

# Burning mouth syndrome: A diagnostic dilemma

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## ABSTRACT

Burning mouth syndrome (BMS) has been considered an enigmatic condition because the intensity of pain rarely corresponds to the clinical signs of the disease. Various local, systemic and psychological factors are associated with BMS, but its etiology is not fully understood. Also, there is no consensus on the diagnosis and classification of BMS. A substantial volume of research has been focused on BMS during the last two decades. Progress has been made, but the condition remains a fascinating, yet poorly understood area, in the field of oral medicine. Recently, there has been a resurgence of interest in this disorder with the discovery that the pain of BMS may be neuropathic in origin and originate both centrally and peripherally. The aim of this paper is to explore the condition of BMS with the specific outcome of increasing awareness of the condition.

**Key words:** Burning mouth syndrome, oral dysesthesia, pain management, stomatodynia

## INTRODUCTION

The patient with a complaint of a burning sensation of the oral mucosa presents one of the most difficult challenges to the health care professionals. There is a variety of names applied to this presentation includes burning mouth syndrome (BMS) (the most widely accepted), stomatodynia, stomatopyrosis, glossopyrosis, glossodynia, sore mouth, sore tongue and oral dysesthesia.<sup>[1]</sup>

Burning mouth syndromes defined by the International Association for the Study of Pain as burning pain in the

tongue or other oral mucous membrane associated with normal signs and laboratory findings lasting at least 4-6 months.<sup>[2]</sup> The International Headache Society in the International Classification of Headache Disorders II classifies BMS in the category of cranial neuralgias and central causes of facial pain within the subcategory of central causes of facial pain.<sup>[3]</sup>

Burning mouth syndrome is described as an intraoral burning sensation for which no medical or dental cause can be found. It is usually described as oral burning pain, sometimes with dysesthetic qualities similar to those present in other neuropathic pain conditions with the absence of clinical and laboratory abnormalities. As a result of the variations in experienced symptoms and despite the fact that numerous studies have been carried out, there is no universal consensus on the diagnosis, etiology and treatment of BMS. This leads to patients being referred from one health care professional to another, causing an increased burden on both the health care system and the patient.<sup>[4]</sup> Various groups of investigators have attempted to provide an answer to the questions regarding this topic, which is the subject of considerable controversy. The multiplicity of factors related with this nosologic entity, which in one form or another are involved in the appearance of the symptoms have made it currently one of the most debated issues.<sup>[5]</sup>

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## EPIDEMIOLOGY

The prevalence of BMS reported from international studies ranges from 0.7% to 4.6%.<sup>[5]</sup> It seems the prevalence of BMS increases with age in both males and females, with this syndrome mainly affecting females in the fifth to seventh decade.<sup>[6]</sup> The mean age of BMS is between 55 and 60 years, with the occurrence under 30 being rare.<sup>[7,8]</sup> The ratio between females and males varies from 3:116:1.<sup>[9]</sup> These gender differences may be explained by biologic, psychologic, and socio-cultural factors; however, these factors are yet to be defined. It seems from these epidemiologic studies that menopausal females have a particularly high incidence of burning mouth.<sup>[10]</sup> This syndrome has never been described in children or adolescents. No studies exist in relation to any occupational, educational or social grouping.<sup>[11]</sup>

## CLASSIFICATION

There have been several proposed classification schemes to characterize better and define BMS. One of the proposed classifications is based on daily fluctuations of the symptoms.<sup>[7,10]</sup>

- a. Type 1: Characterized by progressive pain, patients wake up without pain, which then increases throughout the day, affects approximately 35% of patients. This type may be associated with systemic diseases, such as nutritional deficiencies.
- b. Type 2: Symptoms are constant throughout the day and patients find it difficult to get to sleep, represents 55%. These patients usually present associated psychological disorders.
- c. Type 3: Symptoms are intermittent, with atypical location and pain. Constitutes 10% of patients. It seems that the contact with oral allergens could play an important etiologic role in this group.

A more pragmatic approach is proposed by Scala *et al.*<sup>[5]</sup> who organize BMS into two clinical forms, “primary” or essential/idiopathic BMS, in which the causes cannot be identified, “secondary” BMS, resulting from local factors or systemic conditions. Thus, these idiopathic and secondary criteria form two different subgroups of the same pathology.

## ETIOPATHOGENESIS

The etiology of BMS is poorly understood. Most support a multi-factorial syndrome involving the interaction of biological and psychological systems. A number of etiologies has been proposed suggesting BMS involves alterations in both central and peripheral nervous systems.<sup>[12]</sup> The various factors related with the etiopathogenesis of this syndrome have been divided into local, systemic and psychological [Table 1].

### Local factors

Pseudomembranous and erythematous candidiasis have been associated with BMS.<sup>[13]</sup> The diagnosis of candidiasis

**Table 1: Etiologic factors for BMS**

Etiologic factors	
Local	
	Poorly fitting prosthesis
	Dental treatment
	Parafunctional habits — clenching, bruxism
	Allergic contact stomatitis
	Taste alterations
	Infection — bacterial, fungal, viral
	Xerostomia
Systemic	
	Endocrine — hypothyroidism, menopause, diabetes
	Anemia
	Deficiencies — iron, Vitamin B complex, zinc
	Medications such as captopril
	Esophageal reflux
	Sjogren’s syndrome
Psychologic	
	Cancerphobia
	Stress
	Hypochondriasis
	Anxiety
	Depression
	Compulsive disorders
Miscellaneous	

BMS: Burning mouth syndrome

is often presumptive, made on the response to antifungal therapy and rarely based on cytologic or histologic studies. Gorsky *et al.*<sup>[14]</sup> reported that in patients with BMS having no clinical signs of candidiasis, condition of BMS improved in 86% after using antifungal lozenges and 13% had complete elimination of their symptoms.<sup>[15]</sup>

Glossodynia may be caused by oral cancer, which is normally present on the lateral borders of the tongue or the oropharynx. Premalignant entities such as leukoplakia or erythroplakia may also present with burning or painful sensation.<sup>[16]</sup>

A faulty denture design may promote the burning sensation due to an increased level of functional stress to the circumoral or lingual musculature.<sup>[17]</sup> BMS patients were found to have significantly less daily denture use, reduced tongue space, incorrect placement of the denture occlusal table, and increased denture vertical dimension.<sup>[18]</sup>

Xerostomia is a concomitant symptom in patients with BMS, prevalence varying between 34 % and 39%.<sup>[11]</sup>

### Systemic factors

Systemic factors implicated in BMS; many of these are deficiencies, such as vitamin deficiencies (Vitamin B12, B6, C and folic acid), anemias and low levels of zinc. Hormonal changes (reduced plasma estrogens), diabetes mellitus, hypothyroidism and immunological diseases have also been described.<sup>[19,20]</sup> Many medications are intimately related with burning mouth; among which are found anti-histamines, neuroleptics, some anti-hypertensives, antiarrhythmics and benzodiazepines. Anti-hypertensives are among the most

frequently implicated medicines, principally those that act on the renin-angiotensin system.<sup>[19]</sup>

### Psychological factors

Personality and mood changes have been consistently demonstrated in patients with BMS and have been used to suggest that the disorder is a psychogenic problem.<sup>[21]</sup> Browning *et al.* concluded that 44% of burning mouth patients had an associated psychiatric disorder.<sup>[22]</sup> Lamb *et al.* indicated that 60% of burning mouth patients has had psychological factors, and anxiety was most difficult to control.<sup>[23]</sup> The reported success of bio-behavioral techniques in the treatment of BMS may be related more to an improvement in pain-coping strategies than to a “cure” of the disorder.<sup>[24]</sup> Similarly, the usefulness of tricyclic anti-depressants and some benzodiazepines may be more closely related to their analgesic and anti-convulsant properties, and to the possible effect of benzodiazepines on taste-pain pathways.<sup>[9]</sup>

### CLINICAL PRESENTATION

In more than one-half of patients with BMS, the onset of pain is spontaneous, with no identifiable precipitating factor. Approximately, one-third of patients relate time of onset to a dental procedure, recent illness or medication course. Regardless of the nature of pain onset, once the oral burning starts, it often persists for a prolonged period.<sup>[25]</sup> The predominant pain character reported by BMS patients is a prolonged “burning” sensation of the oral mucosa described as moderate to severe intensity that may vary throughout the course of the day.<sup>[5,26]</sup> The mean severity of pain has been assessed at about 5-8 cm on a 10 cm visual analogue scale, where 0 cm represents “no pain” and 10 cm corresponds to the “worst possible pain” [Table 2].<sup>[27]</sup>

The burning sensation often occurs in more than one oral site, with the anterior two-thirds of the tongue, the anterior hard palate and the mucosa of the lower lip most frequently involved.<sup>[28]</sup> Alterations in taste occur in as many as two-thirds of patients and often include complaints of persistent tastes (bitter, metallic, or both) or changes in the intensity of taste perception. Damage to the taste has been reported in association with BMS, because of disinhibition of pain signaling.<sup>[8]</sup> In many patients with the syndrome, pain is absent during the night but occurs at a mild to moderate level by middle to late morning. Patients often report that the pain interferes with their ability to fall asleep.<sup>[1]</sup> Perhaps because of sleep disturbances, constant pain, or both, patients with oral burning pain often have mood changes, including irritability, anxiety, and depression.<sup>[29]</sup> Minimal information is available on the natural course of the condition.<sup>[1]</sup> In most cases, the syndrome follows a protracted course with an average duration of 3.4 years but may last for 12 years or more with recovery in up to two-thirds of patients within 6-7 years of onset.<sup>[1,6]</sup> It has also been reported that BMS has a negative impact on health-related quality of life of individuals.<sup>[30]</sup> The location of oral pain

is most commonly bilateral and importantly does not follow the anatomical distribution of a peripheral sensory nerve.<sup>[31]</sup>

### DIAGNOSIS

History taking is the key to diagnosis of BMS. Both diagnosis and management may be difficult because patients often present with multiple oral complaints, may be focused on their symptoms and may be anxious or depressed, which intensifies the pain experience.<sup>[15]</sup> BMS is characterized by an oral burning sensation in the absence of any organic disorders of the oral cavity.<sup>[32]</sup> Scala *et al.* proposed a series of differential diagnostic criteria for identifying BMS. In this context, they established a distinction between fundamental and additional criteria for diagnosing the disease [Table 3].

The clinical history is helpful in diagnosing BMS. Most patients with the disorder report an increase in pain intensity from morning to night, decreased pain while eating, oral dryness that waxes and wanes with the burning, and the frequent presence of taste disturbances.<sup>[33]</sup> The clinical examination is more to rule out any possible local factors that may be responsible for the oral burning complaints. The clinical examination should include an extra-oral and intraoral examination of temporomandibular joint function; inspection and palpation of the masticatory muscles, oral mucosa, tongue mobility, and dental hard and soft tissues; and evaluation of any prosthetic devices. Objective measurements of salivary flow rates (whole stimulated and unstimulated saliva) and taste function should be

**Table 2: Clinical features that are helpful in the diagnosis of BMS**

Clinical features
Unilateral or bilateral burning pain localized to tongue, palate, lips and gingiva
Pain that gets worse over the day
Decreased pain on eating
Decreased pain with sleep
Absence of clinical finding
Presence of abnormal or dysgeusic tastes, usually metallic, bitter or sour
Complaint of dry mouth in presence of normal flows
Sensory changes or paresthesias including complaints of areas of roughness or irritation

BMS: Burning mouth syndrome

**Table 3: Criteria developed by Scala for the diagnosis of BMS**

Fundamental inclusion criteria
Daily and deep burning sensation of the oral mucosa (bilateral)
Burning sensation for at least 4-6 months
Constant intensity, or increasing intensity during the day
No worsening on eating or drinking. The symptoms may improve
No interference with sleep
Additional inclusion criteria
Dysgeusia and/or xerostomia
Sensory or chemosensory alterations
Mood changes or psychopathological alterations

BMS: Burning mouth syndrome

taken.<sup>[34]</sup> Neurologic imaging and consultation should be a consideration if patients present with more complex, confounding, or atypical symptoms, including sensory, motor, and autonomic changes, to rule out any neurodegenerative disorders or central nervous system pathology [Table 4].<sup>[10]</sup>

The diagnosis is usually late, often due to a lack of understanding of the nature of this entity, in addition to the patients taking up many health resources since they frequently consult various specialists.<sup>[1]</sup> It is important to highlight that the diagnosis of BMS should be established only when all other possible causes have been discounted, being a diagnosis by elimination.<sup>[11]</sup>

## TREATMENT

Owing to the large variety of associated factors, the protocol for BMS management is complex<sup>[15]</sup> [Table 5].

**Table 4: Clinical tests for BMS**

Clinical test
Oral cultures
Fungal, viral or bacterial (if suspected)
Hematologic tests
Complete blood count
Glucose levels
Nutritional factors
Autoimmune panel
Salivary flow rates
Unstimulated (0.3-0.4 g/min)
Stimulated (0.75-2.0 g/min)
Imaging
MRI, CT scans and nuclear medicine (to rule out central changes or patient is not responding to medication)
Salivary uptake scans
If low salivary flow rates and Sjogren syndrome suspected
Allergy testing
If needed, especially for a dental panel and allergens
Trial of discontinuation of certain medications
Including ACE inhibitors
Gastric reflux studies

MRI: Magnetic resonance imaging; CT: Computed tomography; ACE: Angiotensin converting enzymes; BMS: Burning mouth syndrome

**Table 5: Treatment of BMS**

Treatment
Topical therapy
Clonazepam- 1 mg tab to be dissolved and hold in mouth
Lidocaine- 2% gel
Capsaicin- 0.025% cream
Benzylamine hydrochlorate- 0.15%
Systemic therapy
Amitriptyline- 10-75 mg/day
Paroxetine- 20 mg/day
Amisulpride- 50 mg/day
Clonazepam- 0.25-2 mg/day
Gabapentin- 300-2400 mg/day
Alpha-lipoic acid- 200 mg tid
Capsaicin- 0.25% capsules tid
Behavioral interventions
Cognitive behavioral therapy

BMS: Burning mouth syndrome

The management of BMS has been quite disappointing to date, this in part being due to our lack of knowledge of the specific mechanisms underlying the syndrome.<sup>[1]</sup> Paramount to the clinical management of BMS is obtaining the correct diagnosis. Also, it has been proved that the sooner treatment is prescribed after the diagnosis of BMS, the better the results obtained.<sup>[35]</sup> Initially, the clinician must determine if the patient is suffering from primary BMS or secondary BMS. Secondary BMS requires appropriate diagnosis and treatment of the underlying condition to manage symptoms. In primary BMS, the cause is unclear, so treatment options are based on patients' symptomatology. Three approaches or combinations that can be considered part of the management strategy include topical medications, systemic medications, and behavioral interventions.

The most-used medications to treat this syndrome are anti-depressants, anti-psychotics, anti-epileptics, analgesics and oral mucosa protectors. The tricyclic anti-depressants such as amitriptyline and nortriptyline at low doses are useful in BMS. Studies generally support the use of low dosages of clonazepam (Klonopin),<sup>[36]</sup> chlordiazepoxide (Librium) and tricyclic anti-depressants (e.g., amitriptyline [Elavil]).<sup>[37]</sup> Evidence also supports the utility of a low dosage of gabapentin (Neurontin).<sup>[38]</sup> Studies have not shown any benefit from treatment with selective serotonin reuptake inhibitors or other serotonergic anti-depressants (e.g., trazodone).<sup>[39]</sup> Topical capsaicin has also been applied in BMS, used as a desensitizing agent in patients with BMS, but it is usually unaccepted by patients due to its taste. Topical capsaicin has been used as a treatment alternative for controlling neuropathic pain in general. The drug is normally used at concentrations of between 0.025% and 0.075%, inducing desensitization to thermal, chemical and mechanical stimuli when applied topically. However, it should be noted that there are clear limitations to the use of topical capsaicin, such as limited effect over time and a limited magnitude of improvement. Systemic capsaicin has been used (0.25%, 3 times a day, for 30 days) with a significant reduction in pain intensity compared with a placebo group.

Alpha lipoic acid is a powerful neuroprotector that prevents damage to nerve cells by free radicals. It significantly reduces the symptoms in the majority of patients with an idiopathic dysgeusia. Several studies suggest that alpha lipoic acid can improve the symptoms in BMS, showing that at 2 months, 97% of the patients treated with alpha lipoic acid (200 mg, 3 times a day) experienced an improvement in the symptoms. Topical steroid hormones and anti-inflammatory rinses have been tried with little evidence of effectiveness in reducing or eliminating the symptoms of BMS, particularly when compared to placebo or spontaneous remission rates. Hormone replacement therapy has also been used, finding that women with symptoms of burning and estrogen receptors in the oral mucosa respond to hormone replacement.<sup>[1]</sup>

## CONCLUSION

Burning mouth syndrome remains a fascinating, though poorly understood, condition in the field of oral medicine. The exact cause of BMS often is difficult to pinpoint. No consensus exists in defining, diagnosing and treating BMS. There is little evidence-based material to assist the practitioner when dealing with these individuals. There is no doubt that innovative and interdisciplinary research is required to elucidate and expand on the knowledge of the etiology and pathogenic factors involved in BMS. The positive aspect is that most patients can be helped, and many achieve a complete cure of their condition. It relies, however, on initial recognition and this is the most critical step.

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