, some patients secrete the virus in their saliva for some time after the lesion has healed[1]. Whilst the presence or recent history of herpes labialis will alert the clinician to the potential risk of HSV-1 infection, similar cross infection implications

apply to patients with recurrent oral ulceration and those individuals who periodically secrete HSV-1 into their saliva[2]. Primary inoculation from a patient resulting in herpetic gingivostomatitis is unlikely in a dental worker but there is an important risk of occupationally acquiring two other forms of HSV-1 infection, namely herpetic whitlow and keratitis.

Herpetic whitlow

In a survey of dentists and their patients, herpetic whitlow was found to occur significantly more frequently in practising dentists than in the general population (2.4% *vs.* 1.7%; $p < 0.01$), when the occurrence of herpes labialis in each of the two groups was taken as the reference point[8]. Herpetic whitlow develops due to introduction of HSV-1 into the subcutaneous tissues of the finger usually either via a break in the skin, which comes in contact with saliva from an HSV-1-infected patient, or through direct contact of the finger with a herpes labialis lesion[9,10]. Development of herpetic whitlow is a recognised complication of sharps (needle stick) injuries in dental workers. Although the condition is usually relatively self-limiting, whitlow is associated with severe pain and systemic upset, which will prevent the ability to carry out routine dental work[9]. Healing of herpetic whitlow may take several weeks during which time the sufferer is a potential source of infection to other individuals[2]. Herpetic whitlow may be mistakenly diagnosed as a bacterial infection of the finger and inappropriate management can delay healing further[2,7]. It is important to note that previous HSV-1 infection at other sites does not protect an individual from the development of herpetic whitlow[1].

It has already been stated that the pain associated with herpetic whitlow is likely to prevent a dental worker from carrying out

Figure 3. Recurrent herpes labialis on the lower lip

Figure 4. Recurrent herpes labialis on the upper lip

their normal duties. However, it is also ethically advisable for dental workers to refrain from clinical work whilst they have an active infection due to the highly infectious nature of HSV-1[6,7]. An epidemiological study investigating an outbreak of HSV-1 gingivostomatitis in 20 of 46 patients attending a dental hygienist over a period of four days, found that the hygienist providing treatment had an herpetic whitlow[11]. Fortunately, the incidence of herpetic whitlow in dental workers has reduced considerably in recent years due to the routine wearing of gloves.

Keratitis

HSV-1 can infect the eye causing a rare, but serious, condition known as keratitis or ocular herpes. Inflammation of the cornea[12] results in pain, erythema, watering, discharge, itching and lid swelling. In severe cases there is photophobia, vesiculation of the lid, ulceration and blurred vision[13]. Keratitis is an occupational risk for dental workers since HSV-1 in saliva can spread to the eyes of the clinician if not protected by glasses. The aerosols generated by dental high-speed handpieces and ultrasonic scalers represent a particularly important route of transmission of HSV-1 to dental workers. Recently in the UK, the development of HSV-1 keratitis has been the basis of legal action for negligence in both dental workers and patients who have developed this condition. Although the risk of transmission of HSV-1 in these circumstances is relatively low[8], appropriate eye protection must be

Figure 5. Recurrent herpes simplex infection in the nose

Figure 6. Recurrent herpes simplex infection in the nose
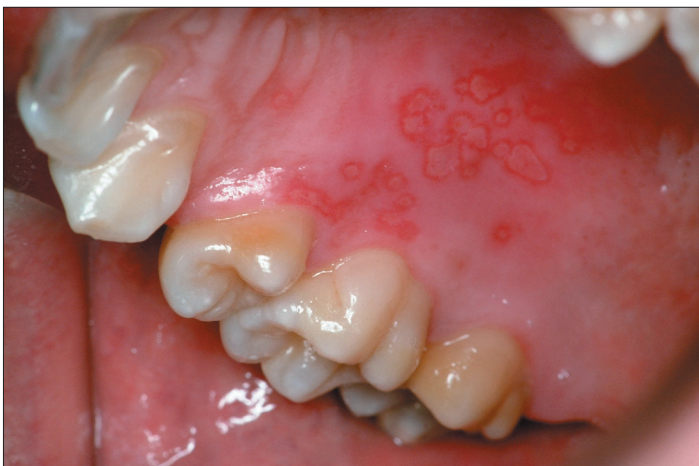
Figure 7. Ulceration to the hard palate due to reactivation of herpes simplex virus

worn by the clinicians and the patient. Fortunately, most cases of keratitis may be treated successfully with antiviral agents. However, recurrent keratitis often reduces visual acuity[7] and failure of therapy can result in loss of vision in the affected eye[12].

Dental treatment: a trigger for reactivation of HSV-1
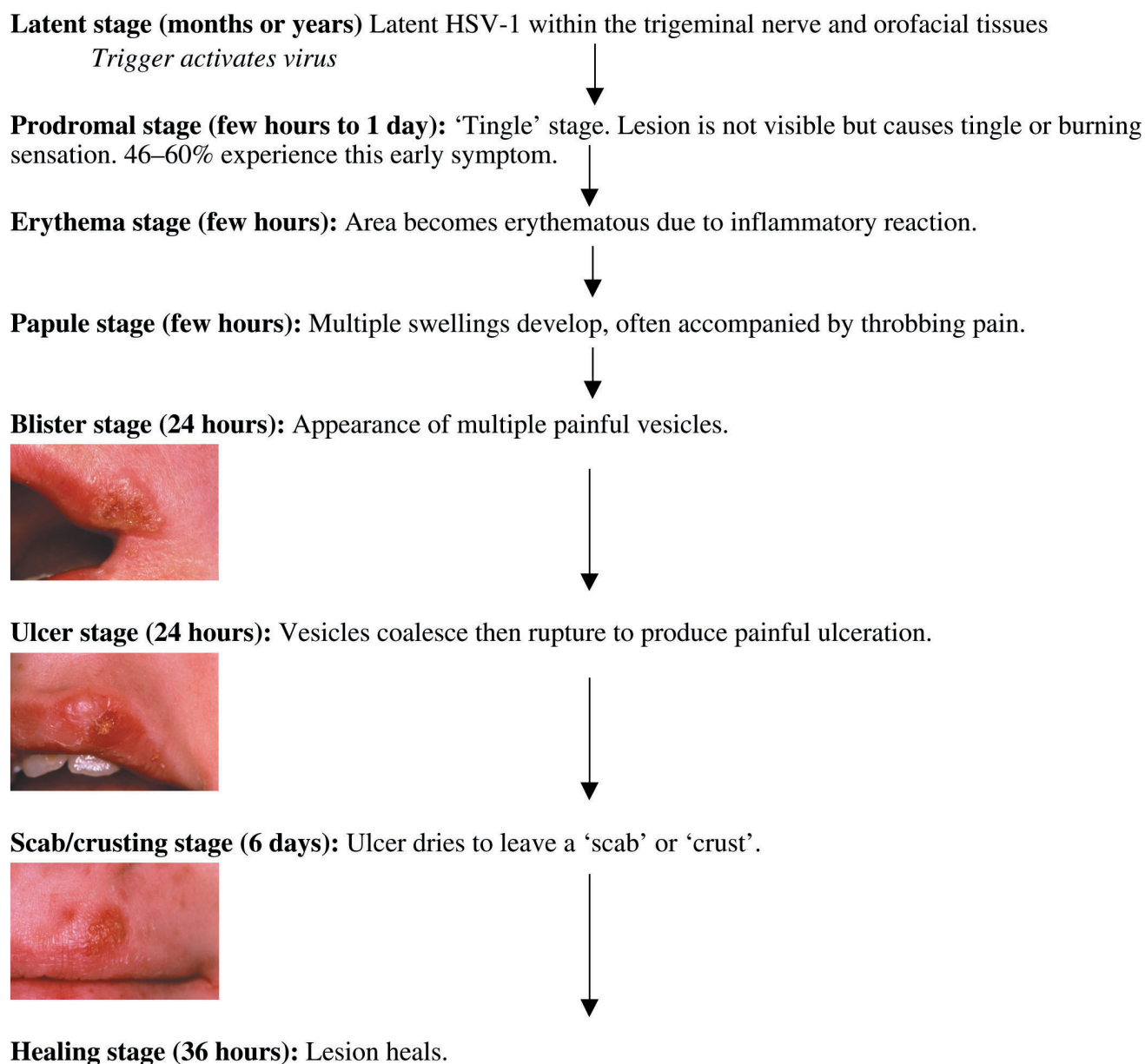
Dental treatment itself may result in reactivation of latent HSV-1 in and around the mouth. For example, the removal of a tooth may trigger herpes labialis due to local trauma of the tissues either as a result of placement of the local anaesthetic or the extraction itself[5]. Injury of the tissues is believed to stimulate migration of HSV-1 from the trigeminal ganglion, down the nerves to the lip or other parts of the face where it undergoes rapid replication[5]. A survey of trigger factors in people who regularly experience herpes labialis reported that 89% of individuals who implicated trauma as a trigger factor identified dental treatment as the cause[14]. The stretching of the orofacial tissues during the provision of dental treatment can also result in local spread of an active lesion thereby causing greater discomfort and pain for the patient[2].

The removal of teeth is contraindicated in patients with herpes labialis due to the risk of development of severe pain at the site of extraction, similar to that caused by dry socket[9].

Impact of HSV-1 infection in at-risk patients

HSV-1 can cause significant morbidity and mortality in immunocompromised patients, particularly those who have acquired immune deficiency syndrome (AIDS)[15] or are receiving immunosuppressive drug therapy. Immunocompromised individuals tend to suffer severe and persistent HSV-1 orofacial lesions[15] and the unusual clinical presentation in such cases may delay diagnosis or provision of antiviral treatment[16]. In some patients HSV-1 infection may progress to involve the central nervous system, lungs, gastrointestinal system, liver or adrenal glands but this subject is beyond the scope of this article[15].

Individuals, often children, with atopic eczema are particularly susceptible to the HSV-1 virus. The virus has been shown to replicate

Latent stage (months or years) Latent HSV-1 within the trigeminal nerve and orofacial tissues
    Trigger activates virus

Prodromal stage (few hours to 1 day): 'Tingle' stage. Lesion is not visible but causes tingle or burning sensation. 46–60% experience this early symptom.

Erythema stage (few hours): Area becomes erythematous due to inflammatory reaction.

Papule stage (few hours): Multiple swellings develop, often accompanied by throbbing pain.

Blister stage (24 hours): Appearance of multiple painful vesicles.

Ulcer stage (24 hours): Vesicles coalesce then rupture to produce painful ulceration.

Scab/crusting stage (6 days): Ulcer dries to leave a 'scab' or 'crust'.

Healing stage (36 hours): Lesion heals.

Figure 8. Key stages and duration of the typical herpes labialis cycle

more rapidly in eczematous skin than normal skin and may progress into a disseminated infection known as eczema herpeticum[17,18]. Eczema herpeticum is a potentially life-threatening complication of HSV-1 infection since it is associated with the development of encephalitis[13]. HSV-1 infection of atopic patients has also been associated with severe herpetic eye infections[18].

Particular care is required to prevent spread of HSV-1 in susceptible individuals and a dental worker with an active lesion should not come into close contact with such patients. It is also important to identify at-risk patients before dental treatment is initiated, since dental trauma is often implicated as the trigger for the development of herpes labialis.

Treatment of HSV-1 infection

The primary aim of antiviral therapy, if used in the treatment of HSV-1 infection, is to reduce viral replication in order to accelerate healing[3]. Antiviral agents have been shown to reduce the duration of the clinical infection and accompanying symptoms, most notably pain and distressing appearance[13]. Antivirals also reduce viral shedding, which in turn is likely to limit the spread of the infection[13]. The treatment of recurrent herpes labialis is predominantly based on the use of topical agents. Herpetic whitlow is treated systemically by the oral route and keratitis may be treated topically or orally. Intravenous administration of an antiviral is only usually required for the treatment of severe forms of HSV-1 infection.

Topical agents

Aciclovir and penciclovir are the two antiviral agents used most

frequently for topical treatment of herpes labialis. Foscarnet[19] and cidovir[20] may be used topically in immuno-compromised patients with aciclovir-resistant recurrent herpes labialis.

Topical therapy of herpes labialis is the most appropriate form of routine treatment since it has the benefits of convenience, reduced systemic exposure to antiviral and specific targeting of the drug to the site of infection[3,21]. Two large-scale randomised, placebo-controlled studies[22] have recently shown that aciclovir cream significantly reduces the duration of herpes labialis and the duration of associated pain. One of the studies reported that aciclovir reduced the duration of the herpes labialis episode, as measured from initiation of treatment to loss of the hard crust if a blister formed or from initiation of treatment to return to normal skin if no blister formed, by 0.5 day ($p = 0.007$). The duration of lesion pain in this study was reduced by 0.3 day ($p = 0.017$) compared with placebo[22]. The second study demonstrated a reduction in lesion episode of 0.6 day ($p = 0.006$) and of lesion pain by 0.4 day ($p = 0.014$)[22]. Aciclovir cream has also been found to have a clinical benefit whether treatment is initiated early at the prodromal stage or late at the blister stage[22]. Similar findings have been reported for penciclovir cream[23]. For maximum efficacy, it would appear that the antiviral cream should be applied frequently. Aciclovir cream should be applied five times daily for five days and continued for a further five days if the lesion has not healed. It has been recommended that penciclovir cream is applied every two hours (while awake) for a period of four days. Aciclovir is also available as an ointment specifically for treatment of herpes simplex infections of the eye. There is no similar preparation of penciclovir for use in the eye.

A new non-prescription topical treatment for recurrent herpes labialis using docosanol has recently been launched in the USA. Docosanol cream has been shown to have antiviral activity and is most effective when applied during the prodromal or erythema stage of herpes labialis[24]. The drug is thought to work by reducing replication of the HSV-1 by inhibiting fusion between the plasma membrane of healthy cells and the HSV-1 envelope[25]. This activity contrasts with that of aciclovir and penciclovir, both of which block viral DNA synthesis after selectively entering herpes virus-infected cells and being activated to their triphosphate forms[26]. Docosanol cream, when applied five times daily, has been shown to be effective and have a safety profile comparable with placebo[27]. Two double-blind, placebo-controlled trials have shown that docosanol shortens the median time to healing by 18 hours ($p = 0.008$)[27]. The drug has also been found to reduce the time from treatment initiation to cessation of pain and other symptoms of itching, burning and/or tingling ($p = 0.002$), the time to complete healing of lesions ($p = 0.023$) and to cessation of the ulcer or soft crust stage of lesions ($p < 0.001$). Docosanol cream also has the advantage of drying to a clear film, which allows make-up to be applied over it.

Systemic agents

Whilst topical treatments have been shown to be effective for the management of herpes labialis, systemic treatment may be more appropriate in individuals who suffer lesions frequently[28]. A five day course of 200mg aciclovir taken orally five times daily and started at the onset of symptoms, has been recommended for such patients. Oral aciclovir is also used prophylactically in immunocompromised patients and for prevention of HSV-1 lesions in those sufferers with frequent secondary infections. Following initial doses of 400mg twice daily, treatment is reduced to 200mg two or three times daily and interrupted every 6–12 months[28]. A break from medication rather than constant use is believed to help reduce the likelihood of the development of resistance to aciclovir.

Oral aciclovir has been shown to accelerate the time to lesion healing among patients who started treatment at the prodromal or erythema stage. In these patients, the mean duration of pain was reduced by 36% ($p = 0.02$) and the mean healing time to loss of crust by 27% ($p = 0.03$)[29]. Oral aciclovir, 400mg twice daily has also been shown to be effective in suppressing herpes labialis in immunocompetent patients with frequently recurring herpes labialis[30]. Compared with placebo, treatment with aciclovir reduced the number of clinical recurrences by 53% and the virus culture-positive recurrences by 71%[30]. In contrast, some studies indicate a lack of response to oral aciclovir. For example, a 2-year randomised, placebo-controlled study found that oral aciclovir 800mg twice daily was not significantly different from placebo in terms of effectiveness and prevention of recurrent herpes labialis[31].

Limited data suggest that a five day course of oral aciclovir is beneficial for herpetic whitlow and may reduce the frequency of recurrence of the infection[1]. One case report indicated a good response to prophylactic treatment with oral aciclovir in a patient with a four year history of recurrent herpetic whitlow[32]. A small study of eight patients with recurrent herpetic whitlow showed that aciclovir given during the prodromal stage of the infection can abort lesion development[33]. Similarly, treatment with oral aciclovir of three HIV-infected patients with prolonged herpetic whitlow resulted in complete recovery[16].

Although a number of studies have shown that oral aciclovir is an effective therapy for herpes labialis,

the drug usually needs to be taken several times daily due to its low oral bioavailability. Newer drugs, such as valaciclovir and famciclovir, the oral prodrugs of aciclovir and penciclovir, respectively, have greater oral bioavailability and may therefore provide greater convenience for the patient[34].

Valaciclovir may be used on a twice-daily basis for five days as a treatment for herpes labialis and is also indicated for suppression of recurrent HSV-1 lesions[28]. Valaciclovir has also recently been launched in the USA as the first oral one-day treatment for herpes labialis. Two large, double-blind, placebo-controlled trials have shown that 2g of valaciclovir taken twice daily for one day reduced the mean duration of herpes labialis lesions by approximately 1 day[35]. However, to be effective the treatment needs to be initiated early at the first sign of symptoms and before any visual signs of the lesion are apparent[35]. Famciclovir is currently indicated for the treatment of recurrent herpes labialis infections in HIV-infected patients as a twice-daily regimen over seven days[36].

What is the most appropriate treatment for herpes labialis?

Whilst clinical efficacy should be the key deciding factor in the choice of treatment for herpes labialis, accessibility, patient preference and compliance also need to be considered. Antiviral therapies presently available vary in terms of the length of the treatment, availability (prescription versus non-prescription) and route of administration. Therapy should ideally be tailored to the need of the individual patient.

Although the majority of antiviral agents require prescription by a medical doctor, aciclovir for topical or oral administration and penciclovir cream may be prescribed by a dentist in a number of countries. Furthermore, aciclovir cream is available without prescription in some countries. Aciclovir cream is not available without prescription in the USA although docosanol topical treatment has recently been launched there. In addition to antiviral agents, a variety of non-specific preparations containing substances such as phenol, zinc oxide, urea, povidone iodine or lidocaine are widely available. Non-prescription treatments offer the patient convenience and rapid access to treatment. Topical treatment is likely to suit a patient who suffers with occasional herpes labialis and is looking for rapid access to treatment rather than an approach involving systemic medication.

Antiviral therapy taken orally usually requires up to five doses per day for a number of days, which is likely to reduce patient compliance. However, valaciclovir provides an extremely convenient one-day oral treatment and this therapeutic approach is likely to become the treatment of choice in the USA. However, such treatment is only possible if the patient has rapid access to a clinician since valaciclovir is a prescription-only drug. Ideally antiviral treatment should start at the prodrome stage and any delay will reduce the efficacy.

Is antiviral resistance a potential problem?

Resistance to all antimicrobial agents, including antiviral agents, is of increasing concern worldwide. The recurrent nature of herpes labialis and the widespread use of antiviral agents, particularly those that are available without prescription, such as aciclovir cream, could potentially result in rapid development of resistance. However, surveillance data suggest that antiviral resistance of HSV does not appear to have increased over the last two decades[37]. Studies indicate that the prevalence of resistant HSV in immunocompetent patients with recurrent HSV infection, such as herpes labialis, is rare (0.1–0.6%) with no apparent difference between treated and untreated patients[37-40]. The prevalence of actual clinical resistance or failure to respond to treatment is even rarer and is predominantly limited to patients who are severely immunocompromised[37].

Resistance to antiviral therapy is an important issue for immunocompromised patients, particularly those with AIDS or recipients of organ transplantation[19]. Interestingly, the reported prevalence of antiviral resistance in such patients has varied. Whilst a number of studies suggest that resistance occurs in around 6% of immunocompromised individuals[40], one study estimated resistance to be as high as 15%[41]. However, a review of resistance over the last 20 years found no evidence to suggest that the problem is increasing in this population[37].

Concerns regarding the effect of increased availability of topical antiviral creams on the prevalence of resistance have not been substantiated. A comparison of two surveys, one performed in the UK[39] and the other in the USA[38], revealed that there was no difference in the prevalence of antiviral resistance despite the widespread use and availability of topical aciclovir in the UK compared to restricted use in the USA[37]. However, in order to limit the potential for misuse of antiviral products, patients should be advised to read the patient information leaflet carefully and follow the instructions.

Reducing the transmission of HSV-1 within dental practice

It is generally accepted that there is a risk of a dental worker acquiring HSV-1 infection whilst providing treatment to patients. HSV-1 will be eliminated from dental instruments during standard sterilisation procedures. However, prevention and control of infection measures, particularly the wearing of gloves, mask and eye protection for treatment of all patients, are essential to minimise any risk of transmission

Table 1   Measures to reduce the risk of transmission of HSV-1 within the dental practice[6-8,10].

Acquisition: Occupational exposure Patient to dental worker	Transmission: Dental worker to patient
• Be aware of the signs and symptoms of HSV-1 infection • Postpone treatment of a patient until HSV-1 lesion has healed • Routinely cover all cuts and abrasions on the hands • Routinely use protective equipment (gloves*, mask and eye protection) • Do not touch own eyes, nose and mouth while treating a patient • Use high volume aspiration to reduce aerosols • Sterilise instruments (autoclave, dry heat, ethylene oxide gas) after use or use disposable instruments	• Be aware of the signs and symptoms of HSV-1 infection • Do not undertake dental treatment whilst HSV-1 lesion is present • Routinely cover all cuts and abrasions on the hands • Routinely use protective equipment (gloves*, mask and eye protection) • Patient must wear eye protection during treatment • Do not touch own eyes, nose and mouth whilst treating a patient • Sterilise instruments (autoclave, dry heat, ethylene oxide gas) after use or use disposable instruments

* Certain dental materials can render latex gloves permeable to herpes viruses (e.g. acrylic monomer, chloroform, oragne solvent)[43]

- **Cold sores are caused by the herpes simplex virus.**
- **The herpes simplex virus can easily be spread by direct (lip) or indirect (finger) contact, especially when a cold sore is present.**
- **Inform your dentist if you suffer from cold sores or ulcers in your mouth.**
- **Postpone a dental appointment when a cold sore is developing (tingle stage) or if one is present until the lesion has completely healed.**
- **Antiviral treatment for cold sores is available as a topical cream and can be bought from a pharmacy without a prescription (only in some countries).**
- **Antiviral treatment is effective at the tingle and blister stages of a cold sore.**

Figure 9. Information to be included on a dental practice poster or leaflet to increase awareness of herpes labialis (cold sore, fever blister).

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of infection by other routes (*Table 1*). It is also advisable to postpone treatment in a patient with an active HSV-1 lesion[42]. Similarly, a dental healthcare worker should not provide treatment whilst they themselves have an active HSV-1 infection.

Patient information

Informing patients of the infectious nature of herpes labialis is likely to reduce the risk of spread of the disease not only within the dental practice but also the wider community (*Figure 9*). Dental healthcare workers are ideally placed to raise awareness of HSV-1 infection, in particular herpes labialis and the availability of effective treatment. An important factor in preventing transmission of HSV-1 within the dental practice is to identify those patients who suffer with recurrent herpes labialis. This information can be gained during routine history taking or updating of the patient's medical history. However, care

should be taken when questioning patients about herpes, since the term 'herpes' has a social stigma in some countries, which may cause embarrassment. Use of the terms cold sores or fever blisters when questioning the patient is preferable.

Patients who suffer with recurrent HSV-1 infections should be encouraged to inform the dental practice if they have a herpes labialis lesion prior to their appointment to allow the visit to be rescheduled and help avoid lost work time[2].

Conclusions

The high prevalence and infectious nature of HSV-1 makes this virus an occupational hazard for the dental practice. However, appropriate infection control measures and education of patients can help minimise the risks associated with HSV-1 both for the clinician and the patient. Patients who experience recurrent herpes labialis should be advised on the use of topical or oral antiviral therapies since these

can reduce the duration of the lesion. Treatment should be tailored to the needs of the individual patient according to the nature of the symptoms and accessibility to prescription or non-prescription medication.

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