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REVIEW ARTICLE

# Burning Mouth Syndrome

**C. Brufau-Redondo,[a] R. Martín-Brufau,[b] R. Corbalán-Velez,[c] and A. de Concepción-Salesa[d]**

[a]Servicio de Dermatología, Hospital General Universitario Reina Sofía, Murcia, Spain
[b]Departamento de Personalidad, Facultad de Psicología, Universidad de Murcia, Spain
[c]Servicio de Dermatología, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain
[d]Complejo Residencial Psicogeriátrico, Espinardo, Murcia, Spain

Abstract. Burning mouth syndrome is characterized by a painful burning or stinging sensation affecting the tongue or other areas of the mouth without obvious signs of an organic cause on physical examination. A burning mouth sensation can occur in several cutaneous or systemic diseases that must be ruled out prior to making a diagnosis of burning mouth syndrome, since this term is used exclusively to refer to idiopathic forms and is included within the cutaneous sensory disorders. In most cases, patients with burning mouth syndrome have accompanying psychological or psychiatric conditions. Consequently, the syndrome has traditionally been included among the psychogenic dermatoses. However, it is currently unclear whether psychological factors are a cause or a consequence of the syndrome, or whether each exacerbates the other. Recent studies propose the etiology to be neurologic, either neuropathic or related to taste.

Key words: burning mouth, orodynia, glossodynia, oral dysesthesia, xerostomia, dysgeusia.

## SÍNDROME DE LA BOCA URENTE

Resumen. El síndrome de la boca urente (SBU) se refiere a la sensación de dolor, ardor o escozor, localizado en la lengua o en otra zona de la cavidad oral, sin causa orgánica objetivable en el examen físico. La sensación de boca urente puede aparecer en algunas enfermedades cutáneas o sistémicas, que habrá que descartar antes de establecer el diagnóstico de SBU, ya que dicho término se refiere exclusivamente a las formas idiopáticas y se encuadra dentro de los trastornos sensitivos (o sensoriales) cutáneos.

En la mayoría de los casos los pacientes con boca urente presentan alteraciones psíquicas o psiquiátricas acompañantes. Por este motivo el SBU se ha incluido clásicamente entre las psicodermatosis. En el momento actual no está claro si los factores psíquicos son causa o consecuencia o simplemente se exacerban mutuamente. Estudios recientes proponen una etiología neurológica, ya sea de tipo neuropático o en relación con el sentido del gusto.

Palabras clave: boca urente, orodinia, glosodinia, disestesia oral, xerostomía, disgeusia.

## Introduction

Burning mouth syndrome (BMS) is characterized by a painful burning or stinging sensation affecting the tongue or other areas of the mouth in the absence of apparent signs of an organic cause on physical examination. Other synonymous terms are orodynia, glossodynia, glossopyrosis, stomatodynia, stomatopyrosis, and oral dysesthesia. Oral burning can also be a symptom of various cutaneous or systemic diseases and these diagnoses must be ruled out before a diagnosis of BMS can be confirmed, since this term is used exclusively to refer to the idiopathic forms (Table 1).

BMS is classified as a cutaneous sensory disorder, a term first used by Koo and Gambla[1] to denote situations in which the patient presenting with cutaneous sensory disturbances, such as burning, itching, or stinging, has no apparent lesions that would justify such symptoms. This group of disorders also includes vulvodynia, coccydynia (affecting the anus), burning feet, scalp dysesthesia or red scalp syndrome, and notalgia paresthetica. In some cases, oral and genital dysesthesias have been reported in the same patient.[2,3]

Nagler et al[4] consider BMS to be part of a broader entity, which they call oral sensorial complaints (OSC). This entity

Correspondence:
Carmen Brufau-Redondo
Servicio de Dermatología
Hospital General Universitario Reina Sofía
Intendente Jorge Palacios, 1
30003 Murcia, Spain
Cbrufau@terra.es

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**Table 1.** Diseases That Must be Ruled Out Before Reaching a Diagnosis of Burning Mouth Syndrome

| *Systemic Diseases* | *Skin Diseases* |
|---|---|
| Sjögren syndrome | Oral candidiasis |
| Diabetes | Lichen planus |
| *Helicobacter pylori* infection | Fissured or geographic tongue |
| Neuralgias | Radiation therapy |
| Deficiencies: Iron, folate, zinc, vitamins | Diseases not clinically apparent: Contact eczema, galvanism |

would include oral burning in addition to other idiopathic sensory complaints, such as taste distortion (dysgeusia) and dry mouth (xerostomia), although not all patients with OSC present all these symptoms. However, saliva analysis, sensory assessment, pain studies, and evaluation of personality traits yielded similar results in these 3 groups of patients, which differed from those of the respective control groups.

Most patients with BMS also have psychological or psychiatric disorders. As a result, the syndrome has traditionally been classified as a psychogenic dermatosis. However, it is currently unclear whether psychological factors are a cause or a consequence of the syndrome, or whether they both play a role and exacerbate each other.

Authors of recent studies have proposed a neurologic etiology, either neuropathic or related to taste.

## Epidemiology

### Prevalence

It is difficult to establish the real prevalence of BMS because of the lack of rigorous diagnostic criteria in many of the published case series. Many authors fail to distinguish between the symptom and the syndrome, reporting cases in which the oral disorders are the symptoms of a disease as idiopathic BMS cases. Consequently, published figures vary widely, from 0.7% to 15%. In the case series reported by Savage et al,[5] prevalence fell from 15% to 11% when cases with organic causes were excluded.

### Age

BMS is particularly common among postmenopausal women aged over 55. It also affects young adults older than 30 to 40 years. Various studies have shown that the prevalence of BMS increases with age in young adults but is independent of age in patients over 55. In a Swedish study in which 6103 pensioners completed a health questionnaire that included questions about somatic diseases, symptoms, habits, and behaviors, the prevalence of BMS was 2.4% among men and 8.5% among women ($P<.0001$).[6] Using logistic regression analysis those authors found prevalence to be independent of age, as did the authors of a Korean study of patients older than 55 years who presented with different types of orofacial pain.[7] Bergdahl and Bergdahl,[8] however, observed an age-related increase in the prevalence of BMS in a randomly selected sample aged between 20 and 69 years in the north of Sweden. Overall, they found a prevalence of 1.6% in men and 5.5% in women, but no cases were found in men younger than 40 or women younger than 30 years. When BMS develops in young women, the patients have often been sterilized while still fertile.[9]

### Sex

All of the studies reviewed reported that BMS is much more frequent among women, with the male-to-female ratio ranging between 1:7[10,11] and 1:13.[12]

## Etiology and Pathogenesis

The etiology and pathogenesis of BMS are poorly understood and probably multifactorial. We will now discuss a number of factors that have been studied in recent years and may play a role in the development of this syndrome.

### Xerostomia

Under normal conditions, salivary flow decreases with age. This has been demonstrated in a study of healthy individuals aged between 18 and 89 years that confirmed both a significant reduction in the flow of saliva and changes in salivary composition in older patients.[4] Given the age of onset of BMS, a certain degree of xerostomia would be expected in this population. However, some patients with BMS have a subjective sensation of dry mouth that does not always correspond to any actual reduction in the volume and flow of saliva.[9,13] Most of the studies carried out show that, despite the sensation of dry mouth they reported, salivary flow in these patients was normal when compared to that of the controls.[12-15] However, salivary composition does appear to be altered in these patients.[16] Studies of patients with BMS, xerostomia, and/or dysgeusia have found similar alterations in salivary composition and significant differences with respect to controls in all 3 groups.[12,13,15] The saliva of the affected patients was found

to have higher levels of sodium, lysozyme, total proteins, immunoglobulin (Ig) A, IgG, IgM, and albumin, especially the last 3. These alterations were not associated with any significant decrease in salivary flow, even in the group of patients who only reported xerostomia. However, they were associated with taste disturbances found in the affected patients as compared to the controls. Nagler et al[13] suggested that these findings indicate a salivary-related local neuropathic mechanism.

The frequency of BMS increases in parallel with the number of nocturnal micturition episodes ($P<.0001$) in women and is higher among patients with nocturnal thirst who are in the habit of drinking at night.[6] This relationship is highly significant and independent of other factors, such as age, sex, and the use of analgesics and diuretics. In addition to the direct association between nocturia and major depression—a condition that may also play a role in the pathogenesis of BMS—it appears that diuresis increases in patients with nocturia, particularly in terms of the proportion of urine excreted at night.[6] In some cases, nocturnal urine output can account for as much as 85% of the total volume of urine excreted over a 24 hour period. This increase is probably caused by an abnormality in the vasopressin system and gives rise to a negative fluid balance, a condition that favors xerostomia and xerophthalmia.[6] Likewise, the use of diuretics is also associated with an increase in dryness of the oral mucosa and with the incidence of BMS in both sexes. Oral dryness also occurs in patients with poorly controlled diabetes because their condition gives rise to increased diuresis and consequently nocturia.

The effect of medications on BMS is very significant.[4] Soares et al[15] found BMS to be significantly associated with xerostomia and the consumption of hypotensives and diuretics.[6] They also reported significant differences between patients with BMS and controls in the number of medicines and xerostomizing agents taken per day, subjective xerostomia, and levels of anxiety and depression (which were higher in the patients with BMS). A number of other drugs have been suggested as possible causes of xerostomia. These include anxiolytics such as clonazepam,[17] angiotensin-converting enzyme inhibitors,[16,18] and a series of other medications, including aspirin, codeine, and vitamins.

It has been suggested that BMS may be caused by allergic contact dermatitis, particularly in patients who report intermittent symptoms throughout the day. Allergic reactions have, in fact, been confirmed by positive patch test results in some patients with BMS who had no apparent mucosal lesions; in these cases the problem resolved once contact with the allergen was eliminated.[19] It is debatable whether these patients with oral burning symptoms and clinically relevant positive patch test results should be considered as cases of BMS or as cases of subclinical contact dermatitis. In any case, these findings are useful in the diagnosis and treatment of the subgroup of patients with intermittent symptoms.

Some authors have suggested that BMS may be related to zinc deficiency.[10,20]

## Infections

Adler et al[21] studied 124 patients with different gastric diseases; 46 had burning sensations with halitosis and tongue hyperplasia, and 78 had other diseases unrelated to BMS. Using biopsy and molecular biology, the authors detected *Helicobacter pylori* in the oral mucosa of 86% of patients who complained of a burning tongue sensation, halitosis, and tongue hyperplasia. By contrast, this microorganism was only isolated in 2.6% of the patients who did not report oral symptoms. A higher prevalence of BMS has not been found in association with other infections, such as candidiasis, although infection with *Candida* species may produce a burning pain.[16]

## Neurologic Abnormalities

A growing body of evidence supports the hypothesis that BMS is caused by an underlying neurologic disorder (a regional neuropathy). In a study of 35 patients with OSC and 19 healthy controls, Granot and Nagler[14] analyzed oral sensory perception, salivary flow and composition, and the patients' personality traits. The findings were similar in all the patients with OSC, irrespective of the symptoms reported (BMS, dysgeusia, or xerostomia) and were suggestive of a regional neuropathy.

The different abnormal responses detected in patients with BMS who undergo quantitative sensory tests also suggest a neuropathic etiology.[22] Moreover, the presence of taste disturbances and the fact that many patients with BMS are "supertasters" (individuals with a greater than normal capacity for perceiving tastes) would suggest an interaction between the gustatory and nociceptive mechanisms connecting the sensations of taste and oral pain in the central nervous system and would indicate that BMS involves central and peripheral nervous system disorders caused by alterations in the gustatory system at the level of the tympanic chord and/or the glossopharyngeal nerve. This would give rise to a loss of central inhibition leading to hyperactivity of the trigeminal pain pathway, which in turn would result in a more intense response to oral irritants and eventually to the development of phantom oral pains caused by this abnormality of the gustatory system.[16,23]

The following are some of the results of sensory tests carried out in different studies:

1. A decrease in thermal sensation taking the form of elevated hot and cold sensory thresholds and low scores for tonic pain stimuli in the oral cavity. These results are

similar to those found in areas of skin affected by polyneuropathies and mononeuropathies.[14]
2. Reduced heat pain tolerance at the tip of the tongue in 85% of patients with BMS, a finding that points to changes in peripheral sensory functions.[26,27]
3. Abnormalities in the blink reflex of patients with BMS (which may represent subclinical trigeminal neuropathy) and abnormalities in the sensory threshold indicative of thin fiber dysfunction.[28]
4. Altered salivary composition with respect to controls, a phenomenon that directly influences the patients' perception of tastes.[14]
5. A discrepancy between the sensation of oral dryness and the presence of a normal amount of saliva.[12,14,15]

These findings could be attributed to a regional small-fiber idiopathic neuropathy affecting salivary secretion and oral sensation in patients with OSC.[14]

Using immunohistochemical and confocal microscopy studies on tongue biopsies, Lauria et al[29] demonstrated that patients with BMS had a lower density of epithelial and subpapillary nerve fibers than healthy controls. These changes, which reflect axonal degeneration, led the authors to conclude that BMS is caused by a trigeminal small-fiber sensory neuropathy.

Central neuropathic mechanisms were also demonstrated when functional magnetic resonance imaging was used to map areas of brain activation after thermal stimulation of the trigeminal nerve in 8 patients with BMS and 8 controls.[30] The patients with BMS showed brain activation patterns similar to those found in patients with other painful neuropathic conditions, and appeared to process painful thermal stimulation of the trigeminal nerve in a qualitatively and quantitatively different way than normal individuals. These findings suggest that brain hypoactivity may be an important factor in the pathogenesis of BMS.

The fact that ciguatera poisoning, which involves ingestion of a neurotoxin, produces symptoms very similar to those of oral burning[31] supports the hypothesis that the etiology of BMS is neuropathic.

### Psychological Factors

Although the relationship is still a matter of debate,[32] an anxious personality is a common trait found in patients with BMS,[5] and some authors have even found a significant correlation between BMS and personality disorders.[33,34] BMS is very often associated with depression and anxiety, with estimates of up to 62% of patients. Soares et al[15] found significant differences between a group of 40 patients with BMS and 40 controls with respect to the presence of anxiety and depression. In many cases, the depression is subclinical and the patient is not aware of his or her condition.[35] Romaní de Gabriel and Chesa[35] interpreted this phenomenon as a process of somatization following a very stressful life event that leaves the patient more vulnerable than before, and in many cases a triggering psychological factor is identified.[36,37] In fact, Granot and Nagler[32] found an increased level of somatization in these patients. Common examples of these life events in our setting include the death of a close relative, family conflicts related to children, the departure of children from the family home, and a diagnosis of cancer; there can be a considerable time lag between the triggering event and onset of the condition.[35,37]

However, it is not clear whether the personality disorders observed in these patients are a cause or a consequence of BMS.[11,38] In many cases anxiety and/or depression are not present when the oral symptoms first appear, but develop later, and patients often assert that they are depressed and/or anxious because of the unbearable nature of their disease; this is also typical of many other chronic or long term diseases and it is difficult to establish the cause and effect relationship.[39] Danhauer et al[40] studied the psychological characteristics of 69 subjects with either BMS or oral burning secondary to other diseases and found no psychological abnormalities in either group of patients. However, other studies in the literature suggest that psychopathologic factors may play an important role in BMS and some authors have advanced the hypothesis of a multifactorial etiology in which physical changes interact with psychological factors, such as personality, humour, anxiety, and tension.[41]

Cancer phobia is present in 20% to 30% of patients with BMS. According to Lamey et al[37] subjects with BMS are 2.7 times more likely to be cancer phobic than controls.

### Other Factors

Some studies suggest that BMS may be associated with low serum zinc levels.[20] Because of the high frequency of BMS among postmenopausal women, it has also been suggested that endocrine factors may play a role in the onset of this disorder. Nevertheless, hormone replacement therapy has not been shown to be an effective treatment.[16] Femiano et al[11] found abnormal perception of tastes associated with thyroid dysfunction (hypothyroidism and antithyroid antibodies) in patients with BMS.

## Clinical Presentation

The clinical manifestations of BMS are not constant in either onset or intensity, but are rather many, diverse, and variable. They are symptoms rather than signs, that is, the clinical presentation is subjective. Patients often report symptoms which only they perceive. The patient's personality influences the description of their symptoms, which are

reported with very personal nuances. What is clear, however, is that the symptoms are persistent and unbearable in all of these patients.

In our experience, when patients are asked to describe the characteristics of their symptoms, they generally find the task difficult. In many cases it is hard for them to define the sensations they perceive, although they emphasize the intensity of the discomfort and spend a great deal of time complaining about the repercussions of the symptoms on their lives. In many cases, the problem of oral burning occupies center stage in the patient's life. Diagnosis of the disorder generally takes a long time (mean delay of 34 months[42]), and perhaps for this reason these patients are high consumers of health care resources. Riley et al[43] found a mean of 8 consultations related to this symptom in the preceding 12 months in 50% of patients with BMS, while the mean in a study by Mignona et al was 3.[42]

Some of the symptoms are universal, that is, they occur in all or the great majority of these patients (a sensation of pain or burning, dry mouth, and the sensation of having a foreign body in the oral cavity). Other symptoms are variable:

1. The pain or burning sensation generally affects the anterior two thirds of the tongue, particularly the sides and the tip, but can also affect the oral mucosa of the lips and cheek, and the hard palate. Onset is spontaneous and there is no precipitating factor in more than 50% of these patients. One third of patients relate the onset of symptoms to a dental procedure, recent illness, medication, or a stressful personal or family event.[5] Once it starts, the pain persists for many years.[16] Most patients with BMS experience a subjective sensation of dry mouth that does not always correspond to an actual reduction in the volume and flow of saliva.[5,9]
2. The sensation of having a foreign body inside the mouth, described by patients as a sensation of having sand, hairs, paste, or threads, among other things, in the mouth, or as a sensation of roughness.
3. Dysgeusia that increases or diminishes when food is ingested. This is a very common symptom. Some patients experience an alteration in their perception of the intensity of normal food flavors, while in others this symptom takes the form of a strange persistent flavor in the mouth, often salty, bitter, metallic, or sour. Dysgeusia is usually accompanied by a sensation of dry mouth (as demonstrated by Nagler and Hershkovich[13]) and may be associated with hypothyroidism.[11] Often a predominant complaint in the beginning, dysgeusia is one of the first symptoms to improve once treatment is started, and this early response can be used on the subsequent visit to indicate that progress is being made and to encourage the patient to adopt a more positive attitude.[5]
4. Comorbid dental problems that patients relate, often obsessively, to the onset of oral pain or discomfort although no cause and effect relationship can be demonstrated even when the patient relates the onset of symptoms to a specific dental or prosthetic procedure.
5. Parafunctional behavior taking the form of a variety of parafunctional habits repeated constantly by the patient (fixed movements of the tongue, which is pressed against the teeth, bruxism, etc). While this behavior could be interpreted as a sign of anxiety,[38] for many patients these habits are a cause rather than a consequence of anxiety. Patients sometimes complain of headaches and pain on palpation of the masticatory muscles in the morning.
6. The psychological symptoms, such as anxiety and depression, mentioned earlier in the section on pathogenesis are also included as symptoms since they appear in many patients after the syndrome has been established and are apparently caused by the stress of living with oral discomfort and pain. One finding that does appear to have been demonstrated is that the use of anxiolytics is significantly higher among patients with BMS than controls.[18]
7. Halitosis is a highly subjective symptom that should be verified by talking to family members. This socially debilitating condition may play some role in the onset and persistence of BMS.[5]
8. Cancer phobia is also common among patients with BMS (some 20% of patients), and patients in this group attribute their problems to the presence of a malignant process.

Brailo et al,[18] who studied 150 patients with BMS, found a significantly greater proportion of patients with gastritis compared to a control group.

The symptoms reported do not generally interfere with sleep, but they do worsen progressively throughout the course of the day.[16] Three different types of BMS patients have been identified on the basis of the evolution of symptoms throughout the day[5]: *a)* Type 1: progressive pain. These patients are symptom free on waking but pain increases progressively throughout the day (35%). Associated psychological factors are not usually found in these patients. *b)* Type 2: symptoms are continuous throughout the day and the patients have difficulty going to sleep (55%). These patients generally present psychological disorders. *c)* Type 3: intermittent symptoms affecting unusual sites and involving atypical pain (10%). It appears that contact dermatitis secondary to oral allergens may be a significant etiologic factor in this group of patients.[19]

## Course

In general, only slight improvement is noted in response to the different forms of treatment. In a retrospective study of 53 patients carried out by Sardella et al,[44] only 28.3%

reported moderate improvement after treatment, while 49% reported no change, and symptoms worsened in 18.9%. Complete remission of symptoms without treatment has been observed in only very few cases (3.7%).[44] Despite the fact that Grushka et al[16] reported an improvement in symptoms in two thirds of patients after 6 to 7 years, spontaneous remission of symptoms has not as yet been clearly demonstrated.[45]

## Diagnosis

The following steps are required in the diagnosis of BMS:

1. Rule out systemic diseases and conditions that present symptoms similar to those of BMS, such as Sjögren syndrome, diabetes, candidiasis, and iron, folate, zinc, or vitamin B deficiencies (Table 1). It is important to differentiate between BMS and oral burning secondary to other diseases because the therapeutic options are different in the 2 groups and it has been shown that the efficacy of treatment depends on a correct initial diagnosis.[40]
2. Rule out skin diseases, both those that are visible and those that are not so immediately obvious, such as galvanism and contact eczema. Patch tests should be used, especially in patients with intermittent symptoms (test for allergy to chrome or other substances used in dental prosthesis, and to food additives, preservatives, and fragrances) (Table 1).[19]

All the elements discussed in the following sections should also be included in the diagnostic procedure for BMS (Table 2).

**Table 2.** Diagnosis of Burning Mouth Syndrome

| |
|---|
| Detailed medical, dental, and psychological history |
| Medication |
| Examination of mucosa |
| Odontological examination |
| Patch tests for metals, prothesis, and food products (additives, preservatives, fragrances) |
| Bacteriologic and mycologic culture |
| Tongue biopsy, hematoxylin-eosin, immunohistochemistry |
| Laboratory tests: complete blood count, blood sugar, iron, folates, vitamin B, zinc, serology for Sjögren syndrome |
| Gastroenterologic examination. *Helicobacter pylori* test |
| Psychiatric/psychological assessment. |

### Detailed Medical History

It is essential to obtain a complete medical, dental, and psychological history, to quantify the sensation of pain on a linear scale from 0 to 10, and to record the characteristics, duration, and timing of symptoms as well as the relationship between insertion of any prosthesis and onset of symptoms. Particular attention must be paid to the possible intake of any drugs that might produce xerostomia (anxiolytics and angiotensin-converting enzyme inhibitors, as well as others, such as aspirin, codeine, and vitamins), and the presence of parafunctional habits. The physician should also endeavor to uncover any underlying mood problems.[9] Romaní and Chesa[35] advise dermatologists to use a basic psychiatric questionnaire designed to reveal depressive disorders: Are you sleeping well? Do you get up in the morning with enthusiasm for starting the day? Have you ever felt so sad that you wanted to cry?

### Examination of the Oral Mucosa

The oral mucosa should be examined carefully to rule out the presence of skin lesions, such as erythema, erosions, depapillation, or any changes characteristic of lichen planus, fissured tongue, geographic tongue, etc. The presence of any of these signs would invalidate the diagnosis of BMS. It should be remembered that autoimmune blistering diseases often begin with disorders that affect the oral mucosa. According to Romaní and Chesa,[35] the presence of a smooth and glossy area in the anterior part of the tongue is indicative of a constant habit of friction and scraping with the teeth. It is important to check for xerostomia as well as crenations or notches on the sides of the tongue.

### Odontological Examination

An odontological examination should be carried out to ascertain whether the patient has any dental problems. This should include revision of any prothesis, occlusion of prosthesis, the likelihood of oral galvanism, and the volume of salivary flow.

### Laboratory Tests

The workup should include a complete blood count, blood sugar, iron, serum ferritin, folates, vitamin B12, zinc, and serology for Sjögren syndrome and *H pylori* infection.[18]

A culture for *Candida* species must also be ordered. The sample should be taken from the oral mucosa or the palate rather than the dorsum of the tongue, since the results from that area can be deceptive. Since dental protheses can be a

reservoir of *Candida* species, a culture of prosthetic devices is also useful.

### Patch Tests

Patch tests should be performed in selected patients, particularly those who present intermittent symptoms (testing allergy to metals and other possible allergens used in dental protheses, as well as food products, additives, preservatives, and fragrances).[19]

### Additional Studies

A biopsy of the tip of the tongue may be useful as it will identify abnormalities in the epithelial and subpapillary nerve fibers, such as a significant decrease in the density of epithelial nerve fibers.[45] The techniques that can be used are immunohistochemistry and confocal microscopy. [29] Some authors consider biopsy to be unnecessary if the results of the physical examination are sufficiently clear.

It is also important to order a gastroenterological examination to rule out the possibility of gastritis.[18]

Granot and Nagler[32] recommend studying the patient's salivary profile and investigating the presence of sensory and taste disturbances with a view to treating these symptoms.

### Psychiatric Assessment

A psychiatric or psychological assessment should be carried out, particularly when the patient reports a significantly high intake of anxiolytics.[18] Anxiety or depression are observed in 62% of patients with BMS.

## Differential Diagnosis

Occasionally, when the tongue has to work excessively to maintain mandibular stability, for example in patients with malocclusions, no teeth, or a dysfunctional temporomandibular joint, muscle fatigue produces a very specific pain that must be differentiated from BMS.[46]

Glossodynia limited to one side of the mouth may be caused by brain tumors or metastasis, as well as by nerve irritation in the glossopharyngeal or hypoglossal regions.[46]

## Treatment

Treatment is symptomatic. The remedies used to treat other painful neuropathic abnormalities are also useful in BMS (Table 3).[16]

It is crucial that the patient understands and accepts the diagnosis and has a realistic understanding of the likelihood of being cured. For this reason, the relationship that physicians establish with patients who have BMS is of the utmost importance. Patients may be somewhat distrustful or even suspicious because they have usually already consulted a number of physicians and have undergone various treatments with frustrating outcomes; they often feel misunderstood. Moreover, as dermatologists we may find patients with BMS trying or we may even fear them because we are frustrated by the fact that we can do so little to improve their condition. At the outset, therefore, the conditions for establishing a good doctor-patient relationship are unfavorable on both sides, but this relationship is, nonetheless, so critical that the subjective improvement of the patient's condition depends upon it to a large degree. However, these patients feel relieved from the moment a physician takes their complaint seriously and starts to record their medical history.

It is important to dedicate sufficient time to the patient at some point early in the treatment and to schedule regular follow-up visits so that he or she will feel well cared for; individuals with BMS need empathy and sympathy. After listening to patients and carrying out a comprehensive physical examination, it is important to inform them that they do not have cancer, if they are concerned about this possibility. This assurance will help the patient to tolerate the glossodynia and the condition may stop being an obsession and become merely a source of discomfort. The patient should also be informed about the idiopathic nature

**Table 3.** Treatment of Burning Mouth Syndrome

| |
|---|
| **Symptomatic** |
| Spend time, empathy |
| Inform the patient. Address cancer phobia |
| **Topical treatment** |
| Capsaicin, Tabasco sauce |
| Sialagogues |
| **Systemic treatment** |
| Low doses of tricyclic antidepressants |
| Selective serotonin reuptake inhibitors |
| Dual-action antidepressants |
| Antipsychotics |
| Benzodiazepines |
| Gabapentin 300-1600 mg/d (start with 100 mg) |
| Alpha-lipoic acid 600 mg/d |
| **Cognitive-behavioral therapy** |

of BMS, the lack of any known organic cause, and the difficulties of treatment, but with an emphasis on the benign nature of the condition and the fact that it is in no way related to cancer.

## Topical Treatment

Topical capsaicin has been used as a desensitizing agent in BMS and other disorders characterized by pain and pruritus, but the treatment is not well tolerated by some patients because of its flavour.[16] The mechanism involved is based on the inhibition of substance P. A mouth rinse made of Tabasco sauce mixed with water can be useful in these patients,[38] or alternatively one made of hot pepper and water in a dilution of between 1:2 and 1:1.[16]

Treatment with systemic capsaicin is currently being investigated. Petruzzi et al[47] confirmed the efficacy of systemic oral capsaicin 0.25%, but reported a high level of gastric toxicity.

Sialagogues are useful when the patient has dry mouth.

Another topical treatment used in the form of a mouthwash is benzydamine hydrochloride 0.15% applied 3 times a day, but the efficacy of this regimen has not been shown to be significant.[48]

## Systemic Treatment

### *Tricyclic Antidepressants*

Low doses of amitriptyline and nortriptyline owe their usefulness in BMS more to the antinociceptive properties of the tricyclics than to their antidepressant effect, and consequently antidepressant doses are not necessary.[2] Amitriptyline at a dose of 25 to 50 mg/d raises the threshold of sensitivity. The starting dose should be 5 to 10 mg/d at bedtime, and this should be increased by 5 or 10 mg each week until symptoms disappear or side effects occur. After 8 weeks, the dose will have reached 40 mg/d, a regimen that usually provides good results. In some cases, a dose as high as 150 mg/d may be necessary.[16] Some authors contraindicate this drug in patients with dry mouth because it could aggravate that condition.[38]

Nortriptyline proved useful in a case of stomatodynia associated with penodynia/scrotodynia in which other antidepressants (venlafaxine) had proven ineffective, probably because of the greater efficacy of the tricyclics in controlling neuropathic pain.[2]

### *Serotonin Reuptake Inhibitors*

Serotonin reuptake inhibitors have proved useful in some cases of BMS,[38,41] but not in others.[2,16] However, it seems clear that these drugs are of some use, particularly in patients with depression, and they are better tolerated than certain other antidepressants because they have no anticholinergic effects, in particular dry mouth.[41]

### *Dual-Action Antidepressants*

Among the dual-action antidepressants—drugs that inhibit both serotonin and noradrenaline—duloxetine is particularly useful at a dose of 30 to 60 mg/d.

### *Antipsychotics*

Risperidone is very effective at a dose of 0.5 mg a day (C. Koblenzer, personal communication).

### *Benzodiazepines*

Benzodiazepines are useful, particularly in patients with anxiety disorders. They are effective at low doses, especially in young people. Alprazolam at 0.25 to 2 mg/d is useful. Treatment should be started at 0.25 mg and be increased by 0.25 mg every week until the maximum dose is reached. However, this drug is highly addictive because of its short half-life, and this makes benzodiazepines, which have a longer half-life, preferable. Treatment with low doses of clonazepam have yielded good results in the treatment of BMS pain, probably because it disrupts the underlying neuropathologic mechanism rather than because of any anxiolytic effect.[13] Gruska et al[16] recommend starting clonazepam at a dose of 0.25 mg/d at bedtime, and increasing the dose by 0.25 mg every 4 to 7 days in 1 full dose or 3 divided doses until symptoms disappear or side effects occur. In a few cases, benzodiazepines have been associated with the onset of BMS.[17]

### *Gabapentin*

The dosage of gabapentin should be established either in combination with benzodiazepines or alone and should range from 300 to 1600 mg/d. Treatment should be started with a dose of 100 mg/d at bedtime and this should be increased by 100 mg/d every week. As dosage increases the medication should be taken in 3 divided doses. The efficacy of this regimen may not be apparent until after at least 1 month of treatment.

### *Hormone Replacement Therapy*

Authors who have studied the use of hormone replacement therapy in the treatment of BMS report an improvement in symptoms, especially with tibolone after 3 months of treatment.[49]

### Alpha Lipoic Acid

Alpha lipoic acid is a powerful neuroprotective agent that limits free radical damage to nerve cells, regenerates other antioxidants, such as vitamins C and E, increases levels of intracellular glutathione, and stimulates the production of nerve growth factors.[50] It also protects membranes by interacting with vitamin C and glutathione, which in turn recycles the vitamin.[51] Thanks to its antioxidant activity, alpha lipoic acid significantly reduces symptoms in most patients with idiopathic dysgeusia[32] and reduces symptoms of peripheral neuropathy in patients with diabetes.[49,51] Femiano et al[23] also reported a significant improvement in BMS symptoms after 2 months of treatment with alpha lipoic acid 600 mg/d in a controlled double-blind study of 60 patients. The improvement was maintained at 1 year in 70% of the patients, a result that supports the hypothesis of a neuropathic etiology for BMS. In another study, the authors found that the improvement occurred particularly in patients not previously treated with tranquilizers, who had a better response than patients previously treated with psychotropic drugs. This finding suggests that the origin of the oral symptoms of BMS may be different in these 2 groups of patients.[50] Patients taking alpha lipoic acid must be prescribed concurrent gastric protection medication.[38,49]

### Psychological Treatment

Cognitive-behavioral therapy appears to reduce the intensity of symptoms after a period of 6 months.[49,52]

It is difficult to evaluate the efficacy of the different therapies used because the studies in the literature are not sufficiently uniform in terms of patient selection criteria. Some of these studies enrolled only patients with idiopathic disease (BMS) but others are not comparable because the authors also included patients with similar oral symptoms secondary to systemic causes.[48]

The complex and multifactorial etiology of BMS makes collaboration between various different types of specialists crucial in the management of these patients.[10]

## Conclusions

BMS continues to pose a challenge for those involved in the care of these patients—dermatologists, dentists, and ear, nose, and throat specialists being the physicians most often consulted in these cases (apart from general practitioners). New findings that have emerged during the last few years shed light on the etiology and pathogenesis of BMS and point to a probably neuropathic origin. However, additional studies with strict diagnostic criteria are necessary to allow us to draw reliable conclusions about the etiology and pathogenesis of this syndrome, the real role played by psychological factors, and appropriate treatment (about which very little data is currently available), all of which will help us become more useful to our patients.

**Conflicts of Interest**
The authors declare no conflicts of interest.

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