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03 **Severe herpes simplex virus type-I infections after dental procedures**

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22 **Abstract**

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24 **Background:** Recurrences of herpes labialis (RHL) may be triggered by systemic factors, including stress, menses, and fever. Local stimuli, such as lip injury or sunlight exposure are also associated to RHL. Dental extraction has also been reported as triggering event.

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27 **Case reports:** Seven otherwise healthy patients are presented with severe and extensive RHL occurring about 2-3 days after dental extraction under local anaesthesia. Immunohistochemistry on smears and immunofluorescence on cell culture identified herpes simplex virus type I (HSV-I). Five patients reported more severe prodromal signs than usual. Although all the patients suffered from RHL, none had previously experienced RHL after dental care. Two patients required hospitalisation for intravenous acyclovir therapy, whereas the others were successfully treated with oral valaciclovir or acyclovir.

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33 **Conclusion:** Severe and extensive RHL can occur soon after dental extraction under local anaesthesia. Patients with a previous history of RHL seem to be at higher risk. It is not clear whether RHL is linked to the procedure itself, to the anaesthetic procedure or both. As the incidence is unknown, more studies are required to recommend prophylactic antiviral treatment in RHL patients who are undergoing extractions. Dentists should be aware of this potentially severe post-extraction complication.

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39 **Key words:** *Aciclovir, prevention, herpes labialis, triggering factors.*

40 **Introduction**

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42 Herpes simplex viruses type I (HSV-I) and II (HSV-II) are members of the α -herpesvirus family (1). The primary infection establishes a life-long latency in the sensory nerve ganglia. Subsequent infra-clinical recurrences are common, eventually followed by a clinical recrudescence (1). Recurrent herpes labialis (RHL) affects 16% to 38% of the population (1). In elderly patients, the frequency of RHL sinks to approximately 20%. The recrudescence of HSV infections requires simultaneously viral reactivation at the trigeminal ganglia level as well as a cutaneous permissivity allowing intra-epidermal viral replication that lead to lesion formation (1). Recrudescence is usually occurring at the same anatomical site, in general the vermillion border

of the upper or lower lip. Recrudescences often present a similar clinical course in terms of duration, pain and lesion severity (1). In many instances, RHL follows various initiating events. Systemic stimuli include fever, menses, iatrogenic immunosuppression and stress. Local triggers encompass lip injury, exposure to cold, sunlight, wind, and iatrogenic trauma (1). RHL can also complicate dental procedures, fixed prosthodontic tissue, and surgery of the oral cavity (1-6). Although supposed to be rare, no data on the incidence of dental intervention-associated RHL are available.

Seven patients are described who presented unusual extensive and severe HSV-I infection following dental extraction.

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01 **Case Reports**

02 The salient clinical features of the patients are summar-
 03 ized in table 1. None of the patients presented a remark-
 04 able medical, allergic or surgical previous history. The
 05 patients took no immunosuppressive medication. All the
 06 patients (3males/4females, mean age: 37.2 years, mini-
 07 num: 19 years, maximum: 55 years) suffered from long-
 08 standing RHL, experiencing between 3 and 8 recrudescen-
 09 ces par year. Stress was the most frequent initiating
 10 event. Two patients suffered from sun-exposure related
 11 recrudescences. Previously, none had experienced RHL
 12 after dental care. Five patients systematically recognized
 13 the typical prodromal signs, including stinging, burning,
 14 dysesthesia, and itching, occurring 1 to 2 days before the
 15 recrudescences. Preceding the current episode, the pro-
 16 dromal signs were much more severe than usual.
 17 The patients searched medical advice mainly due to the
 18 unusual severity of the eruption. Five patients visited
 19 the emergency ward and the others consulted their GP
 20 or dermatologist. One of the patients admitted to the
 21 emergency ward was initially misdiagnosed as erysip-
 22 elas and received intravenous antibiotics (Amoxicilline/
 23 clavulanic acid, Augmentin®, 3x1000mg/day, Smith
 24 Kline Beecham). Two patients presented a painful erup-
 25 tion extending to the right cheek, nose, chin, the oral
 26 cavity and upper lip (Fig 1,2). Erythematous, vesicular,

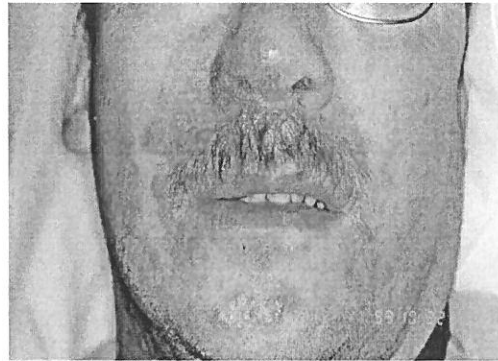


Fig. 1. Severe HSV-I infection following extraction, affecting the lips, cheek, nose, and oral cavity.



Fig. 2. Severe and extensive HSV-I infection after molar extraction.

Table 1. Salient patient characteristics.

Case	Sex Age	Procedure	Anaesthesia	Time interval extraction-RHL	Signs	Site	Test	Serology
1	M 39	Extraction Sup R 3m	Local	2 d	Fe, Ad	Labial inf/sup Cheek, chin	Tz	IgG+, IgM-
2	M 19	Extraction Inf R incisor	Block	2 d	Fe, Ad	Labial inf/sup Cheek, chin	Tz	IgG+, IgM-
3	F 55	Extraction Inf R 2m	Block	2 d	-	Labial sup Chin Nasolabial	CC	NA
4	F 21	Filling Sup R 1m	Local	3 d	-	Labial sup Chin Nasolabial	ND	NA
5	F 30	Extraction Inf L 3m	Block	3 d	-	Labial inf/sup	Tz	IgG+, IgM-
6	M 46	Extraction Inf R 3m	Block	2d	-	Labial inf/sup	Tz	NA
7	F 51	Extraction Inf R 2m	Block	3d	-	Labial inf Chin, cheek	Tz	IgG+, IgM-

M: Male, F: Female, Fe: Fever, Ad: Loco-regional adenopathy, Tz: Tzanck smear test, CC: cell culture, Inf: inferior, Sup: superior, R: right, L: left, m: molar, d: days, NA: not available.

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01 and crusted lesions were present. Both had fever (39°C),
02 a regional adenopathy and were not able to eat. Further
03 physical examination was unremarkable. Due to the
04 severity, two patients required hospitalization and in-
05 travenous acyclovir (5mg/kg/day for 8 days, Zovirax®,
06 GSK). Both individuals had a positive past serostatus for
07 HSV (IgG: +, IgM: -). Topical and intraoral disinfection
08 with povidone iodine (Isobetadine®, MEDA Pharma)
09 was administered three times daily. Blood screening
10 only revealed a mild increase of the sedimentation rate.
11 Other laboratory examinations, including liver, renal,
12 and thyroid functions as well as red and white blood cell
13 counts were in normal range. Serology was negative for
14 HIV, hepatitis A and B.

15 In the five other patients the eruption extended beyond
16 the usual site of recrudescence to the nasolabial fold,
17 the chin, and the cheek, predominantly affecting the site
18 where the procedure had taken place. The patients were
19 treated with oral valaciclovir (Zelitrex®, 500mg b.i.d.
20 for 7 days) or oral acyclovir (5 x 200 mg for 7 days).

21 All the patients presented the recrudescence 2 to 3 days
22 after the dental interventions. All the procedures (Table
23 1) were performed under local anaesthesia using lido-
24 caine (either block anaesthesia of the inferior alveolar
25 nerve or local periodontal infiltration for upper molars).
26 The procedures were molar extractions (5), incisor ex-
27 traction (1) and renewal of a filling (1).

28 Tzanck smears were performed in 6 patients showing
29 multinucleated, syncytial giant cells and numerous
30 polynuclear neutrophils, suggesting an α -herpesvirus
31 infection. Immunohistochemistry using specific anti-
32 bodies directed against HSV-I, HSV-II and Varicella
33 Zoster Virus (VZV) (7) revealed a positive signal for
34 HSV-I, whereas the other antibodies revealed a negative
35 staining. In one patient, a swab was performed for viral
36 cell culture, revealing HSV-I by immunofluorescence
37 after 48 hours.

38 The alveolar healing process after extraction was not
39 impaired or delayed.

40 Two patients required subsequent molar extractions and
41 prophylactic oral valaciclovir (500mg b.i.d., Zelitrex®,
42 Glaxo Smith Kline) was administered 48 hours before
43 until three days after dental care. No further herpetic
44 recurrences were observed in both patients. The drug
45 was well tolerated.

46 Discussion

48 Seven cases of severe dental-extraction-related HSV
49 infections are presented. The imputability to dental
50 injury should be taken with precaution. Nevertheless,
51 all the patients had a previous history of RHL, no his-
52 tory of RHL following dental fillings, no RHL at the
53 time of extraction, a significantly more severe erup-
54 tion than usual, local anaesthesia, a time-interval of 2-3
55 days, and an increased healing time of the eruption in
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common. All the recrudescences started at the site of
prior episodes. Although dental extraction is usually
incriminated as initiating factor, HSV may also com-
plicate fixed prosthodontic tissue (4). There are no data
concerning other common dental procedures, such as
fillings or removal of dental plaque. Data on frequency
of extraction-related RHL are sparse and contradictory.
In a study, 4/20 patients with a previous history of RHL
experienced RHL after dental extraction whereas no re-
currences were noted in 19 patients without a history
of RHL (2). However, in a large study evaluating the
post-extraction complications of 3818 extractions, no
single case of HSV was evidenced (8). In another study
comprising 48 patients undergoing third molar extrac-
tion showed that the frequency of HSV-1 positive nested
polymerase chain reaction (PCR) was low (4,2%) and
not statistically significant with a control group under-
going conventional procedures (5)

The triggering may be multi-factorial. First, it has been
demonstrated that fear and stress for dental procedures
increases HSV asymptomatic shedding (9). This may
be further increased by the nerve injury during extrac-
tion (9). In fact, during surgical procedures involving
the trigeminal nerve root, HSV reactivation occurs in
up to 50 % of the patients (10). However, HSV shed-
ding seems to occur independently from clinical recur-
rences (11,12). Third, nerve irritation by the anaesthetic
block may also conduct to viral reactivation and recrudes-
cence, as the inferior alveolar nerve is a branch of
the mandibular nerve, which is itself the third branch of
the trigeminal nerve, where viral latency is established.
These three elements probably lead to a higher viral
load, explaining the increased severity of the eruption.
Extension of HSV cutaneous extension is often facilitat-
ed by keratinocytic injury, observed during deep chemi-
cal peelings, abrasive laser resurfacing, dermabrasion
and other cosmetic procedures (13). These procedures
systematically require a prophylactic antiviral treatment
(13). However, no signs of prior skin injury were present
in the patient. It is unclear, whether the manipulation
and extension of the lips during the dental procedure
constitutes a risk factor.

The alveolar healing process after extraction seems not
delayed or impaired.

The clinical diagnosis of extraction-related RHL is usu-
ally evident. However, immunohistochemical confir-
mation on a Tzanck smear is suggested (7), in particu-
lar as post-extraction herpes zoster has been described
(14,15). As sero-prevalence achieves 90 to 95% in the
adult population, serology is not a recommended diag-
nostic method.

The treatment of these extraction-related HSV infec-
tions relies on oral or intravenous antiviral therapy,
according to the clinical severity. In two patients, pro-
phylactic antiviral treatment was effective as no RHL

01 was observed after subsequent molar extractions under
02 local anaesthesia. More data is however required to rec-
03 ommend prophylactic antiviral therapy. Currently, only
04 selected individuals with a history of RHL are eligible
05 for antiviral prophylaxis. In analogy to prophylactic an-
06 tiviral treatment for abrasive cosmetic procedures, the
07 following scheme could be proposed; oral valaciclovir
08 (500mg b.i.d., Zelitrex®, Glaxo Smith Kline), 48 hours
09 before until three days after dental care. Famciclovir or
10 acyclovir may also be considered (13).

11 In conclusion, recrudescence of HSV can be triggered
12 by dental extraction. These infections seem to be more
13 severe than usual outbreaks. Data on incidence are lack-
14 ing. Prophylactic antiviral treatment could be consid-
15 ered for RHL patients on an individual basis. Dentists
16 should be aware of this potentially severe complication
17 of dental extraction.

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19 References

- 20 1. Nikkels AF, Pièrard GE. Treatment of muco-cutaneous presenta-
21 tions of herpes simplex virus infections. *Am J Clin Dermatol.* 2002;
22 3: 475-87.
- 23 2. Openshaw H, Bennet HE. Recurrence of herpes simplex virus af-
24 ter dental extraction. *J Infect Dis.* 1982; 146: 707.
- 25 3. Scott DA, Coulter WA, Lamey PJ. Oral shedding of herpes simplex
26 virus type 1: a review. *J Oral Pathol Med.* 1997; 26: 441-7.
- 27 4. Williamson RT. Diagnosis and management of recurrent herpes
28 simplex induced by fixed prosthodontic tissue management: a clinical
29 report. *J Prosthet Dent.* 1999; 82: 1-2.
- 30 5. Marques-Silva L, Castro WH, Gomez EL, Guimarães AL, Silva
31 MS, Gomez RS. The impact of dental surgery on HSV-1 reactivation
32 in the oral mucosa of seropositive patients. *J Oral Maxillofac Surg.*
33 2007; 65: 2269-72.
- 34 6. Guggenheimer J, Fletcher RD. Traumatic induction of an intraoral
35 reinfection with herpes simplex virus. *Oral Surg Oral Med Oral*
36 *Pathol.* 1974; 38: 546-9.
- 37 7. Nikkels AF, Debrus S, Sadzot-Delvaux C, Piette J, Rentier B,
38 Pièrard GE. Immunohistochemical identification of varicella-zoster
39 virus gene 63-encoded protein(IE63) and late (gE) protein on smears
40 and cutaneous biopsies : implications for diagnostic use. *J Med Virol.*
41 1995; 47: 342-7.
- 42 8. Simon E, Matee M. Post-extraction complications seen at a refer-
43 ral dental clinic in Dar Es Salaam, Tanzania. *Intern Dental J.* 2001;
44 51: 273-6.
- 45 9. Hyland PL, Coulter WA, Abu-Ruman I, Fulton CD, O'Neill HJ,
46 Coyle PV, et al. Asymptomatic shedding of HSV-1 in patients under-
47 going oral surgical procedures and attending for noninvasive treat-
48 ment. *Oral Dis.* 2007; 13: 414-8.
- 49 10. Pazin GJ, Ho M, Jannetta PJ. Reactivation of herpes simplex vi-
50 rus after decompression of the trigeminal nerve root. *J Infect Dis.*
51 1978; 138: 405-9.
- 52 11. Knaup B, Schünemann S, Wolff MH. Subclinical reactivation of
53 herpes simplex virus type 1 in the oral cavity. *Oral Microbiol Im-*
54 *munol.* 2000; 15: 281-3.
- 55 12. da Silva LM, Guimarães AL, Victória JM, Gomes CC, Gomez
56 RS. Herpes simplex virus type 1 shedding in the oral cavity of sero-
57 positive patients. *Oral Dis.* 2005; 11: 13-6.
- 58 13. Nestor MS. Prophylaxis for and treatment of uncomplicated skin
59 and skin structure infections in laser and cosmetic surgery. *J Drugs*
Dermatol. 2005; 4: s20-5.
14. Maini S, Preece M. Herpes zoster oticus following mandibular
block. *J Laryngol Otol.* 2000; 114: 212-3.
15. van Gemert JT, Koole R. An unusual skin disorder after tooth
extraction. *Ned Tijdschr Tandheelkd.* 2007; 114: 98-103.

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