Burning mouth syndrome (BMS) is currently defined as a condition in which burning pain in the tongue or other oral mucous membranes occurs in association with normal signs and normal laboratory findings. Although there is no clear understanding of pathogenesis of BMS, recent concepts are dramatically affecting the manner in which clinicians conceptualize this disorder and the way in which these patients are managed.

In BMS, pain intensity and other symptoms commonly develop gradually over time, although in some patients, onset is sudden and precipitous. The most common sites of burning are the anterior tongue, anterior hard palate, and lower lip, but the distribution of oral sites affected does not appear to affect the natural history of the disorder or the response to treatment. Burning mouth syndrome may persist for many years.

Although the majority of patients cannot identify an apparent cause of onset, approximately one-third of patients attribute the onset of their symptoms to a previous dental procedure, illness, or a course of antibiotics. Thus, for some patients the possibility exists of neurologic change as an etiologic factor by virtue of viral infection, mechanical damage, or neurotoxic effect of local anesthetics.

Nocturnal pain is not common for most patients with BMS, rather, the pain, usually of moderate to severe intensity, gradually increases throughout the day, reaching maximum intensity by late evening. As a result, it is not uncommon for patients with BMS to report having difficulty falling asleep at night and experiencing interrupted sleep. Reported mood changes, such as irritability and decreased desire to socialize, may be related to altered sleep patterns.

Personality characteristics including depression and anxiety are commonly reported in patients with BMS and may affect the pain report or be secondary to the chronic pain. The significance of the diurnal variation is unknown but may be related to postural changes in blood flow or to central nervous system (CNS) changes during sleep. There is some support for this concept in the literature, which has demonstrated decreased tongue temperature in BMS during the day; nighttime temperature has not been measured.

Most clinical studies suggest that oral burning is frequently accompanied by dry mouth and thirst (despite lack of evidence of decreased salivary flow in most patients); altered taste (dysgeusia); and additional pain complaints, including facial pain and pain at other sites. Taste and pain are both mediated by small-diameter fibers, whereas salivary stimulation is under the control of the parasympathetic and sympathetic nervous system. Interestingly, whereas both oral burning and altered taste are decreased by stimulation with food, rinsing with a local anesthetic elixir usually increases the oral burning pain but decreases the dysgeusia.

Although BMS may persist for many years following onset, partial remissions have been found to occur in approximately two-thirds of patients within 6 to 7 years after onset. No significant differences in age, gender, duration of disease, or distribution of burning sites have been found among individuals who experience partial or full remission compared with those whose burning continues. Recent studies, however, have suggested that responsiveness to treatment in BMS may be enhanced with shorter disease duration. It is not known what effect treatment has in the long-term on the disease process itself. Further, no studies have yet investigated whether earlier intervention or earlier and better pain control also lead to earlier disease remission.
**Suggested etiologies**

There is a widespread belief that BMS may be the result of specific systemic diseases or nutritional deficiencies, including B vitamins and iron. However, no consistent relation has been found to support this belief. Further, even when abnormal laboratory results are identified, management and correction of these findings usually do not lessen the oral burning and other associated complaints.

The current definition of BMS excludes patients with clinical mucosal conditions. However, a higher incidence of oral soft-tissue lesions, such as gingivitis, periodontitis, ulcerative or erosive lesions, or geographic, fissured, scalloped, or erythematous tongue has been reported in patients with BMS, and the possibility that these conditions may cause irreversible neuropathic changes has not yet been fully explored. Similarly, the possibility that conditions such as Sjögren syndrome, other connective tissue diseases, and diabetes may cause neuropathic changes that result in oral burning also requires consideration.

Burning pain, the main feature in BMS, is also a characteristic feature of some post-traumatic nerve injuries. In contrast to other post-traumatic nerve injuries, alterations in perception to touch, temperature, two-point discrimination, and threshold pain have been noted infrequently in BMS. On the other hand, abnormalities in taste and heat pain tolerance have been noted, and a recent report by Lauritano and colleagues has demonstrated subclinical polyneuropathy in 50% of patients with BMS, involving a loss of function in small-diameter nerve fibers. In this study, polyneuropathy was determined by means of quantitative sensory examination, tongue and face telethermography, and selected tongue biopsy. Qualitative and quantitative differences in some sensory functions of patients with BMS have also been noted, with argon laser stimulation. Other recent studies have identified loss of taste, especially to bitter, in the taste buds subserved by the chorda tympani nerve. Abnormalities in the blink reflex of patients with BMS, associated with disease duration, also suggest a possible generalized pathologic involvement of the nervous system, leading to modification in peripheral or CNS processing in BMS.

Although there is strong evidence from clinical studies to suggest that BMS is most prevalent in postmenopausal women in their mid- to late fifties, some recent epidemiologic data suggest a more equal male to female ratio. If menopause does appear to play a role in BMS, its mechanism remains unclear, since most reports suggest that oral burning is not usually reversible with hormone replacement therapy.

It is also notable that in BMS most studies have not demonstrated a significant decrease in salivary flow rate despite subjective complaints of mouth dryness and thirst. In contrast, significant alterations in salivary pH, buffering capacity, proteins, mucin, and immunoglobulins have been documented. Changes in salivary constituents rather than overall reduction in flow rate appear to be of significance in BMS and suggest involvement of sympathetic or parasympathetic function in BMS in addition to neuropathic injury. The mechanism whereby the autonomic nervous system is involved in BMS has also gone largely unexplored.

Although current evidence clearly indicates a strong psychological component within BMS, there still exists no evidence of a close causal relation between psychogenic factors and burning mouth. Personality characteristics, such as depression and anxiety, which are common to BMS, may be secondary to the pain in accord with the types of personality changes noted in other chronic pain conditions.

Most studies have also not supported chemical irritation or allergic reaction to dental materials as a significant cause of BMS; similarly, there has been little support for galvanic currents as a causative factor. However, mechanical irritation caused by dentures may be a factor in some patients, since errors in denture design and parafunctional habits with associated myofascial pain have been reported in BMS. Whether the parafunction is secondary to pain or is part of the disorder is unknown.

Interestingly, there have recently been case reports of oral burning secondary to the use of angiotensin-converting enzyme (ACE) inhibitors, such as captopril, enalapril, and lisinopril, which has remitted following discontinuation of the medication. Loss of taste sensation has also been reported to occur with use of ACE inhibitors, suggesting an additional link between pain and taste.

**Evolving concept of etiology**

Continuing research suggests that BMS may represent a peripheral or centrally mediated neuropathic condition with multiple etiologies. In view of the increase in oral burning after a topical anesthetic rinse, it has been suggested that oral burning may be a centrally based neuropathic condition that results in decreased peripheral inhibition of the trigeminal nerve. This is in accord with taste studies that have shown that loss of inhibition between the central projection areas of the chorda tympani and glossopharyngeal taste nerves following peripheral injury to either nerve can result in the production of phantom tastes. Preliminary spatial taste
testing in patients with BMS has provided further support for the possibility that for some patients, oral burning may result from the loss of inhibition of nociceptive trigeminal fibers secondary to injury to either the chorda tympani or the glossopharyngeal nerves.

Recent studies have demonstrated a relation between pain, taste, and alterations in the perception of oral dryness. For instance, there have been reports that taste loss, burning pain of the tongue and lips, tingling, and drooling can follow mild nerve injury after local anesthetic block (without extraction) to the inferior alveolar and lingual nerves. Similarly, paresthesias, pain, abnormal tastes, and drooling have been reported to follow damage to the inferior alveolar nerve and lingual nerve during mandibular third molar extraction. Moreover, although a male:female ratio of 30:70 in patients who have suffered injury to the trigeminal nerve during lower third molar extraction has been demonstrated, women and older patients tended to have the most severe complaints.

**Management**

For many years BMS has been managed with low-dose tricyclic antidepressants (TCA) based on earlier reports of their effectiveness as analgesics in alleviating oral burning in some patients with BMS. Many tricyclics have been used, including amitriptyline, desipramine, nortriptyline, imipramine, and clomipramine, although only amitriptyline has been evaluated in controlled clinical trials. In contrast, controlled trials of trazodone, a selective serotonin reuptake inhibitor (SSRI), have failed to document relief of BMS. There are no data that indicate that other SSRIs are effective in BMS.

Recently, several studies have suggested that various benzodiazepines, including clonazepam, a GABA (gamma-aminobutyric acid) receptor agonist, may be effective for various orofacial pain disorders, including BMS. Clonazepam is thought to have both peripheral and central effects and to bind more to central than to peripheral GABA receptor sites than other benzo-

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**Figure 34–1** Proposed workup for the diagnosis of burning mouth syndrome. GERD = gastroesophageal reflex disease.
diazeepines. Notably, the study by Grushka and colleagues showed that clonazepam was effective in relieving taste dysgeusias and oral dryness along with the oral burning.

Other medications and treatments recommended for the symptomatic relief of the burning pain include topical capsaicin; the monoamine oxidase inhibitor tranylcypromine sulphate in combination with diazepam, and the systemic anesthetic mexiletine, a use-dependent sodium channel blocker, all of which have been used for other neuropathic pain conditions. However, there are no controlled studies validating the effectiveness of any of these medications.

**Workup and hypothetic model**

A new approach to the diagnosis of BMS, based on the above review, is outlined in Figure 34–1. Based on the assumption that BMS is a neuropathic pain condition secondary to loss of inhibition of the trigeminal nociceptive fibers, this approach seeks objective evidence of oral dryness, taste disturbance, and effect of topical anesthetic. In contrast to earlier diagnostic paradigms, this diagnostic paradigm is one of inclusion and not exclusion. Hopefully, with this type of modeling, criteria for inclusion, much as for other diseases like Sjögren syndrome, will be developed.

Figure 34–2 presents a hypothetic model of the multifactorial nature of BMS. This includes burning pain as the result of increased excitatory output of the trigeminal nerve either from direct injury to the nerve, leading to increased output, or from decreased inhibition of the trigeminal nerve, leading to increased spontaneous output. Treatment depends on the mechanism of injury and helps direct investigation. This is thought to be the first easily testable model of BMS.

**Summary and conclusions**

It is currently believed that morphologic alterations in peripheral tissue attributable to injury or disease can cause biochemical and pathophysiologic changes in nociceptive neurons in the CNS. As a result of these changes, ongoing neuronal activity, referral of pain, and response of nociceptive-specific neurons to previously non-noxious stimuli can occur. These types of conditions may occur in BMS as a result of common systemic or local disorders in which nerve damage occurs to either the trigeminal nerve directly or other cranial nerves, which usually inhibit oral nociceptive activity. Hopefully, with further testing, further elucidation of the model will occur and universally accepted criteria for the diagnosis of BMS will be established.

**Figure 34–2** Hypothetic model for burning mouth syndrome.

**Suggested reading**


