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Guidelines

French guidelines for the management of oral lichen planus (excluding pharmacological therapy)

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SUMMARY

Introduction: Oral lichen is a chronic inflammatory disease for which diagnostic management and follow-up are heterogeneous given the absence of specific guidelines in France. Our objective was to develop French multidisciplinary guidelines for the management of oral lichen.
Materials and methods: Working groups from the *Groupe d'Etude de la Muqueuse Buccale (GEMUB)* formulated a list of research questions and the corresponding recommendations according to the "formal consensus" method for developing practice guidelines. These recommendations were submitted to a group of experts and the degree of agreement for each recommendation was assessed by a scoring group.
Results: Twenty-two research questions, divided into 3 themes (nosological classification and initial assessment, induced oral lichenoid lesions, and follow-up) resulted in 22 recommendations. Initial biopsy for histology is recommended in the absence of reticulated lesions. Biopsy for direct immunofluorescence is recommended for ulcerated, erosive, bullous types and for diffuse erythematous gingivitis. Management should include a periodontal and dental check-up, and investigation for extra-oral lesions. Hepatitis C testing is recommended only if risk factors are present. Definitions, triggering factors and the management of "induced oral lichenoid lesions" were clarified. Oral lichen must be monitored by a practitioner familiar with the disease at least once a year, using objective tools.
Conclusion: This formalised consensus of multidisciplinary experts provides clinical practice guidelines on the management and monitoring of oral lichen.

Oral lichen is a chronic inflammatory disease whose management involves different practitioners: dermatologists, oral surgeons, stomatologists, maxillofacial surgeons, dental surgeons and pathologists. There are no evidence-based recommendations available in France or in Europe for the management of oral lichen. In the United States, the AAOMP (American Academy of Oral and Maxillofacial Pathology) and the AAOM (American Association of Oral Medicine) have drawn up monodisciplinary recommendations not based on any systematic methodology [1,2]. Furthermore, systematic reviews of therapeutic interventions for oral lichen planus – which include two Cochrane reviews – do not address

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initial assessment and work up, management of "induced oral lichenoid lesions", or patient follow-up [3,4].

Our objective was therefore to produce multidisciplinary recommendations for the management of oral lichen.

1. Methods

These recommendations were established between 15 December 2017 and 6 December 2019 by the French GEMUB group (*Groupe d'Etude de la Muqueuse Buccale*) on the basis of the methodology of the "Haute Autorité de Santé" for developing good practice recommendations by formalized consensus. These recommendations include the initial management and further monitoring of oral lichen planus, excluding drug treatment. Under the coordination of a steering group, four working groups developed the research questions then carried out a bibliographic analysis and proposed recommendations in response to each question, based on a set of arguments. Each group consisted of 4 to 6 practitioners specialized in oral lichen, with representatives from medical specialties (dermatology, oral surgery, pathology, stomatology, maxillo-facial surgery) and odontological disciplines (oral surgery, oral medicine), from both public and private practice and from different parts of France. The bibliographical analysis was carried out using the MEDLINE database between 1 March and 1 June 2019 (inclusion criteria: articles written in English and French; search period between 01/01/1990 and 31/12/2018; clinical trials, systematic reviews with meta-analyses, case series greater than or equal to 3 cases, recommendations for clinical practice and consensus conferences). Selected articles were analysed using predefined extraction grids and were graded according to level of evidence (Table 1). In response to each question, the working groups drafted arguments and recommendations, and these were revised by an external multidisciplinary group of experts with representation from medical specialties (dermatology, oral surgery, anatomical-cyto-pathology, stomatology, maxillofacial surgery) and odontological disciplines (oral surgery, oral medicine). The degree of agreement on the final version of the recommendations was assessed using an interactive voting system by a scoring group. Each voter rated each draft recommendation from 1 to 9, according to degree of acceptability.

2. Results

The working group identified 22 research questions, divided into three themes: nosological classification and initial assessment of oral lichen; induced oral lichenoid lesions (IOLL); follow-up of oral lichen. The flow chart of the literature search is shown in Fig. 1. A total of 150 articles were analysed. The degree of agreement of the scoring group for each recommendation is shown in Table 2.

2.1. Theme 1. Nosological classification and initial assessment of oral lichen

Question 1: In patients with suspected oral lichen, are there any clinical and histological criteria that should be examined at initial assessment in order to distinguish between oral lichen planus and oral lichenoid lesions?

The diagnostic criteria adopted by the WHO in 2003 (Table 3) distinguish between oral lichen planus (OLP) and oral lichenoid lesions (OLL) based on "typical" or "consistent" clinical and histological features [5,6]. Any lesion not meeting the "typical" clinical and histological criteria is classified as an OLL [5,6]. However, this classification does not define or include "lichenoid reactions", which, by definition, improve or disappear after exclusion of the causative agent (e.g. a systemic condition, a local triggering factor, or a drug). There is therefore some confusion of terminology between "lichenoid lesions" and (induced) "lichenoid reactions". Furthermore, the WHO classification does not take into account the histopathological course of OLP over time and under the influence of extrinsic factors. Some clinical types, such as diffuse erythematous gingivitis (*i.e.* erosive gingivitis, desquamative gingivitis) and some long-lasting OLPs, do not or no longer have the "typical" features and would therefore be classified *de facto* as OLLs on the WHO classification.

This terminology has been clarified by the working group in order to distinguish OLP and OLLs, as defined by the WHO, from IOLLs, classically referred to as "lichenoid reactions", which improve or disappear after suppression of the inducing factor (Table 4).

The generic denomination "oral lichen" encompasses all three entities: OLP, OLL and IOLL.

Recommendation 1: Presence of factors inducing oral lichen, such as general disease (e.g. graft-versus-host disease, lupus, Good's syndrome), a local factor or a drug, should be sought in order to distinguish IOLL from other types of oral lichen. A diagnosis of IOLL is retained only if the lesion disappears/improves after suppression of the inducing factor. Distinction between OLP and OLL does not affect overall management (EO).

Question 2. In patients with suspected oral lichen, should biopsy be routinely performed during the initial assessment?

According to the WHO criteria, biopsy is part of the initial assessment of oral lichen [5]. Its purpose is:

- to differentiate OLP from OLL where clinical features are "typical" of OLP;
- to differentiate OLP from other differential diagnoses where clinical features are "consistent" solely with OLP;
- to rule out autoimmune bullous dermatosis, especially in the case of diffuse erythematous gingivitis [2];
- to screen for dysplasia [7].

However, the correlation between the clinical and histological diagnosis of OLP was found to be low. In a study of 100 patients with oral lichen, Hiremath et al. made a clinical diagnosis of OLP in 80% of cases and of OLL in 20%, whereas a pathologist diagnosed OLP in 38% of cases and OLL in 62% of cases [7]. Mravak-Stipetic *et al.* found clinicopathological diagnostic correlation in only 52.5% of OLP cases and 42.9% of OLL cases [8]. These studies also found the clinicopathological correlation to be improved when the biopsy was taken from a keratotic zone rather than an erosive zone [7,8].

Recommendation 2: In the presence of typical white reticulations, biopsy should not be routinely performed for the diagnosis of oral lichen. Biopsy is recommended in the absence of typical white reticulations. The biopsy should be performed outside erosive or ulcerated areas. (EO)

Question 3. In patients with suspected oral lichen, should biopsy for direct immunofluorescence (DIF) be routinely performed during the initial assessment?

Question 4. In patients with suspected oral lichen, when should lichen planus pemphigoides be considered and how can the diagnosis be confirmed?

DIF of oral lichen shows linear fibrinogen deposits on the basal membrane. This finding is non-specific and its sensitivity depends

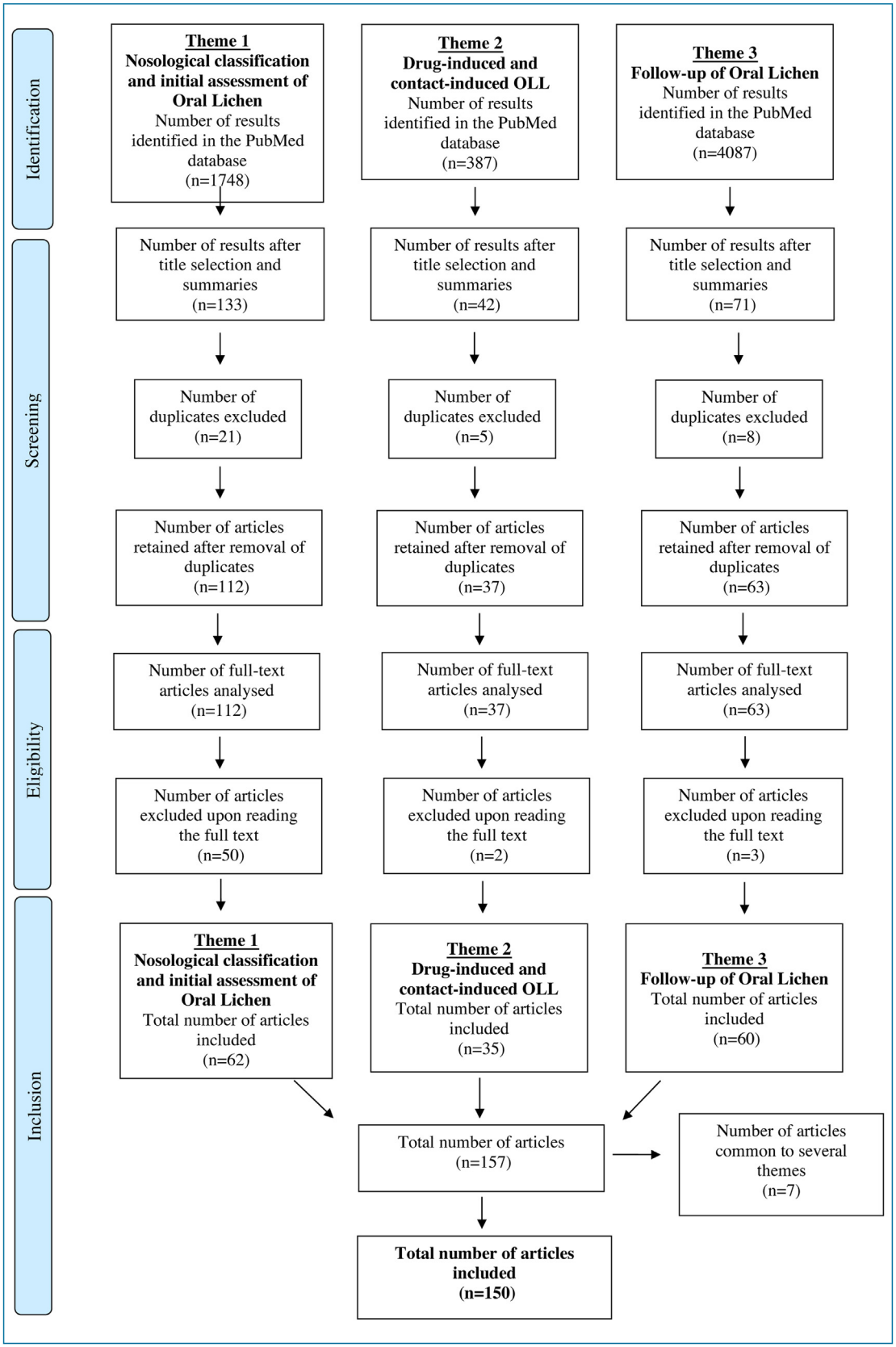

Fig. 1. Flow chart of the literature search.

Table 1
Grade of recommendations.

Grade of recommendations	
Grade A	**Established scientific evidence** Based on studies with a high level of evidence (level of evidence 1): high-powered randomised controlled trials with no major bias or meta-analysis of randomised controlled trials, decision analysis based on well-conducted studies
Grade B	**Scientific presumption** Based on a scientific presumption provided by intermediate level of evidence studies (level of evidence 2), such as low-powered randomised controlled trials, well-conducted non-randomized controlled studies, and cohort studies
Grade C	**Low level of evidence** Based on studies with a lower level of evidence, such as case-control studies (evidence level 3), retrospective studies, case series, and comparative studies with significant bias (evidence level 4)
EO	**Expert opinion** In the absence of studies, the recommendations are based on agreement between experts in the working group after consultation with the reading group. Absence of gradation does not mean that the recommendations are not relevant or useful. It should, however, encourage the undertaking of further studies

Table 2
Voting results and level of agreement.

Recommendation	Number of voters (number of excluded)	Median rating (range)	Level of agreement
1	31 (3)	8 (5–9)	Relative agreement
2	31 (3)	9 (7–9)	Strong agreement
3	32 (3)	7 (1–9)	No consensus
4	34 (3)	9 (7–9)	Strong agreement
5	34 (3)	9 (7–9)	Strong agreement
6	31 (3)	9 (7–9)	Strong agreement
7	32 (3)	8 (5–9)	Relative agreement
8	33 (3)	8 (5–9)	Relative agreement
9	32 (3)	9 (5–9)	Relative agreement
10	32 (3)	9 (5–9)	Relative agreement
11	32 (3)	9 (7–9)	Strong agreement
12	28 (2)	8 (1–9)	No consensus
13	29 (2)	8 (1–9)	No consensus
14	27 (2)	8 (1–9)	No consensus
15	29 (2)	8 (1–9)	No consensus
16	27 (2)	8 (1–9)	No consensus
17	29 (2)	9 (7–9)	Strong agreement
18	28 (2)	8 (5–9)	Relative agreement
19	25 (2)	8 (1–9)	No consensus
20	25 (2)	8 (1–9)	No consensus
21	20 (2)	8 (5–9)	Relative agreement
22	23 (2)	9 (5–9)	Relative agreement

Each voter assigns a number from 1 to 9 depending on the degree of acceptance of each proposed recommendation. For each proposed recommendation, the steering group eliminated from its analysis one extreme response, which was out of line with the rest of the ratings, for each allotment of 15 responses, in accordance with the HAS methodological guide for recommendations by consensus.

Table 3
Summary of OLP and OLL definitions according to WHO and Van der Waals and Van der Meij, 2003.

Clinical criteria
Presence of bilateral and more or less symmetrical lesions
Presence of grey/white reticulated networks
Erosive, atrophic, bullous and plaque lesions are only accepted as subtypes in the presence of reticulated networks on the oral mucosa
For all other lesions resembling OLP but not meeting the above criteria, the term 'clinically consistent' should be used
Histological criteria
Presence of a band-like inflammatory infiltrate limited to the superficial part of the chorion, consisting mainly of lymphocytes
Signs of vacuolar degeneration of the basal epithelium layer
Absence of epithelial dysplasia
Where histopathological signs are less obvious, the statement "histopathologically consistent with OLP" should be used
Final diagnosis OLP/OLL: in order to establish the final diagnosis, clinical and histopathological criteria must be met
OLP: Diagnosis requires that both clinical and histopathological criteria are met
OLL: this diagnosis will be confirmed in the following circumstances:
• Clinically typical OLP, but only histopathologically consistent,
• Histopathologically typical OLP, but only clinically consistent,
• Clinically and histopathologically consistent OLP

OLP: oral lichen planus; OLL: oral lichenoid lesions.

on the biopsy site. A positive DIF has been suggested as an indicator of oral lichen severity [9]. In a study including 138 biopsies of oral lichen, a positive DIF was more frequent in cases of OLP (n = 30; 73.3% positive DIF) than in cases of OLL (n = 26, 38.4% positive DIF) (OR = 3.73; IC95%, 1.23–11.38) [10]. Three studies showed that DIF assists with differential diagnosis between oral bullous lichen and autoimmune bullous diseases, particularly in cases of diffuse erythematous gingivitis [10–12]. DIF confirms the diagnosis of lichen

Table 4
Summary of oral lichen definitions, GEMUB 2020.

Oral Lichen	Clinical features	Histopathological features	Inducing factor*
OLP	Typical	Typical	No
OLL	Typical	Consistent	No
	Consistent	Typical	No
	Consistent	Consistent	No
IOLL	Typical	Typical	Yes
	Typica*l	Consistent	Yes
	Consistent	Typical	Yes
	Consistent	Consistent	Yes

* Inducing factors include systemic diseases (such as graft-versus-host disease), a local factor or a systemic drug. OLP, oral lichen planus; OLL, oral lichenoid lesions; IOLL, induced oral lichenoid lesions

planus pemphigoides, which combines histological features of OLP with linear IgG, IgA or C3 deposits at the chorioepithelial junction [13].

Recommendation 3: DIF should not be performed routinely in the initial assessment of oral lichen. DIF is recommended in ulcerated, erosive, bullous types, and in diffuse erythematous gingivitis, particularly to rule out autoimmune bullous disease. (EO)

Recommendation 4: Lichen planus pemphigoides should be considered in the case of oral lichen with blistering lesions. A biopsy of healthy mucosae is needed for a direct immunofluorescence study (frozen or storage medium: Michel's medium) and a biopsy of an oral lichen lesion (storage medium: formalin) for histology. The diagnosis is confirmed if the DIF shows linear deposits of IgG, IgA or C3 at the chorioepithelial junction associated with histological evidence of lichen. (Grade C)

Question 5 In patients with oral lichen, is routine screening for viral hepatitis essential?

Studies investigating the link between HBV and oral lichen found no evidence of an association between OLP and HBV infection [14–18]. However, four meta-analyses showed an association between OLP and HCV infection [19–22]. Nevertheless, the latter association varies considerably across countries and few studies have been carried out in countries with low HCV prevalence such as metropolitan France. Since the last meta-analysis, two studies have found no association between HCV infection and OLP, while conversely, one Italian study found an association between the two entities [14,15,22,23]. In France, two studies, including 52 and 102 patients respectively, concluded that there was no significant difference in the prevalence of HCV infection between patients with OLP (3.8 and 4.9%) and controls (2.6 and 4.5%) [24,25]. There is little data available on the clinical types of oral lichen associated with hepatitis C.

Recommendation 5: Routine screening for hepatitis B in patients with oral lichen is not recommended. (Grade C)

As the prevalence of hepatitis C in France is low, routine screening for hepatitis C in patients with oral lichen is not recommended. (Grade C)

HCV serology can be performed in the case of individual risk factors (recommendations of the Haute Autorité de Santé) and/or in case of erosive or treatment-resistant oral lichen. (EO)

Question 6: In patients with oral lichen, should a periodontal and dental check-up be routinely performed at initial assessment?

Case-control studies have shown that periodontal parameters were significantly impaired in patients with OLP, particularly in the atrophic and erosive forms, compared to healthy subjects [26–29]. Periodontopathogenic bacteria were significantly increased in 27 OLP patients compared to 26 controls [30]. Oral hygiene education, periodontal sanitation and conservative dental care decreased the plaque index, the severity of symptoms, and the severity of lesions in patients with gingival OLP [31–35].

Recommendation 6: Periodontal and dental care (oral hygiene education, dental scaling, removal of traumatic factors) is recommended in patients with oral lichen. (Grade C)

Question 7. In patients with oral lichen, should genital involvement be routinely investigated?

In a retrospective series of 584 patients with oral lichen, 19% (77/399 females) had erosive (60%) or asymptomatic reticulated (25%) vulvovaginal lichen. All females with both oral and genital lichen had gingival involvement. There was no correlation of severity between oral and genital locations. By contrast, only 4.6% (8/174) of males with oral lichen also had genital involvement [36]. Similarly, a prospective study involving routine vulvar examination in 41 women with oral lichen also showed vulvar involvement in 31 cases (75%) [37].

Vulvovaginal-gingival syndrome has been described as a plurimucosal erosive lichen combining oral and vulvovaginal involvement [36–38]. In a study of 126 patients with lichen planus (regardless of location) (110 women, of whom 63.5% had cutaneous lichen), Olszewska et al. reported 12.7% of vulvovaginal-gingival syndrome [38]. Oral involvement consisted mostly of isolated diffuse erythematous gingivitis, but was also associated with other oral locations, whether erosive or not [38]. Clinical forms and severity of lesions were not systematically correlated between the two locations [37]. In two series, the first symptoms of vulvovaginal-gingival syndrome were oral in 33.6 to 45% of cases and genital in 22.7 to 35% of cases, while both symptoms appeared concomitantly in 20 to 43.7% of cases [39,40]. In order of frequency, vulvovaginal-gingival syndrome may also be associated with involvement of the scalp, skin, nails, perianal area, oesophagus, tear ducts, pharynx and external auditory canals [36,38,40,41]. Association of oral and genital lichen has also been described in males (peno-gingival syndrome) [36,42,43].

By contrast, the association of oral lichen and vulvar lichen sclerosus seems fortuitous (0.6% in a cohort of 1328 cases) [44].

In addition to genital involvement, extra-oral locations of oral lichen include the skin, scalp, nails, perianal, oesophagus, pharynx and eye. Investigations of such extra-oral locations are summarized in Table 5.

Table 5
Extra-oral and extra-genital locations of lichen planus.

Location	Investigations
Skin	Routine skin examination
Scalp	Routine skin examination
Nail	Routine skin examination
Oesophagus	Routine fibroscopy is indicated in case of functional symptoms (odynophagia, dysphagia) Routine fibroscopy may be indicated for patients with plurierosive oral and genital involvement
Anus	Routine examination is indicated in case of functional symptoms (pruritus, anal pain) Routine examination is indicated for patients with plurierosive oral and genital involvement
Pharynx, larynx	Routine fibroscopy is indicated in case of functional symptoms (dysphonia, dysphagia) Routine fibroscopy may be indicated for patients with erosive oral and genital involvement
Eye (eyelid, cornea, conjunctiva, lacrimal ducts)	Ophthalmological examination is indicated in case of functional symptoms (blurred vision, lacrimation, eye dryness) Ophthalmological examination may be indicated for patients with erosive oral and genital involvement

Recommendation 7: Women with oral lichen should routinely undergo genital examination. (Grade C). Men with oral lichen should be advised to undergo genital examination. (Grade C)

Extra-oral lichen involvement (cutaneous, adnexal, anal, oesophageal, pharyngeal, ophthalmic) should be routinely sought. (EO)

2.2. Theme 2: Induced oral lichenoid lesions

Question 8: In patients with oral lichen, what clinical and histological characteristics suggest drug-induced OLL?

The literature does not describe any specific clinical or histological criteria of drug-induced OLL compared to OLP/OLL. Drug-induced OLL were reported as being bilateral, keratotic or erosive, and located on lingual, jugal, labial and/or gingival mucosae [45–48]. Histological testing was not systematically reported in the literature but a literature review did not find any histological criteria allowing differentiation between drug-induced OLL and OLP/OLL [49]. In a systematic review in 2017, the mean time to onset of drug-induced OLL following drug introduction was 165 days (range: 60–406) [48].

Recommendation 8: Drug-induced oral lichenoid lesion has no specific clinical or histological criteria. (Grade C).

A diagnosis of drug-induced oral lichenoid lesion should be considered in the case of:

- **appearance of oral lichen within one year of the introduction of a drug (EO),**
- **treatment-resistant oral lichen in a patient taking a potentially inducing drug (EO).**

Question 9: In patients with suspected drug-induced OLL, which are the inducing drugs and what is the time to disease onset?

Two case-control studies have shown that patients with oral lichen had a higher consumption of non-steroidal anti-inflammatory drugs (NSAIDs) compared with controls [50,51]. NSAIDs were reported to induce lichen planus in one literature review [49]. As such, naproxen intake was associated with the occurrence of 28 cases of oral lichen in a series of 55 patients with lichen planus [52].

Immune checkpoint inhibitors (anti-PD-1 and anti-PD-L1 antibodies) in 3 series and imatinib in 2 series and one literature review were reported as having induced mostly cutaneous, but also oral, lichen planus [46,48,53–56]. Case series of oral lichen have been described following treatment with pegylated interferon and ribavirin [45], alpha interferon [47], anti-TNF alpha antibodies [47], or methyldopa [48,57]. Two literature reviews reported numerous other inducing drugs from isolated cases (quinacrine, ketoconazole, D-penicillamine, allopurinol, amiphenazole) [48,49].

Drug-induced OLL occurs with a variable timescale. For instance, drug-induced OLL was reported to appear on average 4 months (3 days to 13 months) after introduction of immune checkpoint inhibitors, and prevalence increased with treatment duration [46,53,54]. The median time to onset was 8 weeks after imatinib introduction [55], 2 weeks to 3 months after naproxen [52], 2 months after pegylated interferon/ribavirin, and 2 to 6 months after anti-TNF alpha antibodies [45].

Recommendation 9: Many drugs have been reported as inducing oral lichenoid lesions, mostly through isolated case reports. The main reported molecules are non-steroidal anti-inflammatory drugs, immune checkpoint inhibitors, imatinib, anti-TNF alpha, interferon, methyldopa, and D-penicillamine (Grade C). There is no scientific evidence for constituting an exhaustive list of drugs that induce OLL (EO). Time to drug-induced OLL varies widely, with onset most commonly after the first month of introduction of the drug (EO).

Question 10: In patients with suspected drug-induced OLL, should the inducing drug be adjusted or stopped?

In a literature review of 54 cases of drug-induced OLL, the drug was stopped in 37 cases (68.5%), with or without associated treatment, leading to an improvement or disappearance of the lesions. The median time to partial/complete response was 56 days (range: 28–90) [48]. In a series of drug-induced OLL in 20 patients treated with anti-PD-1 antibodies, 6 patients required temporary or permanent discontinuation of the drug [46]. In the imatinib series, drug dosage was adjusted in 5 of 46 cases, leading to improvement in induced lesions [55]. Discontinuation of naproxen resulted in stabilization of the disease, with no new lesions [52]. In the cases of OLL induced by pegylated interferon, ribavirin or anti-TNF alpha, the drugs were initially maintained and drug-induced OLL was treated by local corticosteroid therapy. Given the variable response, discontinuation of the inducing drugs was necessary in some cases [45,47].

Question 11: In patients with suspected drug-induced OLL and for whom the inducing drug is maintained, which specific treatment of drug-induced OLL should be recommended?

Therapeutic management of drug-induced OLL was reported in 5 articles and was based on topical or oral corticosteroid therapy [45–47,54,55]. In the case of refractory lesions, the authors recommended re-assessing whether the inducing drug should be maintained.

Recommendation 10: Asymptomatic drug-induced OLL does not require discontinuation of the drug (EO). Symptomatic drug-induced OLL requires discontinuation of the drug in cooperation with the prescriber (EO). Depending on the benefit/risk ratio, this may result in maintenance, dosage adjustment or withdrawal of the inducing drug.

Recommendation 11: If the inducing drug is maintained, local corticosteroids are the first line of treatment for symptomatic drug-induced OLL, with close monitoring. (Grade C)

Question 12: In patients with oral lichen, what clinical or histological features may suggest a contact-induced oral lichenoid lesion?

The clinical appearance and oral location of contact-induced OLL is similar to that of OLP/OLL [58–69]. However, this assumption is limited by the lack of a consensual definition of contact-induced OLL. Some authors consider that only oral lichenoid lesions close to dental material can be defined as contact-induced OLL [59–61,70]. On the other hand, the topographic relationship between contact-induced OLL and dental material was also reported as varying according to the strength of the association (strict contact, close contact, distant contact) [58,62–66]. According to studies, the histology of contact-induced OLL has been described as "typical of" (30–100% of cases), "consistent with" (24–100%) or "nonspecific for" oral lichen (18–35%) [65,66,69].

In patients with oral lichen, patch tests (performed using a European standard battery and a dental material battery) are more often positive when the oral lichen lesions are situated close to dental materials [59,64,65,71]. In addition, resolution of lesions after removal of the material is much more frequent where patch-tests are positive [67–71]. Conversely, a lack of correlation between clinical appearance, histological features and patch-testing reactivity has also been reported [69]. On the other hand, no clinical aspect of diffuse erythematous gingivitis was observed among contact-induced OLLs [71]. Similarly, no extra-oral lichen lesions have been reported in patients with contact-induced OLL related to dental amalgams [60,72]. Lichen lesions in the vicinity of dental materials refractory to well-conducted therapies are likely to be contact-induced OLL [73].

Recommendation 12: Contact-induced OLL has no specific clinical or histological criteria. (Grade C)

A diagnosis of contact-induced OLL should be considered in the presence of the following criteria (EO):

- **Clinical criteria**:
  - **Complete or partial direct topographic relationship between the lesion and the dental restorative material (Grade B)**,
  - **Absence or poor response to treatments (EO)**
- **Histology consistent with oral lichen (Grade B)**
- **Positive patch-test results (Grade B)**.

Isolated erosive gingival lichen or cutaneous lichen do not support a diagnosis of contact-induced OLL (Grade B).

Extra-oral lichen involvement does not support a diagnosis of contact-induced OLL (EO).

Question 13: Should patients with suspected contact-induced OLL be checked for dental materials?

Question 14: In patients with suspected contact-induced OLL related to dental restoration, which epicutaneous tests should be carried out?

Contact-induced OLL was reported most frequently with dental amalgam [58–60,63,65–68,72–75]. Other materials such as palladium, composite resins, acrylic resins, gold and metallic or ceramic-metallic dental crowns were described more sporadically [58,61,68,69,74,76].

Recommendation 13: Any metallic or non-metallic dental material may be involved in contact-induced OLL (EO). Mercurials (amalgam) are the most often incriminated and should be sought first. (Grade B)

Recommendation 14: If contact-induced OLL are thought be related to dental restorations, patch testing with a standard battery and a dental material battery is recommended. (Grade C)

Question 15: In patients with suspected contact-induced OLL associated with dental restoration, should the suspected dental material be replaced?

Numerous studies have evaluated the course of contact-induced OLLs after removal or replacement of suspected materials. The main limitations of these studies are: heterogeneity of the definitions of contact-induced OLL, heterogeneity of the criteria for removing or replacing materials (systematic removal/replacement or according to topography and/or according to epicutaneous tests), heterogeneity of times to evaluation of efficacy, and heterogeneity of efficacy criteria (clinical and/or histological resolution of oral lichen *versus* "improvement" of oral lichen), with the latter being difficult to interpret in such chronic, relapsing disease. Overall, partial or complete resolution of symptomatic lesions was observed following removal/replacement of dental materials in 46 to 97% of cases and was correlated with the topographical proximity of the lesions to the dental material [58,59,63–68,71,72].

Recommendation 15: In case of persistent, symptomatic suspected contact-induced OLL, replacement of the dental restoration in partial or total contact should be considered. (EO)

Question 16: In patients with suspected contact-induced OLL associated with dental restorations, how should the alternative dental material be selected?

Amalgam has been replaced by different materials such as composite resins, glass-ionomer cements, gold or ceramic restorations, metal-ceramic crowns, titanium, or a combination of different materials [59,63,67,70,72]. Composite resins have been replaced by ceramics, glass-ionomer cement or acrylic resin [61]. Patients with positive patch-tests more frequently showed improvement (60–100%) than those with negative patch-tests (33%) [75]. The choice of material most often depended on the patch-tests results [62,66,67,70].

Recommendation 16: There is no evidence for recommending any alternative material (EO). The choice of alternative dental material should take into account the results of patch tests if performed as part of the diagnosis of contact-induced OLL (EO).

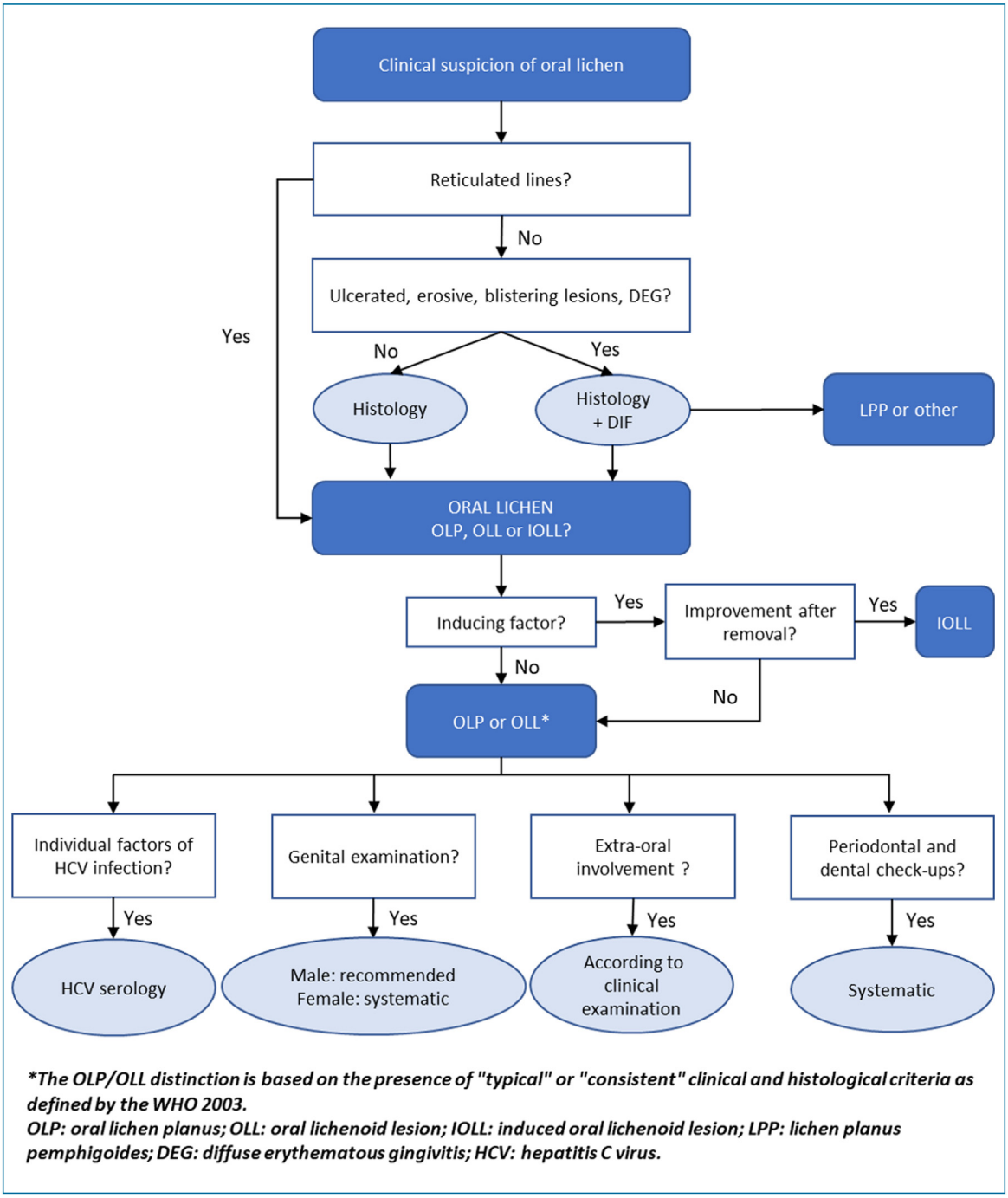

Fig. 2. Initial assessment of oral lichen: decision tree.

2.3. Theme 3: Monitoring oral lichen

Question 17: In patients with oral lichen, which medical practitioner should provide follow-up?

No studies have specifically addressed which practitioners should follow up patients with oral lichen. The specialities evaluated (dental surgeons, oral surgeons and maxillofacial surgeons) appeared to have insufficient knowledge of oral mucosal conditions [77–81]. Dental surgeons performed biopsies only very rarely and the technique was insufficiently mastered [77,82]. Inter- and intra-observer agreement for monitoring oral disease from photographs was greater in oral surgeons than in dental surgeons [81].

Recommendation 17: Monitoring of oral lichen should be carried out by a practitioner with knowledge of the disease, its treatment and complications. (EO)

Question 18: In patients with oral lichen, what should be the duration of follow-up?

All authors agree that oral lichen should be monitored at least annually in the long-term, with follow-up adjusted to each individual case. For atrophic or erosive lesions, which are at increased risk of transformation into cancer, follow-up every 2 to 6 months

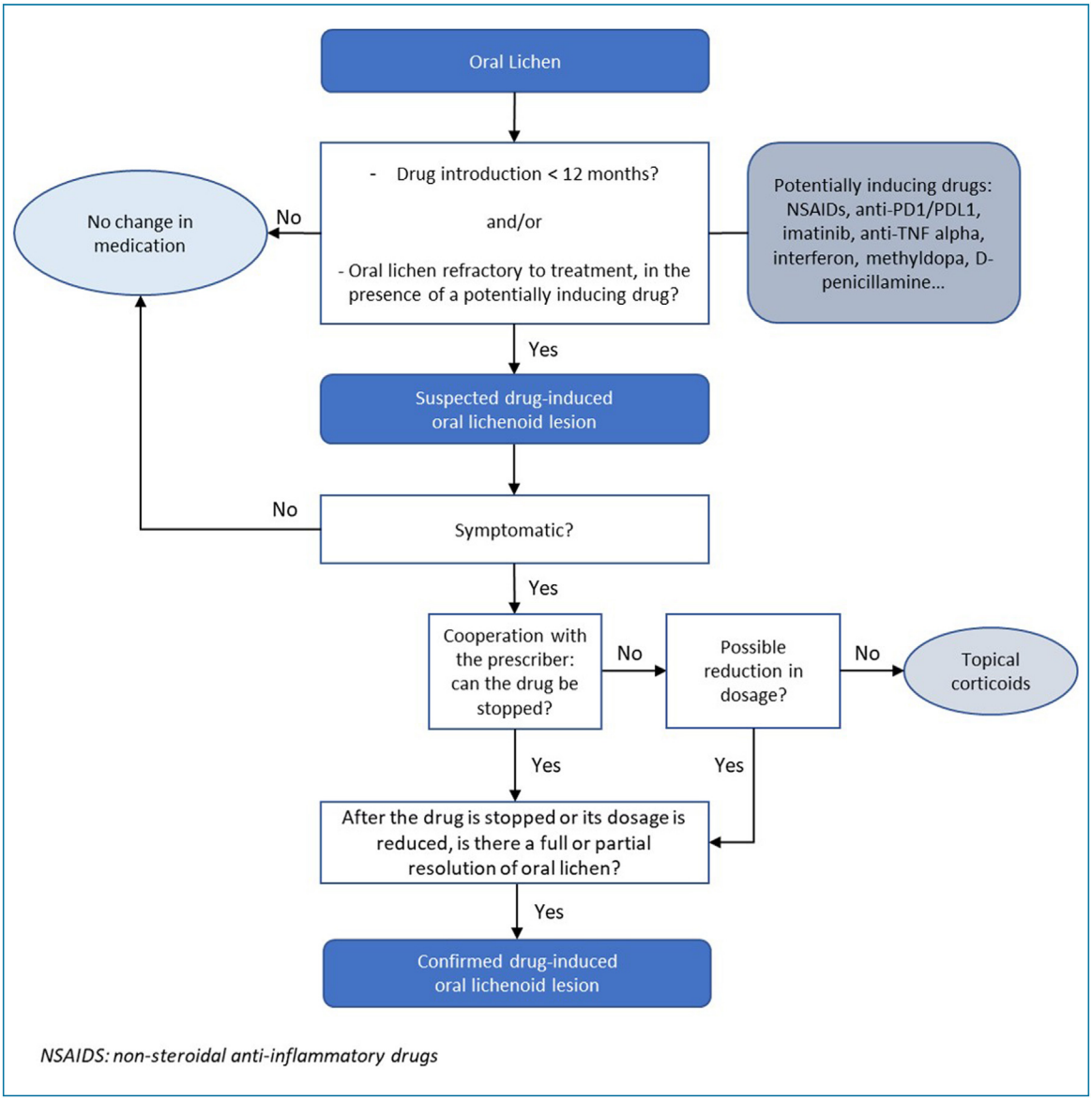

Fig. 3. Drug-induced OLL: decision tree.

is recommended [83–91]. However, another study did not find a multiyear follow up to decrease morbidity [83].

After removal of local causes or initiation of specific treatment, several authors proposed that the patient should be re-evaluated within 2 to 4 weeks [84,85,92,93]. However, Thongprasom *et al.*, in their Cochrane review of 28 trials on the efficacy of OLP treatments, reported that the available data did not allow any recommendations regarding the frequency of monitoring [3].

Recommendation 18: Monitoring of oral lichen should be at least annual (for asymptomatic reticulated types). For other types, follow-up should be adjusted every 2-6 months, depending on clinical severity and treatment efficacy. (EO)

Question 19: In patients with oral lichen, what are the evaluation criteria during follow-up?

There are many scoring systems for oral lichen designed to evaluate disease severity and objective assessment during follow up: Carrozzo and Gandolfo's index, Thongprasom's WEA score, Kaliakatsou's WEA-MOD score, Pibooniym's REU scale, Escudier's score and Chainani's CSS scale [94–100]. These scoring systems, although not comparable with each other and without any demonstrated superiority of one over the others, allow reproducible and objective monitoring [101–105]. Photography, whether associated with a transparent graduated ruler or not, is considered an objective monitoring tool, but can be difficult to use in the case of diffuse lesions [98,99,102]. A diagram of the lesions and/or a clinical description and/or an assessment of pain using a digital or visual analog scale can also constitute monitoring tools [99,100]. Assessment of quality of life using specific scores such as OHQOL-UK or OHIP-14 has also proved useful [103,106]. Biopsy is necessary if suspicious changes occur in the lesions [84–86].

Question 20: In patients with oral lichen, what information should be provided during follow-up?

Patient concern about the risk of malignant transformation, contagiousness, and lack of information about the disease have been reported [107,108]. A review article emphasised the value of patient education (application of topical treatment and oral hygiene), and of an information sheet and self-examination to

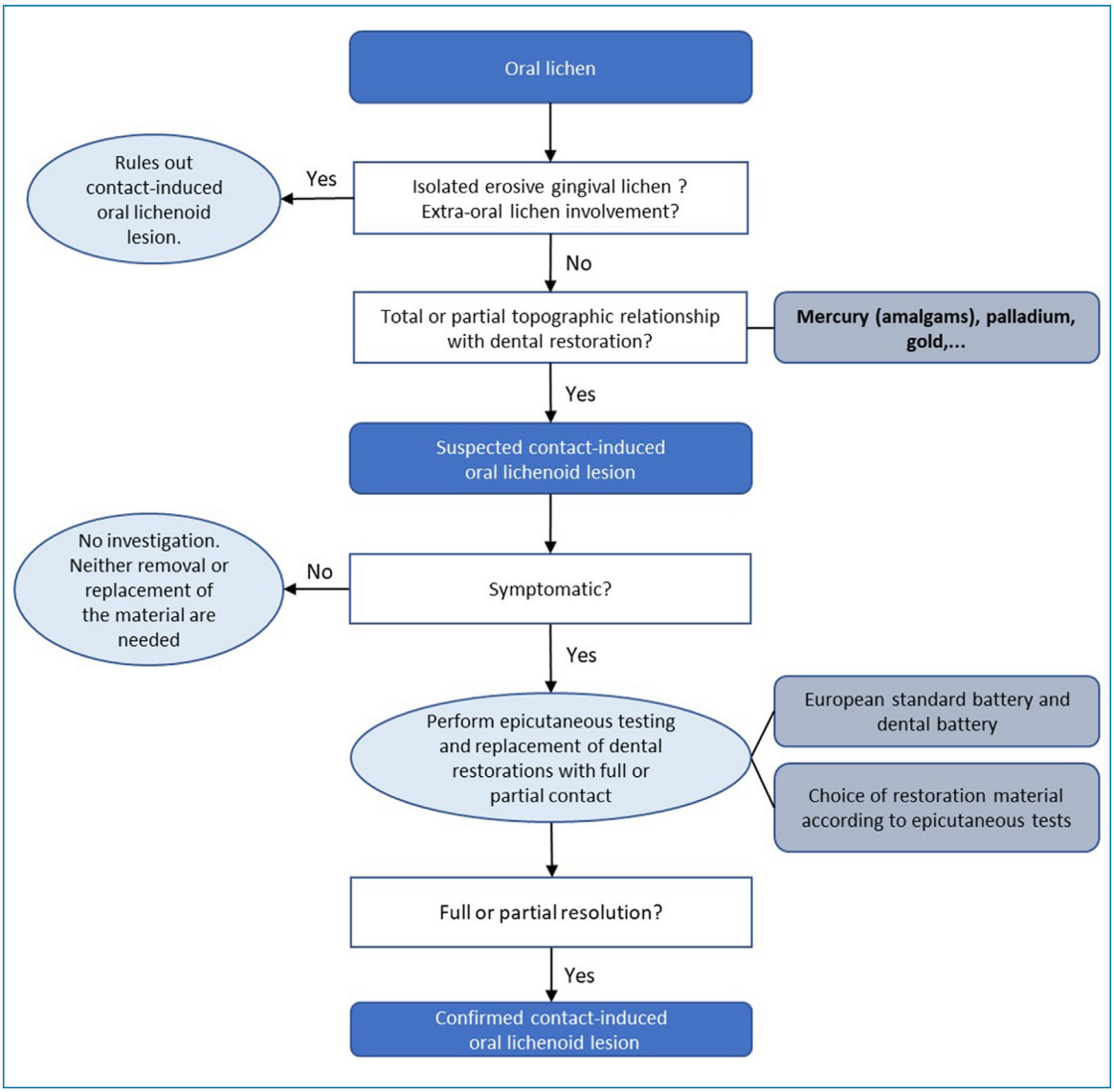

Fig. 4. Contact-induced OLL: decision tree.

Recommendation 19: Oral lichen should be monitored using objective (disease-specific score and/or photograph and/or diagram and/or description) and subjective criteria (pain assessment scale and/or quality of life questionnaire) (EO).

Biopsy must be performed if there is a suspicious change in a lesion (Grade C).

detect any change in lesions and assess treatment response [108]. As such, an information sheet for patients, in the French language, has been prepared by the GEMUB group (available at http://www.sfdermato.org/pour-la-pratique/fiches-information-patients.html and www.gemub.org/fiches-patients).

The risk of transformation of OLP into squamous cell carcinoma is estimated at 1.1% and that of OLL at between 2.5 and 3.2% according to the two most recent meta-analyses. The mean time to transformation was between 51.4 and 58.55 months, with a mean age of between 58.5 and 60.8 years. No gender difference was found [109–111]. The tongue was the most frequently reported transformation site [109]. Erosive and atrophic lichens were more at risk of transformation [109,110,112].

Recommendation 20: Patient information and education (application of topicals, oral hygiene) and patient self-monitoring are essential in the management of oral lichen (EO). Patients should be informed that oral lichen is a chronic, non-infectious, non-contagious inflammatory disease with low risk of malignant transformation (1–3%) (Grade B). Self-examination should be advised to allow earlier consultation and/or adjustment of treatment in the event of a change in the lesion (EO).

Question 21: In patients with oral lichen, how should the factors triggering inflammatory flare-ups be managed?

Stress is the most frequently reported (17–77% of cases) inducing factor for oral lichen [113–116]. In other studies, anxiety and depression scores were found to be significantly higher in patients with OLP than controls [117–119]. In a retrospective study of 51 patients with oral lichen, spicy food (50%), citrus fruits (40%), alco-

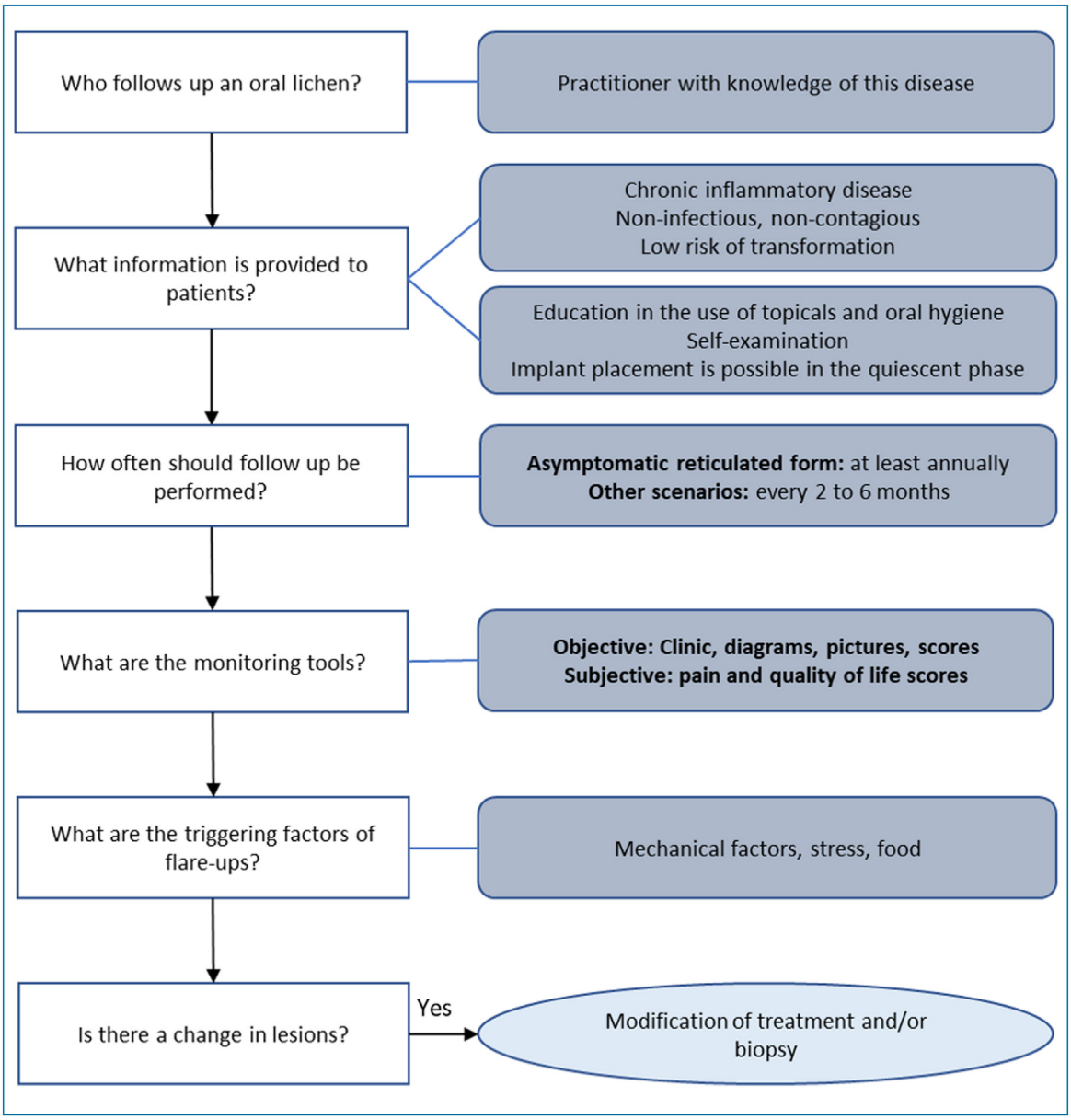

Fig. 5. Monitoring of oral lichen.

hol, vinegar, nuts, mustard or raw fruit (20%), cinnamon or raw vegetables (10%) were described as exacerbating oral lichen: 79% of patients avoided these foods and of these, 70% reported a decrease in the frequency of flare-ups [120]. Koebner's phenomenon as well as dental care, rubbing by poorly fitting braces, ill-fitting crowns and amalgam fillings were cited as triggers, but have not been evaluated to date [114].

Recommendation 21: Factors favouring inflammatory flare-ups or pain are stressful life events, certain foods, and mechanical factors (Koebner's phenomenon). (EO)

In the event of a flare-up or pain, the following factors should be investigated:

- **triggering food, if identified, should be avoided (EO).**
- **oral mechanical factors (rubbing of ill-fitting dentures, traumatic dental restorations, etc.) should be corrected. (EO)**

Question 22: Is implant therapy feasible in patients with oral lichen?

The overall survival of dental implants in patients with oral lichen ranged from 96.4 to 98.5% with a follow-up of 42 to 68 months. No difference was found between patients with reticulated types and those with erosive types of lichen [121,122]. Some authors have shown that implants should be placed during the quiescent phase of oral lichen and that active lesions should be treated beforehand [123]. The presence of dental implants did not modify the clinical course of oral lichen over time [124]. The presence of diffuse erythematous gingivitis was associated with a higher percentage of peri-implantitis, but did not affect the implant survival rate [125].

Recommendation 22: Implant placement is not contraindicated in patients with oral lichen, and implant success rates are comparable to those of the general population. (Grade C)

3. Conclusion

These multidisciplinary recommendations propose a nosological classification of oral lichen, including OLP, OLL and IOLL. The initial management of oral lichen lesions, the management of suspected drug-induced or contact OLL, and recommendations for follow-up are summarized in Figs. 2 to 5.

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This study is dedicated to the memory of Francis Pascal.

Disclosure of interest

The authors declare that they have no competing interest.

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