

# Separating oral burning from burning mouth syndrome: unravelling a diagnostic enigma

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## ABSTRACT

Burning mouth syndrome (BMS) is characterized by burning pain in the tongue or other oral mucous membrane often associated with symptoms such as subjective dryness of the mouth, paraesthesia and altered taste for which no medical or dental cause can be found. The difficulty in diagnosing BMS lies in excluding known causes of oral burning. A pragmatic approach in clarifying this issue is to divide patients into either primary (essential/idiopathic) BMS, whereby other disease is not evident or secondary BMS, where oral burning is explained by a clinical abnormality. The purpose of this article was to provide the practitioner with an understanding of the local, systemic and psychosocial factors which may be responsible for oral burning associated with secondary BMS, therefore providing a foundation for diagnosing primary BMS.

**Keywords:** Burning mouth syndrome, local factors, oral burning, psychosocial factors, systemic factors.

**Abbreviations and acronyms:** ACE = angiotensin converting enzyme; BMS = burning mouth syndrome.

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## INTRODUCTION

Burning mouth syndrome (BMS) is defined by the International Association for the Study of Pain<sup>1</sup> as burning pain in the tongue or other oral mucous membrane associated with normal signs and laboratory findings lasting at least four to six months.<sup>2,3</sup> The International Headache Society in The International Classification of Headache Disorders II<sup>4</sup> describes BMS as an intra-oral burning sensation for which no medical or dental cause can be found. It is further commented that the pain may be confined to the tongue (glossodynia) with associated symptoms including subjective dryness of the mouth, paraesthesia and altered taste. From these definitions it is easy to understand the uncertainty this condition creates from both the patient's perspective and the practitioner evaluating these individuals; the patient is experiencing continuous burning pain in the mouth without obvious clinical signs, while the practitioner is unable to definitively diagnose these symptoms even with the use of diagnostic testing or imaging. The lack of a definite and clear distinction between BMS without a known cause and conditions that are responsible for oral burning symptoms creates a diagnostic dilemma. A

pragmatic approach in clarifying this issue is to divide patients into either primary (essential/idiopathic) BMS, whereby other disease is not evident or secondary BMS, where oral burning is explained by a clinical abnormality.

The purpose of this article is to provide the practitioner with an understanding of the local, systemic and psychosocial factors which may be responsible for oral burning associated with secondary BMS, therefore providing a foundation for diagnosing primary BMS (Table 1).

## Local factors

There are a number of local factors that can cause oral burning which must be excluded prior to making a diagnosis of primary BMS. One of the more common causes of oral burning is dry mouth. Dry mouth may either be an objective finding due to hyposalivation or a subjective sensation termed xerostomia. Twenty-five per cent of BMS patients report dry mouth which may either be idiopathic or secondary to medication use such as tricyclic antidepressants and benzodiazepines.<sup>5–9</sup> A list of medications associated with dry mouth may be found in other sources.<sup>10,11</sup> Objective reduction of

**Table 1. Local, systemic and psychosocial factors which may be responsible for oral burning**

Local	Systemic	Psychosocial
Dry mouth • hyposalivation • xerostomia	Haematinic disorders • vitamin B group • iron • folate • zinc	Psychological disorders • depression • anxiety • somatization
Taste alterations	Autoimmune type connective tissue • Sjögren's syndrome • sicca • systemic lupus erythematosus	Personality profiles • neuroticism • extraversion • openness • conscientiousness
Oral infection • fungal • bacterial • viral	Gastroesophageal reflux disease	
Oral mucosal diseases • lichen planus • benign migratory glossitis • hairy tongue • fissured tongue	Endocrine-related disorders • diabetes • thyroid disorders • hormone deficiencies	
Oral parafunction	Medication side effects • tricyclic antidepressants • ACE inhibitors	
Oral galvanism	Central nervous system disorders • multiple sclerosis • Parkinson's disease • trigeminal neuralgia	
Poorly designed dentures	Idiopathic focal conditions • oro-cervical • uro-genital	
Allergic reactions • dental products • food products		

salivary flow (hyposalivation) as measured by sialometry is also reported.<sup>8,12</sup> Patients with normal oral mucosa may present with salivary gland dysfunction upon assessment (hyposalivation) or may not voluntarily admit to oral dryness (xerostomia) unless actively questioned.<sup>8</sup> A lack of lubrication with saliva predisposes the oral mucosa to friction and pain often of burning quality.<sup>6</sup>

The complaint of dry mouth in BMS patients without objective evidence of hyposalivation may be related to the quality of the saliva. Increased levels of chloride, phosphorus and potassium concentrations and decreased low molecular weight proteins were found in BMS subjects compared to controls suggesting a relationship between salivary composition and BMS.<sup>13</sup> Other studies do not support these findings.<sup>14,15</sup> Nagler and Hershkovich<sup>16</sup> found similarities with respect to low salivary flow, as well as salivary and taste analysis among subjects with BMS, taste aberrations or xerostomia compared to controls. This suggests that oral sensorial complaints may have a salivary-related neuropathic mechanism. Specifically, BMS subjects had

higher concentrations of sodium, total protein, albumin, IgA, IgG, IgM, lysozyme, amylase and secretory IgA. Of interest, Nagler and Hershkovich<sup>17</sup> studied the elderly and found an age-related reduction in salivary flow rate and components when compared to younger subjects. Also, 50 per cent of the elderly had oral sensorial complaints including BMS which was more prevalent among those who used medication. These findings suggest a possible aetiological relationship between salivary function and BMS.

Taste disturbances, such as an alteration in taste perception (dysgeusia) and/or a persistently altered taste are often reported by BMS patients.<sup>3,18-20</sup> Grushka<sup>3</sup> reported disturbances of taste in 69 per cent of BMS subjects (n = 49), whereby 88 per cent and 59 per cent reported persistent taste and alteration in taste perception, respectively. Persistent taste reported included bitter (33 per cent), metallic (27 per cent) or combination (10 per cent) which decreased in 60 per cent of subjects after rinsing with distilled and deionized water. Alterations in taste perception of salt (70 per cent) which may be stronger or weaker, sweet (40 per cent) which is typically weaker, sour (40 per cent) and bitter (35 per cent) which are usually stronger were also found. Formaker and Frank<sup>20</sup> reported on taste function among 73 BMS patients (57 females, 16 males) by measuring the intensity ratings and quality identification for a concentration series of sucrose (sweet), NaCl (salty), citric acid (sour), and quinine-HCl (bitter). Compared to age and gender matched controls, 57 female patients reported lower intensity ratings to NaCl and sucrose; whereas no differences were found for citric acid or quinine-HCl between the groups. Among the male BMS patients (n = 16) and controls (n = 14), no differences were evident for any stimulus. Misidentification of detected stimuli quality occurred in 19 per cent of BMS women compared to 8 per cent of controls. Predominantly, NaCl and citric acid were difficult to identify among BMS women. Although these findings are unclear, the literature regarding taste disturbances suggests the possibility of an aetiological relationship between these findings and BMS. Further investigation into this matter is certainly warranted.

Infections involving the oral cavity have been reported as a cause of oral burning.<sup>8,21-28</sup> Oral candidiasis is a common fungal infection implicated in BMS and must be ruled out. Of concern, is the high prevalence of candida species in BMS patients, therefore making it difficult to discern its specific role in causing oral mucosal burning.<sup>24,27</sup> Typically, the presence of fungal infection is often associated with the findings of atrophy, erythema and ulceration of the oral mucosa which may be the cause of burning pain.<sup>27</sup> Patients often report an increased pain upon eating suggestive of candida-induced burning and likely due to irritation of the mucosa.<sup>29,30</sup> On the contrary, a

decrease or abortion of the pain while eating is commonly found in BMS patients.<sup>3</sup> This finding would therefore cast doubt on a fungal infection being the source of the burning pain. Bacterial infections involving spirochetes, fusiform, enterobacter and klebsiella species and helicobacter pylori have been suggested as causative of BMS.<sup>21–24,31</sup> Due to the often described rapid onset of BMS and dysaesthesia, viral (herpes viruses) causes have been considered. Epstein *et al.*<sup>32</sup> investigated this factor and found no evidence of an active viral infection but considered the possibility of a “hit and run” role for viral damage in BMS. In summary, apart from candida-induced burning, it remains unclear if bacterial and/or viral infections can induce oral burning.

Oral mucosal diseases such as lichen planus, benign migratory glossitis, hairy tongue and fissured tongue have been proposed as causative of BMS.<sup>6,7,33,34</sup> Atrophic and ulcerative forms of lichen planus are known to have a burning pain particularly during periods of exacerbation.<sup>35</sup> Benign migratory glossitis is usually painless but burning may occur in areas of depapillation which may be exacerbated by spicy foods, alcohol or stress.<sup>33,34</sup> Fissured tongue is also usually painless unless grooves and fissures become inflamed or infected due to accumulation of debris resulting in a burning sensation.<sup>33</sup> These oral mucosal diseases are all associated with visual clinical findings, yet in BMS patients, the oral mucosa appears normal.

Parafunctional oral habits such as clenching, bruxing, tongue posturing, lip trapping, sucking, licking or mouth breathing have been proposed as causative in BMS.<sup>8,36,37</sup> To date, studies do not support the assertion that parafunctional habits may cause BMS.<sup>38</sup>

The role of oral galvanism due to electrochemical potential differences between dissimilar metals (restorations and metal prosthesis) as a cause of BMS is rare, but has been reported in the literature.<sup>31</sup>

Poorly designed dentures have been implicated as causative for BMS. Correction of tongue space deficiency because of a lingually positioned occlusal table or incorrect vertical dimension may benefit some patients.<sup>8,39,40</sup> A study by Nater *et al.*<sup>41</sup> found no difference in the denture characteristics such as occlusion, articulation and stability among BMS patients compared to controls suggesting that mechanical factors were unlikely causes of BMS.

Allergic reactions to polymethylmethacrylate, epoxy curing agent, chromium, cobalt, nickel, cadmium, amalgam (mercury), gold, potassium, palladium and related materials in dental products and food-related products such as sorbic acid, propylene glycol, fragrance mix (eugenol, cinnamic aldehyde), benzoic acid, mint and cinnamon may cause allergic contact stomatitis (type IV hypersensitivity reaction) but are rarely

implicated in BMS as, once again, there is a lack of clinical oral mucosa irritation in BMS patients. In cases that are confirmed by patch testing, cessation of exposure to these materials may result in improvement of burning symptoms.<sup>8,42–48</sup>

### Systemic factors

As well as local environmental factors, a number of systemic factors are considered to be involved in causing oral burning sensations. Indeed, oral burning pain may indicate a previously undiagnosed systemic condition. Therefore, before a diagnosis of primary BMS can be made, possible systemic causes of oral burning pain should be ruled out.

Blood disorders associated with anaemias, including vitamin B group, iron and folate deficiencies are associated with a variety of oral manifestations including oral dryness, tongue papillary changes and burning pain. Zinc deficiency has also been associated with burning oral mucosa.<sup>49,50</sup> Blood studies could be utilized to rule out these factors as the cause of the oral burning symptoms.

Similarly, autoimmune type connective tissue disorders such as Sjögren's syndrome, sicca and systemic lupus erythematosus are associated with oral dryness and increased risk of candida infections that may cause oral burning.<sup>51</sup> Even though more than 58 per cent of persons with BMS display abnormal immunological features such as elevated rheumatoid factor and anti-nuclear antibody, no consistent relationship has been found between BMS and a connective tissue disorder,<sup>52</sup> thereby questioning connective tissue disorders as an aetiological factor.

Gastroesophageal reflux disease must be considered in any patient complaining of oral burning. Careful history taking and examination is required for diagnosis and the symptoms should rapidly respond to appropriate management.

Endocrine-related disorders, especially uncontrolled diabetes and thyroid disorders, along with hormonal deficiencies and alterations at menopause have also been associated with oral burning.<sup>12,17,31,53–62</sup>

Medications that may cause hyposalivation such as tricyclic antidepressants have been implicated, but the angiotensin converting enzyme (ACE) inhibitors, namely captopril, enalapril and lisinopril have been particularly associated with oral burning pain.<sup>63–65</sup>

Central nervous system changes associated with conditions such as multiple sclerosis, Parkinson's disease and trigeminal neuralgia may be associated with oral neuropathic pain that may assume a burning nature. The prevalence of BMS has been suggested to be greater in patients with Parkinson's disease than in the general population, suggesting a role of dopaminergic pathways.<sup>66</sup>

Increased frequency of facial pains, pains in other parts of the body and headache in BMS patients has also been reported.<sup>3,39</sup> Also, BMS has been linked with other “dynias”, a group of idiopathic focal conditions with a predilection for the oro-cervical and uro-genital regions such as vulvodynia.<sup>67,68</sup> However, the meaning and relevance of this association remains unclear.

Despite the above evidence supporting a possible association of systemic factors such as nutritional factors, systemic diseases and oestrogen levels with oral burning, the literature is inconsistent and there is a paucity of controlled clinical trials. Attempted treatments where indicated for specific systemic problems such as insulin, vitamin or hormone replacements have not consistently reduced symptoms in patients with oral burning.<sup>5,8,34,69,70</sup> Exceptions include oral burning secondary to the use of the ACE inhibitors where both the oral lesions (when present) and the pain have remitted following discontinuation of the medication and satisfactory resolution of gastroesophageal reflux disease.

### Psychosocial factors

From a historical perspective, the occurrence of BMS has been linked to a patient’s psychological status.<sup>71</sup> The earliest reference for psychological disorders as an aetiological factor for BMS dates back to the 1920s. Lamb *et al.*<sup>72</sup> list many references preceding the date of their publication which address the psychological aspects of BMS. Various disorders, such as depression, anxiety and somatization have been discussed as having a major association with BMS.<sup>73,74</sup> It has been reported that at least one-third of BMS patients may have an underlying psychological diagnosis.<sup>6</sup> Furthermore, a phobic concern regarding cancer has been reported in 20 per cent of patients<sup>8</sup> and is often manifested as repeated self-examination by the patient.<sup>75</sup> In a study<sup>73</sup> comparing 25 BMS subjects to an equivalent number of an age and gender matched group with organically based intra-oral pain disorders, it was found that 44 per cent of the BMS subjects displayed a positive psychological diagnosis as compared to only 16 per cent of the non-BMS group. The identical psychological screening tool (General Health Questionnaire, 28-item version) used in the previous study was also given to 31 consecutive BMS subjects in another study.<sup>76</sup> The authors found that 51.9 per cent of the subjects showed evidence of psychological disorders, especially depression. When compared to other chronic pain populations, using a different psychological screening tool (Irritability, Depression and Anxiety Scale), BMS subjects appeared to have psychological illness more often than other subjects with chronic pain, except those attending a psychiatric clinic. In another study<sup>77</sup> involving 74 BMS subjects, investigating both depression and anxiety (Hamilton’s Depres-

sion and Anxiety Scales), it was found that 51.4 per cent of BMS subjects reported a positive diagnosis, predominantly depression. In a more recent study<sup>78</sup> investigating personality profiles, 32 BMS subjects were compared to 32 matched control subjects using a comprehensive, reliable and validated inventory. The results indicated there were many personality characteristics within the domains of neuroticism, extraversion, openness and conscientiousness differentiating BMS subjects from the control group. Maina *et al.*<sup>79</sup> found a high degree of personality disorders among the BMS subjects compared to both a non-psychiatric population sample and a population with other somatoform disorders. However, they stated their results could not determine whether or not the development of BMS precedes or follows the development of personality disorders. Bergdahl *et al.*<sup>80</sup> reported that when compared to a control group, the BMS subjects had a significantly lower score on the socialization scale and significantly higher scores on the somatic anxiety, muscular tension and psychoasthenia scales. Furthermore, the subjects with BMS were significantly more easily fatigued and more sensitive and showed a tendency to be more concerned about their health. Although it would seem plausible that BMS is no more than a somatic symptom of psychological disorders and/or related to a personality disorder, the association does not always equate to a causal relationship. In a study supporting this non-causal relationship, Carlson *et al.*<sup>81</sup> used standardized psychological assessment instruments (Revised Symptom Checklist and the Multidimensional Pain Inventory) on 33 BMS cases and compared the data to population samples which included both non-BMS chronic pain patients and a normal non-clinical sample. They concluded that there was no evidence for significant clinical elevations on any of the subscales, including depression, anxiety and somatization. Moreover, patients reported significantly fewer disruptions in normal activities as a result of their oral burning pain compared to a large sample of chronic pain patients. They did note that 21 per cent of the BMS cases had substantially elevated psychological distress. In another study<sup>82</sup> using similar methodology, BMS subjects were compared to subjects with oral burning sensations resulting from other clinical abnormalities. The authors found no differences between the groups with respect to age, pain duration, pain intensity, life interference and levels of psychological distress. A recent study<sup>83</sup> was designed to evaluate the psychological profile of BMS and non-BMS subjects in order to identify any psychological disease affecting these patients and to evaluate a possible psychological factor in the aetiopathogenesis of BMS. Twenty-eight BMS and 24 matched control subjects were evaluated for their personality profile using the Minnesota Multiphasic Personality Inventory-2. The authors concluded that there were no significant

differences in personality profiles between the BMS and the control subjects, suggesting the aetiology for BMS is different from the psychogenic hypothesis. These studies certainly cast doubt regarding the evidence of causality.

The findings of high levels of psychological disturbances involving depression, anxiety, somatization and personality disorders are not unusual or unique to BMS patients. These are common findings in the chronic pain population and may contribute to the cause, intensity or urgency of complaint or may be the result of the constant pain.<sup>84,85</sup> In a study by Grushka *et al.*,<sup>56</sup> BMS subjects did show elevations in the following personality characteristics: being more concerned with bodily function, depressed, emotionally repressed, angry, distrustful, anxious and socially isolated as compared to age and gender matched control subjects. However, these characteristics were similar to those seen in other chronic pain patients, and these personality disturbances tended to increase with increased pain. It appears personality characteristics among chronic pain patients, be it BMS or other pain conditions, share a certain commonality. Furthermore, many of the medications used to treat these psychological conditions and personality disorders can cause side effects such as dry mouth and taste alterations that may induce or exacerbate oral burning symptoms.

Therefore, the question remains whether psychological disturbances and personality disorders are aetiologically related to BMS or if chronic oral burning sensations initiate or exacerbate psychosocial disorders. Further large scale studies are necessary to enlighten us in this “chicken and egg” dilemma. Regardless, the presence of these co-morbidities certainly suggests treatment of these problems is necessary, although this does not constitute evidence of causality.

## CONCLUSIONS

The article has reviewed the conditions and diseases that may be responsible for oral burning in an attempt to clarify the differences between secondary BMS from primary BMS when a cause for the burning pain is illusive. Based on the available evidence, it is difficult to draw definitive conclusions for a pragmatic approach for differentiating primary and secondary BMS. Nonetheless, it is prudent for practitioners treating BMS to recognize possible local, systemic and psychological factors that may be responsible for oral burning and in turn manage the patient's symptoms appropriately.

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