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內文：

**[Abstract]**

- **Oral submucosa fibrosis (OSF)** is a premalignant condition associated with the practice of chewing betel quid (containing areca nut) which is a habit common among South Asian people. (South China, South Asia, Middle East)
- OSF is characterized by inflammation, **increased deposition of submucosal collagen and formation of fibrotic bands** in the oral and paraoral tissues, which increasingly limit mouth-opening
- Significant mobility—in terms of loss mouth function as tissues become rigid  
Mortality—transformation into SCC

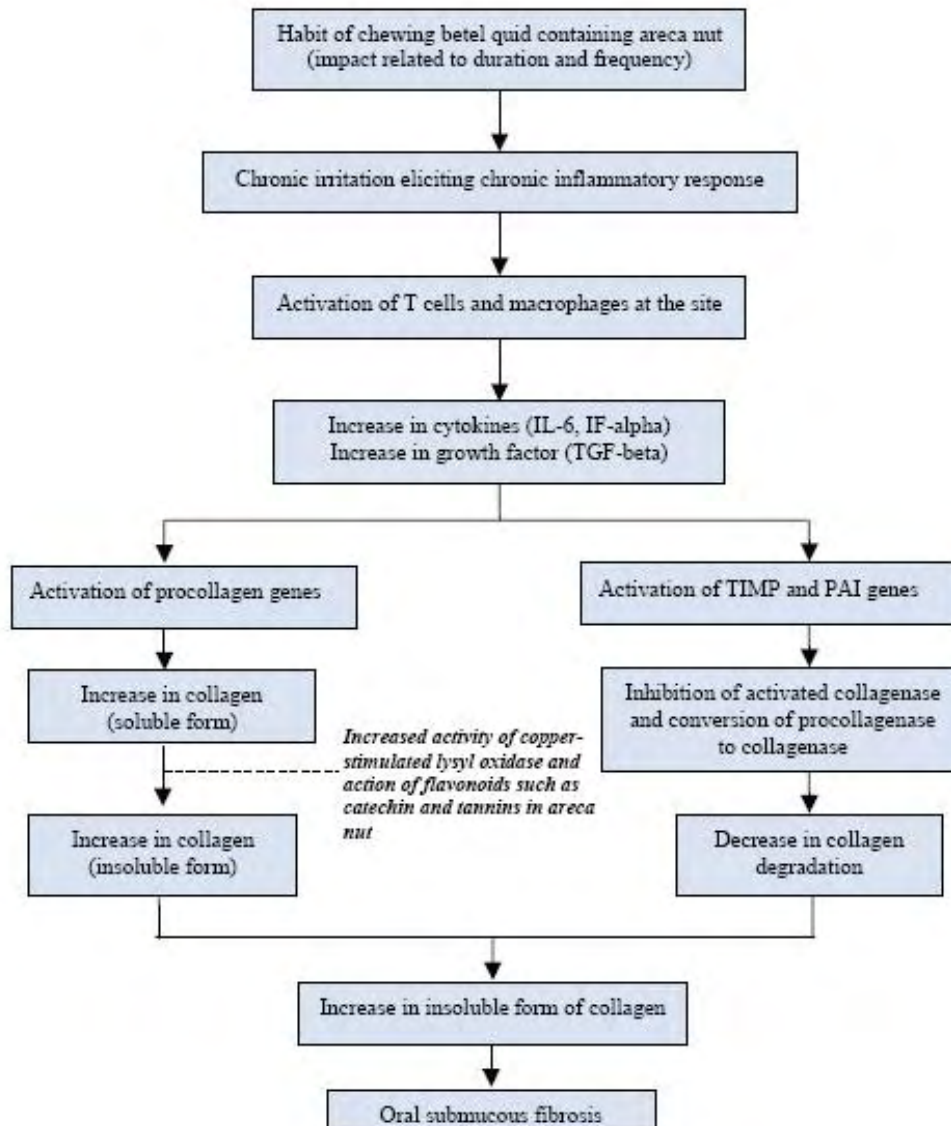
**[Literature Review]**

**Etiology:**

- The amount, frequency and duration are clearly related to the development of OSF
- Besides continuous irrigation, genetic and immunologic predisposition play a role of OSF

**Pathogenesis:**

- Pathogenesis is believed to involve juxta-epithelium inflammatory reaction and fibrosis of oral mucosa, probably due to increased cross-linking of collagen through up-regulation
- Fibrosis results from the effects of areca nut, which increases collagen production and decreases collagen degeneration
- OSF is considered a **collagen metabolic disorder**



### Clinical features

- The period between the initiation of chewing betel quid and the development of clinical symptoms of OSF varies tremendously, ranging from a few months to several decades (type of areca nut, duration, practice habit, individual susceptibility)

#### Early Stage :

- The S/S of OSF is due to inflammation, and primarily, fibrosis.
- **Burning sensation** (especially when eating spicy food), **dry mouth, blanching oral mucosa** and **ulceration**
- **Blanching of oral mucosa** is caused by impairment of local vascularity because of increasing fibrosis. (marble-like appearance) Blanching may be localized, diffuse, or reticular. Sometimes vesicles are formed and making erosion

#### More Advanced Stage :

- **Soft tissues more rigid--** Mouth opening limited, thick and rubbery lip, thick and rigid cheek, fibrosis of tongue (depapillation of tongue), shrunken uvula, blockage of Eustachian tube, esophageal fibrosis

**Pathology :**

- **Initial—juxta-epithelial inflammation** (edema, large fibroblasts, neutrophils, eosinophils) A little later, **collagen bundles with early hyalinization, lymphocytes and plasma cells**, occasionally lichenoid mucositis.
- **More Advanced—thick bands of collagen, hyalinization extending into submucosa layer and decreased vascularity.** Thinner epithelium, lack of melanin and hyperkeratinized. Occasional dysplastic changes, muscle degeneration.

**Treatment :**

- **No known treatment is effective**
- **Intralesional steroid**—injected into fibrotic bands weekly, amount 6~8 weeks
- Patients are advised to do mouth-opening exercises
- Some conservative treatment
  
- If mouth opening is severely limited, surgical such as myotomy, coronoidectomy and excision of fibrotic bands are required
- Reconstruction : buccal pad flap, superficial temporal flap, forearm flap
- Alternative procedures : Physiotherapy (insertion of an oral stent), local heat therapy, mouth exercises

**Outcomes :**

- 2 features : persistence or its potential to become malignant
- OSF may cause atrophy in the epithelium, increasing carcinogen penetration
- Studies suggest—dysplasia of biopsied OSF cases—25%  
transformation to malignancy—3% ~ 19%

**[Case Reports]****Case 1 : A 23 year-old man**

**C.C. :** Burning sensation while chewing spicy food

The patient had a habit of chewing areca nut powder 3~4 times a day for the past 2~3 years ago. He also drank alcohol 750ml on every weekends for 5 years

**O.E. :** **normal mouth opening**

Entire oral mucosa is pale, especially buccal mucosa, showing erosion spots.

Hard palate is wholly blanched

**No fibrotic bands** are palpable

**Pathologic report :** Prominent fibroblasts, increased vascularity, edema, inflammation infiltration (neutrophil and eosinophil)

**Diagnosis :** Early stage OSF

**Tx :** Suggest p't to quid areca nut and keep F/u



**Case 2 : a 43 year-old woman**

**C.C. : progressive difficulty in opening mouth** past 2 years

The patient had a longstanding habit of chewing areca nut (4~5 pouches a day for 20+ years)

**O.E. : Thin lips**

**MMO = 26mm** (< 40mm, average normal opening)

Erosion at corners of her mouth

**Entire oral mucosa is pale, extending to focal area**

Depapillation of tongue

**Extensive fibrosis** occurred on ventral surface, floor of the mouth and buccal mucosa

The patient could not stick out her tongue or touch hard palate with tongue tip.

Difficult to retract the patient's lips

Suspect with dry mouth

Loss of cheek elasticity (puffed-cheek appearance was not seen)



**Diagnosis : OSF at a moderately advanced stage**

**Case 3—a 60 year-old male, diagnosed OSF of 10 years duration**

**C.C. : a swelling on his cheek and on the floor of the mouth** for past 6 months

The patient has begun intralesional steroid 10 years ago on diagnosis of OSF

He ceased treatment after a few visits, and continued to chew areca nut

**O.E. : MMO = 16mm** (< 40mm, averaged normal opening)

Oral cavity was fully blanched, and buccal mucosa was completely fibrotic.

The uvula was also fibrotic and deformed

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2 swelling mass : 1<sup>st</sup> mass is about 3X2cm in size. With an irregular margin, 1<sup>st</sup>

mass was extending from corner of his mouth to molar area  
 Firm and fixed, indurated surrounding mucosa  
 2<sup>nd</sup> mass is about 1cm in diameter, over lingual side of LR  
 premolar region. Small finger-like projections on the mass

A panoramic radiograph showed no bony involvement

**Pathologic report : Squamous cell carcinoma**



**[Conclusion]**

This 3 cases illustrate **the relentless progression of OSF** and its significant mobility and mortality. They also emphasize **the importance of close follow up** of such cases.

Because the significant cancer risk, periodic biopsies of suspicious region of the oral mucosa are essential.

題號	題目
1	有關於OSF的敘述，下列何者為非？ (A) 有許多病患的致病因素是嚼食檳榔造成 (B) 屬於癌前病灶，但轉化為惡性腫瘤機率小於1% (C) 纖維化的範圍甚至會影響懸雍垂與咽喉部位 (D) 張口度會隨病情惡化而逐漸縮小
答案(B)	出處：
題號	題目
2	對於OSF的特性描述，以下何者為非 (A) 目前歸納出最有效的治療方式是手術移除纖維組織 (B) 纖維化可能會影響聽力與吞嚥 (C) 在初期病灶的切片可發現eosinophil的浸潤 (D) 纖維組織可能會造成表皮層的破壞，使癌化物質易進入軟組織
答案(A)	出處：

P.S.

1. Up-regulation：當訊息分子作用於細胞，造成細胞內觀察標的物的增加。



## 2. Treatment of OSF :

Treatment	Treatment details
Micronutrients and minerals <sup>24</sup>	Vitamin A, B complex, C, D and E, iron, copper, calcium, zinc, magnesium, selenium and others
Milk from immunized cows <sup>25</sup>	45 g milk powder twice a day for 3 months
Lycopene <sup>26</sup>	8 mg twice a day for 2 months
Pentoxifylline <sup>27</sup>	400 mg 3 times a day for 7 months
Interferon gamma <sup>28</sup>	Intralesional injection of interferon gamma (0.01–10.0 U/mL) 3 times a day for 6 months
Steroids <sup>29</sup>	Submucosal injections twice a week in multiple sites for 3 months
Steroids <sup>29</sup>	Topical for 3 months
Hyalase + dexamethasone <sup>23</sup>	—
Placental extracts <sup>23</sup>	—
Turmeric <sup>30</sup>	Alcoholic extracts of turmeric (3 g), turmeric oil (600 mg), turmeric oleoresin (600 mg) daily for 3 months
Chymotripsin, hyaluronidase and dexamethasone <sup>31</sup>	Chymotripsin (5000 IU), hyaluronidase (1500 IU) and dexamethasone (4 mg), twice weekly submucosal injections for 10 weeks