

Oral Mucosal Lesions Associated with Use of Quid

(Lésions de la muqueuse buccale associées à l'usage de chiques)

• Sylvie Louise Avon, DMD, MSc •

S o m m a i r e

La chique est un mélange de substances qu'on se met dans la bouche ou qu'on mâche activement pendant une période prolongée, ce qui fait qu'elle reste en contact avec la muqueuse buccale. Elle contient habituellement 1 ou 2 ingrédients de base, soit du tabac et de la noix d'arec. La chique de bétel ou le paan est un mélange de noix d'arec et de chaux, auquel on peut ajouter du tabac. Le tout est enveloppé dans une feuille de bétel. Les composantes particulières du produit peuvent varier entre les collectivités et les personnes. L'habitude de chiquer a un rôle social et culturel important dans les collectivités du sous-continent indien, dans l'Asie du Sud-Est et dans certaines régions du Pacifique ouest. Après l'émigration en provenance de ces pays vers l'Amérique du Nord, principalement dans les régions urbaines, l'habitude est restée prévalente chez ses adeptes. Beaucoup de dentistes ne connaissent pas la prévalence de l'usage de chiques ou du paan dans les populations de patients asiatiques. La reconnaissance du rôle des produits en cause dans l'apparition des lésions pré-malignes ou des cancers de la bouche est d'une grande importance pour le praticien dentaire. En effet, toutes sortes de lésions et de conditions de la muqueuse buccale ont été signalées avec l'usage de chiques et de tabac. L'association de ces affections avec l'apparition du cancer de la bouche renforce l'importance de l'éducation visant à limiter l'usage de ces produits. Dans la plupart des cas, la cessation de l'habitude produit une amélioration des lésions muqueuses et des symptômes cliniques.

Mots clés MeSH : areca/adverse effects; mouth neoplasms/chemically induced; precancerous conditions/chemically induced

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Quid is a substance or mixture of substances (in any manufactured or processed form) that is placed in the mouth, where it is sucked or actively chewed and thus remains in contact with the mucosa over an extended period. It usually contains one or both of 2 basic ingredients, tobacco and areca nut.¹ The composition of betel quid, also known as paan, varies between communities and individuals, although the major constituents are areca nut and slaked lime (from limestone or coral) wrapped within a betel leaf (Fig. 1). The paan is placed between the teeth and the buccal mucosa, and is gently chewed or sucked over a period of several hours.^{1,2} The slaked lime acts to release an alkaloid from the areca nut, which produces a feeling of euphoria and well-being.³ Other substances of local preference may be added, such as grated coconut or a variety of spices, for example, aniseed, peppermint, cardamom and cloves.⁴ Tobacco may also be used as a component of paan, and this ingredient is associated with a significant risk of oral cancer. In addition, the lime has been shown to release reactive oxygen species from extracts of areca

nut, which might contribute to the cytogenetic damage involved in oral cancer.⁵ A synergistic increase in risk of oral cancer has been demonstrated among people who consume alcohol, smoke and chew quid.^{6,7}

Variants of paan include use of sliced areca nut alone (Fig. 2) and addition of sweeteners to make the product particularly attractive to younger children, to whom it is sold under the names sweet supari, gua, mawa or mistee pan (Figs. 3 and 4). Other variants such as kiwam, zarda and mitha pan (also known as gutkha) may contain a variety of substances, including tobacco.^{2,8}

Oral mucosal lesions and conditions associated with use of quid and tobacco have been reported.^{1,9} In an effort to bring some uniformity to the reporting of quid and tobacco-chewing habits and the associated lesions of the oral mucosa, 22 researchers from 11 countries met for a workshop in Kuala Lumpur, Malaysia, from November 25 to 27, 1996.¹ The definitions of quid and tobacco-chewing habits and associated oral mucosal lesions that were agreed upon during that workshop have been used in this article.



Figure 1: Leaf of betel (Piper betle).



Figure 2: Sliced areca nut, one of the major constituents of betel quid (paan), can also be chewed on its own.



Figure 3: Sweeteners are added to children's paan.



Figure 4: Once the ingredients have been placed on the betel leaf, the leaf is folded and the paan is ready to chew or suck.

In addition to defining quid-related terminology, the workshop participants set out guidelines for reporting quid use among research subjects. They note that the specific ingredients should be listed so as to clearly delineate the following 3 basic categories:

- Quid with areca nut but without any tobacco products, which may involve chewing only the areca nut or areca nut quid wrapped in betel leaf (paan).
- Quid with tobacco products but without areca nut, including chewing tobacco, chewing tobacco plus lime, mishri (burned tobacco applied to the teeth and gums), moist snuff, dry snuff, niswar (a different kind of tobacco snuff) and naas (a stronger form of niswar).
- Quid with both areca nut and tobacco products (paan with tobacco).

A variety of packaged products from all 3 of these categories are now available in several countries. It is almost always possible to identify the presence or absence of the 2 principal ingredients of interest, areca nut and tobacco, and thus to allocate the product to a specific category.¹

In 1985, the International Agency for Research on Cancer reported that there is sufficient evidence to conclude that the habit of chewing quid that contains tobacco is carcinogenic to humans, but there is inadequate evidence to conclude that the habit of chewing quid that does not contain tobacco is carcinogenic.⁴ Countries with a high prevalence of areca nut use have higher rates of oral cancers than countries where this habit is not established.¹⁰ However, some authorities believe it is the addition of tobacco, rather than the areca nut itself, that leads to these higher rates.^{4,11,12}

Lesions and Conditions Associated with Quid-Chewing Habits

Some oral mucosal lesions and conditions are specifically associated with quid-chewing habits. Two categories of quid-related lesions are recognized:

- Lesions or conditions that are diffusely outlined, that involve more than one site or that represent a widespread alteration, such as those due to mechanical or chemical trauma. Clinical lesions or conditions such as chewer's

mucosa fall into this category, but transient states of the mucosa, such as quid stains, are excluded.¹

- Lesions that are localized to the site where quid is regularly placed. These lesions are equivalent to snuff-induced lesions or tobacco–lime user's lesions, which arise only on the mucosa in contact with the quid.¹³

The following lesions and conditions are defined on the basis of specific criteria for their diagnosis.¹

Betel Chewer's Mucosa

Betel chewer's mucosa is a condition of the oral mucosa in which, because of either direct action of the quid or the traumatic effect of chewing (or both), there is a tendency for the oral mucosa to desquamate or peel. Loose and detached white tags of tissue can also be seen and felt. The underlying areas assume a pseudomembranous or wrinkled appearance.¹ The area may also show evidence of incorporation of the quid ingredients in the form of yellowish or reddish brown encrustations.¹⁴ This type of lesion should be distinguished from cheek-biting, which leads to a very similar appearance in terms of clinical and histologic features. For example, cheek-biting is unintentional, whereas chewer's mucosa results from an intentional habit. In addition, the average age of people with chewer's mucosa is usually higher, at least 50 years,¹⁵ whereas cheek-biting typically occurs in younger people, around 20–35 years.^{4,15}

Quid-Induced Lesion

A quid-induced lesion is a localized lesion of the oral mucosa corresponding to the regular site of placement of quid. It is characterized by one or more of the following characteristics: change in colour, wrinkled appearance, thickening of the mucosa, scrapable or non-scrapable epithelial surface, and presence of ulceration.¹

Areca-Nut-Related Lesion

Areca nut chewers, like chewers of other kinds of quid, may have clinically healthy mucosa with no textural or colour changes. However, the buccal mucosa, either bilaterally or unilaterally, may show an ill-defined whitish grey discoloration that cannot be rubbed off. In addition, the mucosa may show a rough, linen-like texture, and histologic examination reveals ortho-keratinized or para-keratinized epithelium. Rarely, localized white or red lesions and malignancies may be seen among areca nut chewers; these should be distinguished from lesions arising from other habits.¹

Oral Submucous Fibrosis

Oral submucous fibrosis (OSF) was initially described in 1966 by Pindborg and Sirsat¹⁶ as an insidious, precancerous, chronic disease that may affect the entire oral cavity and that sometimes extends to the pharynx.^{17,18} Although it is occasionally preceded by the formation of vesicles, OSF is always associated with a subepithelial inflammatory reaction followed by fibroelastic changes of the lamina propria, accompanied by epithelial atrophy. This process leads to

stiffness of the oral mucosa, which results in trismus and inability to eat.¹⁸ Various factors have been implicated in the development of OSF, the most common of which is chewing areca nut.^{19,20} Associations with tobacco use and vitamin deficiency have also been reported.²¹

OSF is predominantly seen in people in south Asian countries²² such as Bangladesh, Bhutan, India, Pakistan and Sri Lanka, or in south Asian immigrants to other parts of the world.^{23,24} It is extremely rare in white populations,¹¹ although cases have occasionally been reported in Europeans; it also occurs in people from Taiwan, China, Nepal, Thailand and Vietnam.¹⁹ The condition affects predominantly women (female–male ratio of 3:1)^{8,18} and characteristically presents in adulthood (between the ages of 45 and 54 years).⁸

OSF is diagnosed on the basis of clinical criteria, including oral ulceration, paleness of the oral mucosa, a burning sensation (particularly in the presence of spicy foods), hardening of the tissue and presence of characteristic fibrous bands. The condition is associated with gradual onset of inability to open the mouth⁸ and protrusion of the tongue, which causes difficulty in eating, swallowing and phonation. It has been recognized that OSF may manifest itself at an early stage without the presence of fibrous bands,^{8,25} and although palpable fibrous bands are not always present, a tough leathery mucosa with all the associated symptomatic, clinical and histopathologic characteristics of OSF may be seen.²⁵ It is therefore recommended that the definition of OSF be extended and that this condition be diagnosed on the basis of the presence of one or more of the following characteristics:¹

- palpable fibrous bands
- tough, leathery texture of the mucosa
- blanching of the mucosa (defined as a persistent, white, marble-like appearance of the oral mucosa, which may be localized, diffuse or reticular), accompanied by histopathologic features characteristic of OSF (atrophic epithelium with loss of rete ridges and juxta-epithelial hyalinization of the lamina propria and the underlying muscle).

Betel Quid Lichenoid Lesion

A quid-induced lichenoid oral lesion has been reported exclusively among users of betel quid.²⁶ It resembles oral lichen planus, but there are certain specific differences. The quid-induced lesion is characterized by the presence of fine, white, wavy, parallel lines that do not overlap or criss-cross, are not elevated and in some instances radiate from a central erythematous area. The lesion generally occurs at the site of placement of the quid. This lesion was originally described as a lichen-planus-like lesion, but it is now termed a betel-quid lichenoid lesion (Fig. 5).¹ This lesion may regress with decrease in the frequency or duration of quid use or a change in the site of placement of the quid. There may be complete regression if the quid habit is given up.¹

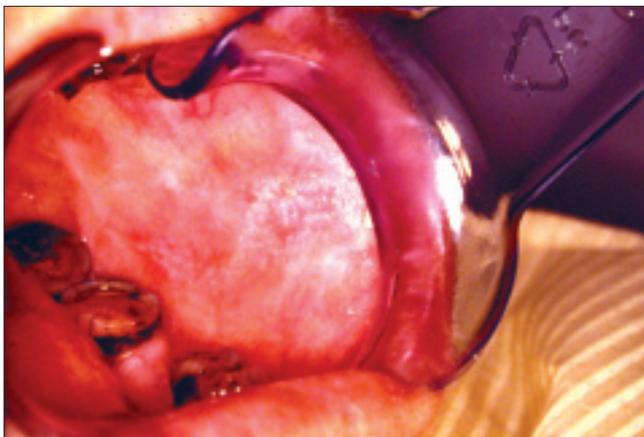


Figure 5: White papular and striated lichenoid lesion induced by betel quid. Photo courtesy of Dr. Karen Burgess.

Conclusions

The association of the conditions described above with the development of oral cancer highlights the importance of education on limiting the use of quid. In particular, there seems to be an association between the use of quid that incorporates tobacco and the occurrence of white lesions.^{14,27} The intraoral locations of white lesions are generally influenced by the person's specific tobacco habits, and there seems to be a significant relationship between tobacco cessation and a decrease in the incidence rate of white lesions.¹⁴

No specific test is available to confirm whether a particular oral lesion was caused by the patient's quid habit. The diagnosis must be made on the basis of a history of repeated exposure to betel quid containing certain ingredients, the clinical appearance and the texture of the tissue (especially for OSF). Incisional biopsy is recommended, specifically biopsy of the most severely affected area (or any area of ulceration) to rule out squamous cell carcinoma.²⁸ Histopathologic examination may show a dense, chronic inflammatory infiltrate with epithelial changes ranging from atrophy accompanied by hyperkeratosis to dysplasia to frank malignancy.

The management of such oral lesions depends on the type of quid-related lesion. The first option is no treatment, accompanied by discontinuation of the betel quid habit and appropriate follow-up. Mild cases of OSF or patients with limited jaw opening that still permits reasonable eating abilities and access for oral hygiene and dental care may be treated without intervention but with a focus on quitting the quid habit. Severe cases can be successfully treated, with return to near-normal jaw opening, by complete excision and surgery using mucosal or nonvascularized split-thickness skin grafts of the affected areas.²⁸ Successful prevention in the early stages of these conditions may lead to improvement in symptoms.⁸ However, when the patient continues his or her betel quid habit, the prognosis for an untreated lesion, regardless of its colour, degree of thickening, ulceration of the epithelial surface or presence of thick fibrous bands, is progressive worsening, with a high risk for squamous cell carcinoma.²⁸

The quid habit has a major social and cultural role in communities throughout the Indian subcontinent, Southeast Asia and locations in the western Pacific. Following migration from these countries to North America, predominantly to inner city areas, the habit has remained prevalent among its practitioners. Dental practitioners in North America should be aware of these conditions and their relation to betel quid use, since they may well be seen more frequently in the future. An active preventive approach is required to limit the potential for the development of oral cancer. ♦



La Dre Avon est spécialiste en pathologie buccale et médecine buccale et professeure à l'Université Laval, Québec (Québec).

Écrire à la : Dre Sylvie-Louise Avon, Faculté de médecine dentaire, Université Laval, Ste-Foy QC G1K 7P4. Courriel : sylvie-louise.avon@fmd.ulaval.ca.

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Références

1. Zain RB, Ikeda N, Gupta PC, Warnakulasuriya KAAS, van Wyk CW, Shrestha P, and other. Oral mucosal lesions associated with betel quid, areca nut and tobacco chewing habits: consensus from a workshop held in Kuala Lumpur, Malaysia, November 25–27, 1996. *J Oral Pathol Med* 1999; 28(1):1–4.
2. Farrand P, Rowe RM, Johnston A, Murdoch H. Prevalence, age of onset and demographic relationships of different areca nut habits amongst children in Tower Hamlets, London. *Br Dent J* 2001; 190(3):150–4.
3. Neville BW, Damm DD, Allen CM, Bouquot JE. Oral and maxillofacial pathology. 2nd ed. Philadelphia: W.B. Saunders Company; 2002. p. 349–50.
4. International Agency for Research on Cancer. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans. Tobacco habits other than smoking; betel-quid and areca-nut chewing; and some related nitrosamines. Vol. 37. 291 pp. Lyon, France: IARC, 1985.
5. Nair UJ, Obe J, Friesen M, Goldberg MT, Bartsch H. The role of lime in the generation of reactive oxygen species from betel quid ingredients. *Environ Health Perspect* 1992; 98:203–5.
6. Gupta PC, Nandakumar A. Oral cancer scene in India. *Oral Dis* 1999; 5(1):1–2.
7. Ko YC, Huang YL, Lee CH, Chen MJ, Lin LM, Tsai CC. Betel quid chewing, cigarette smoking and alcohol consumption related to oral cancer in Taiwan. *J Oral Pathol Med* 1995; 24(10):450–3.
8. Shah B, Lewis MA, Bedi R. Oral submucous fibrosis in a 11-year-old Bangladeshi girl living in the United Kingdom. *Br Dent J* 2001; 191(3):130–2.
9. Yang YH, Lee HY, Tung S, Shieh TY. Epidemiologic survey of oral submucous fibrosis and leukoplakia in aborigines of Taiwan. *J Oral Pathol Med* 2001; 30(4):213–9.
10. Johnson NW. Orofacial neoplasms; global epidemiology, risk factors and recommendations for research. *Int Dent J* 1991; 41(6):365–75.
11. Murti PR, Bhonsle RB, Gupta PC, Daftary DK, Pindborg JJ, Mehta FS. Etiology of oral submucous fibrosis with special reference to the role of areca nut chewing. *J Oral Pathol Med* 1995; 24(4):145–52.
12. Johnson NW, Warnakulasuriya KA. Epidemiology and aetiology of oral cancer in the United Kingdom. *Community Dent Health* 1993; 10 Suppl 1:13–29.
13. Bhonsle RB, Murti PR, Daftary DK, Mehta FS. An oral lesion in tobacco-lime users in Maharashtra, India. *J Oral Pathol* 1979; 8(1):47–52.
14. Gupta PC, Mehta FS, Daftary DK, Pindborg JJ, Bhonsle RB, Jalnawalla PN, and others. Incidence of oral cancer and natural history of oral precancerous lesions in a 10-year follow-up study of Indian villagers.

Community Dent Oral Epidemiol 1980; 8(6):283–333.

15. Reichart PA, Schmidtberg W, Scheifele CH. Betel chewer's mucosa in elderly Cambodian woman. *J Oral Pathol Med* 1996; 25(7):367–70.

16. Pindborg JJ, Sirsat SM. Oral submucous fibrosis. *Oral Surg Oral Med Oral Pathol* 1966; 22(6):764–79.

17. Pindborg JJ, Murti PR, Bhonsle RB, Gupta PC, Daftary DK, Mehta FS. Oral submucous fibrosis as a precancerous condition. *Scand J Dent Res* 1984; 92(3):224–9.

18. Pillai R, Balaram P, Reddiar KS. Pathogenesis of oral submucous fibrosis. Relationship to risk factors associated with oral cancer. *Cancer* 1992; 69(8):2011–20.

19. Lai DR, Chen HR, Lin LM, Huang YL, Tsai CC. Clinical evaluation of different treatment methods for oral submucous fibrosis. A 10-year experience with 150 cases. *J Oral Pathol Med* 1995; 24(9):402–6.

20. Dave BJ, Trivedi AH, Adharyu SG. Role of areca nut consumption in the cause of oral cancers. A cytogenetic assessment. *Cancer* 1992; 70(5):1017–23.

21. Haider SM, Merchant AT, Fikree FF, Rahbar MH. Clinical and functional staging of oral submucous fibrosis. *Br J Oral Maxillofac Surg* 2000; 38(1):12–5.

22. Anuradha CD, Devi CS. Serum protein, ascorbic acid & iron & tissue collagen in oral submucous fibrosis — a preliminary study. *Indian J Med Res* 1993; 98:147–51.

23. van Wyk CW, Grobler-Rabie AF, Martell RW, Hammond MG. HLA-antigens in oral submucous fibrosis. *J Oral Pathol Med* 1994; 23(1):23–7.

24. Maresky LS, de Waal J, Pretorius S, van Zyl AW, Wolfaardt P. Epidemiology of oral precancer and cancer. *J Dent Assoc S Afr* 1989; Suppl 1:18–20.

25. Pindborg JJ, Bhonsle RB, Murt PR, Gupta PC, Daftary DK, Mehta FS. Incidence rate and early forms of oral submucous fibrosis. *Oral Surg Oral Med Oral Pathol* 1980; 50(1):40–4.

26. Daftary DK, Bhonsle RB, Murti PR, Pindborg JJ, Mehta FS. An oral lichen planus-like lesion in India betel-tobacco chewers. *Scand J Dent Res* 1980; 88(3):244–9.

27. Pearson N, Croucher N, Marcenes W, O'Farrell M. Prevalence of oral lesions among a sample of Bangladeshi medical users aged 40 years and over living in Tower Hamlets, UK. *Int Dent J* 2001; 51(1):30–4.

28. Marx RE, Stern D. Oral and maxillofacial pathology. A rationale for diagnosis and treatment. Quintessence Publishing Co, Inc.; 2003. p. 317–9.