Imagine the frustration of having a continuous painful disorder that cannot be definitively diagnosed with any known test or X-ray, interferes with eating, becomes progressively worse with time, has no known cause, and for which there is no highly effective treatment. This is what patients with burning mouth syndrome deal with every day of their lives. BMS typically has a spontaneous onset, although its intensity will increase gradually over time. It is characterized by both positive (burning pain, dysgeusia and dysesthesia) and negative (loss of taste and paraesthesia) sensory symptoms. The primary location for these symptoms are the lips and tongue, mainly the tip and anterior two-thirds. BMS patients complain also of sensory discomfort in the hard palate and alveolar ridges. Conversely, the buccal mucosa and the floor of the mouth are almost never involved. At least for the tongue, the anatomic distribution of the burning pain in BMS patients corresponds to a great degree where taste bud density
is greatest in the mouth. For example, Miller examined taste bud density on the tongue and found that taste bud density was 4.6 times higher on the tip than the mid-tongue region. However, since taste buds are not commonly located on the inner lip mucosa, anterior hard palate or alveolar ridges, this association between taste buds and BMS is not absolute. Nevertheless, most BMS patients report a persistently diminished taste or altered (metallic) taste sensations. Acidic foods such as tomatoes and orange juice cause considerable distress with an increase in burning sensations. These descriptions vary but often include a stinging-burning sensation as if they have scalded the mucosa. Finally, in spite of the vividly described irritated or raw feeling in their oral tissues, most of the time, the tissues appear normal to visual inspection. Most of the common laboratory tests suggested for BMS patients (described later) will be negative as well.

BMS has various synonyms such as stomatopyrosis, glossopyrosis, stomatodynia, glossodynia, sore mouth, sore tongue, and oral dysesthesia. These terms are used to emphasize the quality and/or the location of pain in the oral cavity. The International Association for the Study of Pain has identified BMS as a distinctive named entity characterized by oral burning pain episodes lasting at least four to six months. The International Classification of Disease (version 9) has assigned the term glossodynia, which included the subterms glossopyrosis and painful tongue a specific identity code number (ICD-9 #529.6).

A recent paper suggested that a subpopulation of BMS cases presents with a common triad of symptoms including idiopathic sensorial disturbances of burning mouth, taste disturbance (dysgeusia), and dry mouth. Another paper suggested three subgroups with type 1 being characterized by burning pain increasing throughout the day and reaching its peak in the evening. Type 2 was characterized by complaints of continuous sensory disturbances, and type 3 had intermittent symptoms with free-pain periods during the day. The most pragmatic method of grouping BMS is by dividing patients into the primary BMS sufferers (no other evident disease) and secondary BMS sufferers (defined as oral burning from other clinical abnormalities). In fact, using this classification scheme, one paper examined 69 BMS patients (83 percent) and asked them to fill out both the Multidimensional Pain Inventory and Symptom Checklist 90-Revised. They found that the primary BMS patients and the secondary BMS patients showed no differences with respect to age, pain duration, pain intensity, or levels of psychologic distress. The only substantial difference was that if the associated clinical abnormality was treatable, then the burning sensations would improve in the secondary BMS group, whereas the primary BMS group did not demonstrate remarkable symptom cessation with treatment.

Epidemiology

Burning mouth symptoms are reported in up to 4 percent of adults, and this percentage increases with age being more prevalent in the fifth to seventh decade. One study surveyed 669 men and 758 women randomly selected from 48,500 individuals between the ages of 20 and 69, and reported 53 individuals (3.7 percent) exhibited BMS (11 men or 1.6 percent and 42 women or 5.5 percent). The presence of BMS is very uncommon before the age of 30; 40 years for men. The onset in women usually occurs within three to 12 years after menopause and is higher in women who have more systemic disease.

Another epidemiologic study surveyed U.S. adults and estimated the overall prevalence of burning mouth to be 0.7 percent of the adults up to age 65. This study was repeated on a subset of more than 5,800 individuals aged 65 or older in southern Florida. They reported a prevalence of 1.7 percent for burning mouth pain in this elderly group. Clearly the differences in these prevalence figures are related to sampling bias in surveyed populations and disease definition being used.

Quantitative Sensory Testing in BMS

The frequent occurrence of numbness, pain and dysesthesia in BMS has prompted researchers to perform a quantitative assessment of the sensory and chemosensory functions in these patients. Until recently, researchers have not consistently found a statistically significant alteration in the sensory perception (touch and temperature) of BMS patients. For example, one study carefully examined 20 BMS patients versus 20 controls for different abilities to perceive different shapes of objects with
their tongue. No systematic disparity was evident in the two groups regarding object size perception ability. Of course, detecting the shape of objects with one’s tongue is not the only test of sensory acuity. Several years ago researchers used argon laser stimulation to examine 23 BMS subjects versus 23 age-matched controls for differences in their sensory and pain thresholds. This study used brief laser stimulation to six test sites (tongue tip, lower lip mucosa and skin, buccal mucosa, anterior hard palate, and dorsum of the hand). They reported the sensory thresholds were significantly higher and the ratios between pain and sensory thresholds significantly lower in patients with BMS at all tested sites. The resulting widespread sensory threshold differences seen in this study argues for a centrally mediated sensory amplification abnormality. Another study used an objective electrophysiological examination of the trigeminal-facial nerve system using the blink reflex response in 11 BMS subjects and 10 controls. They reported BMS patients have clear-cut alterations in their blink response to applied stimulation. Finally, a study examined evoked brainwave potentials following lingual nerve stimulation in 22 BMS patients with pain, 10 BMS patients with reported numbness, and six controls. They found that pain thresholds were significantly lower and evoked potential response latencies were significantly different (i.e., shorter) in the BMS with pain group. The latencies in the BMS with numbness group were significantly longer. Overall, these sensory data suggest that peripheral and/or central nervous system changes are clearly present in BMS but they do not pinpoint where in the somatosensory system changes are to be found.

### Biopsy Evidence of BMS changes

Until recently, the primary site of pathology in BMS was not identified; therefore, no diagnostic test was available for this disorder. However, a new study investigated the innervation of the epithelium of the tongue in 12 chronic BMS cases and nine healthy controls using tongue tissue biopsies to assess whether damage of peripheral nerve fibers underlies the pathogenesis of the disease. These researchers used immunohistochemical and microscopic methods to examine for nerve damage in the tongue. They reported a significantly lower density of epithelial nerve fibers for BMS patients than controls. The authors described epithelial and subpapillary nerve fibers changes suggestive of axonal degeneration. They concluded that BMS is caused by a trigeminal small-fiber sensory neuropathy.

### Taste Changes and BMS

Dysgeusia is a term used to describe a distorted gustatory perception or persistent gustatory sensation in the absence of gustatory stimulants. As mentioned earlier, BMS patients frequently report a positive taste sensation, which they describe as a persistently altered (metallic) taste. They also have a diminished ability to detect bitter flavors, and spicy and acidic foods increase their burning sensations. One recent study examined 50 patients with BMS (study group) and 50 healthy subjects (control group), and analyzed their ability to taste three flavors: bitter, acid, and spicy substances. They found that taste sensation was normal in all controls, but in 30 of the BMS patients, they had a diminished response to bitter taste. The use of a spicy substance, pepper sauce, applied to the tongue produced a strong burning to the tongue in 28 patients of the BMS group but the same response was only seen in 10 of the controls.

Another study examined 180 subjects with complaints of BMS, xerostomia, and taste disturbances versus 90 age- and gender-matched healthy controls. They also reported that the BMS patient group had clear-cut taste acuity differences compared to the controls with more of the BMS patients reporting sweet abnormality than with the other three taste substances: salt, bitter, and sour. Lastly, a study examined taste acuity in 73 BMS patients (57 women and 16 men) and 52 control subjects (38 women and 14 men) who were age- and gender-matched to the BMS group. They used various concentrations of sweet, salty, sour, and bitter solutions, and asked subjects to rate the intensity and quality of each solution. They found that the 57 women in the BMS group gave lower intensity ratings for salty and sweet test solutions than the 38 women controls. They also found no group differences for these women on sour or bitter test solutions, but the men in this study showed no group differences on any of the substances tested. The above studies document that taste is consistently altered, although not in a consistent direction in BMS patients.

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**BMS patients frequently report a positive taste sensation, which they describe as a persistently altered (metallic) taste.**
Since metallic dysgeusia is a common early symptom of a BMS disorder, it would be appropriate to review a recent article that describes medication induced dysgeusia. This recent paper reported that the most commonly reported medications linked to metallic dysgeusia are those used to treat bacterial infections, psychosis, arthritis, and hypertension. Specifically, they found case reports for metallic dysgeusia linked with tetracycline, lithium carbonate, D-penicillamine, and catapryl. The Doty and Bromley review paper in 2004 also pointed out that sometimes the underlying medical problems for which medications are being prescribed are the real problem, especially when the disease affects the brain (e.g., epilepsy, migraines, hypothyroidism, schizophrenia). Lastly, one 1985 paper described a link between metallic dysgeusia and Crohn’s disease that is manifesting oral effects as well as the usual intestinal changes.

In summary, metallic dysgeusia is not well understood, but in the absence of medications or a brain disease causing it, the possibility remains that it may be related to damaged peripheral nerves, especially considering the information already presented about small sensory fiber neuropathic changes in the tongue. The hypothesis that pain
and taste pathway are both affected and interact is reasonable and certainly worthy of further testing, especially if an animal model could be developed.

**Other Local Oral Factors and BMS**

Many local and systemic precipitating factors have been suggested beyond the salivary changes and sensory dysfunction changes previously mentioned. The local factors included other diseases that may cause burning sensations such as oral candidal infections, autoimmune mucosal reactions like lichen planus and geographic tongue, and tissue trauma from ill-fitting dentures. Of course, there are always case reports of burning-type pain occurring from oral carcinomas that invade the trigeminal nerve and from a variety of local oral mucosal tissue irritants. These local oral conditions have been seen often enough to suggest that some cases of BMS are secondary BMS cases. Estimates are that more than one-third of all BMS patients presenting for diagnosis have multiple causes and the most common causes of secondary BMS are listed in Table 1.

**Other Common Co-morbid Systemic Diseases**

Various systemic conditions have been associated with BMS, including diabetes, hormonal changes and nutritional/mineral deficiencies. Because the condition is more prominent in female patients over age 40, most suffering from BMS are perimenopausal or postmenopausal at this stage in life. Whether or not the hormonal changes in women that occur with menopause is causally related to BMS is not clear. One study examined this issue by looking at the effect of hormonal replacement therapy, HRT, on BMS. They found that HRT helped in 15 of 27 of their postmenopausal women with BMS. Unfortunately, this study was an open label study and not a randomized, blinded, placebo-controlled study and thus the data are not convincing proof of a causal link between hormone alterations and BMS. Patients with BMS often have high blood glucose levels, but this does not occur on a consistent basis so no causal relationship has been demonstrated. Next, nutritional deficiencies (vitamins B-1, B-2, B-6, B-12, iron, folic acid, zinc, etc.) is yet another reported systemic abnormality associated with BMS. Like hormonal status and diabetes, these suggested nutritional deficiencies are not consistently supported by the literature. Nevertheless, local and systemic factors must be ruled out before final diagnosis of BMS is made. The common diagnostic tests used for BMS are listed in Table 2.

**Psychological Factors**

Various psychological disorders, including depression, anxiety and somato-
tization, have been mentioned as playing a role in BMS. One study examined 25 patients with a diagnosis of primary BMS and 25 age- and gender-matched patients with organically based painful disorders of the mouth and reported a positive psychiatric diagnosis in 44 percent (11/25) of the BMS patients but only in 16 percent (4/25) of the non-BMS controls of the patients with BMS. This study involved an interview by a psychiatrist and a questionnaire that screens for psychiatric disorders. While 44 percent seems a high number when compared to other chronic pain patients, this rate is not unusual or even high. For example, the same 28-item psychiatric screening questionnaire (general health questionnaire (GHQ-28)) used in the prior study was given to 31 consecutive primary BMS subjects. These authors found that although 51.9 percent of the patients showed evidence of psychiatric illness using the GHQ-28 questionnaire, this rate was similar or lower than what had been reported for other chronic pain subjects, except those attending a psychiatric clinic. Anxiety is another often-reported feature of BMS patients and one study examined 74 BMS using a psychiatric interview plus the Hamilton’s Depression and Anxiety Scales, HADS. This study reported a positive psychiatric diagnosis (mostly depression) was established in 38 of the 74 cases (51.4 percent). The HADS questionnaire data suggested that when anxiety was present, it strongly influenced the psychiatric condition of these patients. Findings of an elevated rate of positive findings when a systematic psychometric analysis of BMS patients is performed was confirmed again in a recent study, which examined 32 BMS patients and 32 matched control subjects using a comprehensive, reliable, and validated inventory. Like the studies previously mentioned, results showed highly significant differences between the BMS group and the non-BMS controls with regard to several personality factors. Unfortunately, findings of high levels of anxiety, depression or even somatization tendencies are not unusual or unique to BMS patients.

Chronic pain patients in general have elevated findings when compared to age- and gender-matched nonpain patients. The question remains whether the pain is etiologically related to these personality characteristics or visa versa. In fact, recently, a report on 33 BMS patients suggested that psychological factors are not consistently elevated over control subjects in this population. These authors used the revised Symptom Checklist (SCL-90R) and the Multidimensional Pain Inventory (MPI) on their BMS cases and compared the resulting data to data from population samples that included both non-BMS chronic pain patients and a normal nonclinical sample. They concluded the BMS patient scores were not significantly elevated on the measures of depression, anxiety, and somatization. They did note that 21 percent of the BMS cases (7/33) had a substantially elevated psychologic distress. Of course, the presence of co-morbid psychological disease would suggest treatment of these problems but is not evidence of causality.

Current Etiologic Theories

Searching for the causal link is one of the more difficult endeavors in science. It is a well-known scientific principle that association does not prove causality. Unfortunately, many authors have not made this point clear when reporting on clinical findings that are seen in association with BMS symptoms. For example, it is just as likely that the observed elevated depression and anxiety traits and the elevated somatic focus on their burning pains is an effect of the pain symptoms and not a causative factor. The same could be said about diabetes, menopause, candida infections and their relationship to BMS. For example, it is just as likely that the patients do not clean their mouth as well because of the burning and this causes candida overgrowth.

Other local factors and systemic factors could also be coincidental findings that may have no specific relationship to the causation of the BMS. To establish a causal link between two factors, one must have good consistency of data. This means that the association is present in all cases, no matter how many ways it is studied. The association should be strong and it should account for most of the variability seen in the data. There should be a positive dose-response relationship between the two associated factors. This means that when you have a small amount of the predictor, you see only a small amount of outcome. As the predictor increases so does the outcome response. A bio-
Logically plausible explanation must be available regarding how the predictor variable causes the outcome and the suggested association must be independently verified.

Given the mentioned caveats, there are two current hypotheses for BMS worth discussing. The first deals with the interplay of sensory and taste systems which innervate the tongue. The anterior two-thirds of the tongue send taste sensations centrally via the chorda tympani nerve. Nontaste sensations are supplied by the trigeminal nerve (lingual branch). The essential theory is that burning mouth pain symptoms occur when there is an abnormal interplay between lingual nerve function and chorda tympani function.40,41 These authors have further speculated that there is a specific group of patients at risk for developing burning mouth pain who have a large number of fungiform papillae. They speculate that individuals with increased fungiform papillae innervation (labeled as supertasters) are more at risk for disturbance of the balance between these two nerves (trigeminal and chorda tympani). In other words, if there is damage to the chorda tympani nerve over time, they have the greatest potential to develop pain and taste alterations (dysgeusia). At present, this theory is lacking definitive data that a high prevalence of BMS patients are indeed supertasters.

Their second theory is similar but does not require a disturbed interplay between taste nerves and sensory nerves. It is based on two new studies that suggest that BMS is due to small fiber neurologic damage in the oral cavity. Of course, the idea that a neuropathic change may underlie BMS is not new, but strong evidence supporting this idea has been lacking. The first study of significance is one that examined 52 BMS patients using quantitative sensory tests (QST) in addition to the blink reflex (BR) recordings.42 They suggested that while BMS patients have different types of neural change (some with diminished neural responses and some with elevated neural responses, the majority (90 percent) of those tested had some form of an altered sensory thresholds or reflex reaction. The other critical study supporting a neuropathic etiology for BMS is by Lauria et al. (2005) and it was described earlier in the section on biopsy evidence for BMS. In combination, the QST and the tongue biopsy data suggest that small diameter nerve fibers progressively deteriorate causing the BMS symptoms.

Finally, neuropathic pain phenomena are not limited to peripheral neural changes altering transduction and transmission of impulses into the brain. Most neuropathic disorders also have ongoing altered central modulation of nociceptive information as an integral part of the disease process. In this regard, two additional studies have examined BMS patients for more central neural changes, specifically on dopamine receptors in the basal ganglia.43 The study measured dopaminergic function of the putamen in 10 BMS patients and 14 healthy controls using positron emission tomography. They reported that the presynaptic dopaminergic function was significantly decreased (between 17 percent and 20 percent) in the putamen of the BMS patients compared to control subjects. The above data was supported by a subsequent study using a more specific ligand which specifically bound to dopamine D1 and D2 receptors in these patients.

Again, they examined 10 BMS cases and 11 healthy controls. They concluded from the ligand uptake data that a decline in endogenous dopamine levels in the putamen was present in burning mouth patients.44 The number of available striatal D2 receptors are thought to dictate the extent of central pain suppression.45 All in all, these studies suggest that brain function changes occur along with peripheral nerve changes and support the idea that central modulation of sensory signal occurs in BMS cases. In fact, altered central nociceptive signal processing is an expected consequence with all neuropathic disease processes, not just BMS.

Management

In 2003, a systematic review of the treatment literature for BMS was conducted.46 These authors examined Medline publications and conference proceedings up to September 2001 which contained quality research on interventions used for the treatment of BMS in comparison to a placebo. The authors identified several trials that tested antidepressants, cognitive behavioral therapy, analgesics, hormone replacement therapy, and vitamin complexes used to provide relief of the burning and discomfort in BMS. They found that none of the trials examined was able to provide conclu-
### Table 3

<table>
<thead>
<tr>
<th>Medications (class of drug)</th>
<th>Common Dosage Range</th>
<th>Prescription</th>
<th>Mechanisms of Action/ FDA Approval Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nortriptyline (tricyclic antidepressant)</td>
<td>10 to 75 mg per day</td>
<td>10 mg at bedtime; increase dosage by 10 mg every four to seven days until oral burning is relieved or side effects occur.</td>
<td>Tricyclic antidepressants inhibit the activity of such diverse agents as histamine, 5-hydroxytryptamine, and acetylcholine. It increases the pressor effect of norepinephrine. This drug is approved for use of the symptoms of depression, but is used off-label for neuropathic pain.</td>
</tr>
<tr>
<td>Oral clonazepam (benzodiazepine)</td>
<td>0.25 to 2 mg per day</td>
<td>0.25 mg at bedtime; increase dosage by 0.25 mg every four to seven days until oral burning is relieved or side effects occur. As dosage increases, medication is taken as full dose or in three divided doses.</td>
<td>Mechanism is unknown, although it is believed to enhance the activity of gamma aminobutyric acid (GABA), the major inhibitory neurotransmitter in the CNS. This agent is approved by the FDA for seizures and for panic disorders. It is used off-label for neuropathic pain and BMS in particular.</td>
</tr>
<tr>
<td>Topical clonazepam (benzodiazepine)</td>
<td>1 mg tablet tid, after meals</td>
<td>Let tablet dissolve and hold fluid in mouth in area of most intense burning for three minutes, then spit.</td>
<td>Same as above</td>
</tr>
<tr>
<td>Gabapentin (anticonvulsant)</td>
<td>300 to 2,400 mg per day</td>
<td>100 mg at bedtime; increase dosage by 100 mg every four to seven days until oral burning is relieved or side effects occurs. As dosage increases taken in three divided doses.</td>
<td>Anticonvulsant action is unknown, gabapentin is known to prevent seizures as do other marketed anticonvulsants. This drug is FDA-approved for partial seizures and for post-herpetic neuralgia pain.</td>
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<tr>
<td>Pregabalin (anticonvulsant)</td>
<td>100 mg PO tid</td>
<td>100 mg PO tid</td>
<td>This is a new drug that is being suggested for use in neuropathic pain patients. Its mechanism of action is thought to be similar to gabapentin. It is approved by the FDA as an adjunctive agent in adult patients with partial onset seizures and for post-herpetic neuralgia and diabetic neuropathy.</td>
</tr>
<tr>
<td>Topical lidocaine (anesthetic)</td>
<td>Viscous gel 2%</td>
<td>5 ml qid. Rinse for two minutes and expectorate.</td>
<td>This agent is a sodium channel-blocking agent and provides analgesic effects when applied topically. It is FDA-approved as a topical anesthetic agent but its use is specified as an aid for minor surgeries or skin abrasions.</td>
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</table>
### Table 3: Medications Commonly Used in the Management of BMS

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanisms of Action</th>
<th>FDA Approval Status</th>
<th>Evidence Basis for Use</th>
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<tbody>
<tr>
<td><strong>Lidocaine</strong></td>
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<tr>
<td>Topical lidocaine</td>
<td>Anticonvulsant</td>
<td>No data for BMS is yet available, but it should work similar to gabapentin and it is thought to have better pharmacokinetics. No RBCT study performed.</td>
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<tr>
<td>2% Viscous gel</td>
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<tr>
<td>100 mg PO tid</td>
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<tr>
<td><strong>Clonazepam</strong></td>
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<tr>
<td>Topical clonazepam</td>
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<tr>
<td>5 mg qid, rinse for two min</td>
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<tr>
<td><strong>Conclusions</strong></td>
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Evidence Basis for Use

- **No published evidence for BMS but used commonly for neuropathic pain.**
- **Open clinical trials show some efficacy for BMS. No randomized, blinded placebo-controlled study (note exception below).**
- **RBCT is available showing this approach is helpful in many BMS patients and is better than placebo.**
- **Case report data suggests this agent may be helpful in some patients. No RBCT study performed.**
- **No data for BMS is yet available, but it should work similar to gabapentin and it is thought to have better pharmacokinetics. No RBCT study performed.**

Appendix: Evidence from Multicenter Randomized, Double-Blind, Placebo-Controlled Trials on Alpha-Lipoic Acid Therapy in BMS

**Evidence from Multicenter Randomized, Double-Blind, Placebo-Controlled Trials on Alpha-Lipoic Acid Therapy in BMS**

- **Among these medications, the most widely accepted treatment for BMS is clonazepam.** This drug has been evaluated in open-label studies on BMS with reported positive results. Recently, a randomized, double-blind, placebo-controlled multicenter clinical trial was performed on the efficacy of topical clonazepam for BMS. This study reported on 48 patients (four men and 44 women) who were given either a placebo tablet or a 1 mg tablet of clonazepam to suck on and hold the saliva in the area of burning for three minutes, then spit. This was done three times per day for 14 days. They reported that pain intensity decreased significantly more in the clonazepam group and blood levels of clonazepam were extremely low. They hypothesized that clonazepam, which is classified both as an anticonvulsant and an anxiolytic agent, acts locally to disrupt the mechanism(s) underlying stomatodynia.

The newer drugs, on which there is preliminary data assessing efficacy for possible use in BMS, include gabapentin and alpha-lipoic acid. Gabapentin was approved by the Food and Drug Administration in the United States in May 2002 for treatment of postherpetic neuralgia. Even before this, gabapentin has been used off-label for many types of neuropathic pain disorders including BMS. A meta-analysis of gabapentin shows it to be a promising medication in the treatment of sustained continuous pain, but no good, high-quality study has examined it specifically for BMS. A recent case report showed that at least in one patient, this medication was helpful at reducing burning pain. Another agent that has been suggested as potentially helpful in BMS is alpha-lipoic acid. This is a common nutritional supplement that is promoted for its pain-suppressing effect on diabetic neuropathic pain. The best study on alpha-lipoic acid involved assessment of the short-term effect (three weeks) of 600 mg of alpha-lipoic acid per day for diabetic polyneuropathy. This study was a multicenter, randomized double-blind placebo-controlled trial on...
509 outpatients with neuropathic pain symptoms in the feet. The subjects were randomly assigned to receive either 600 mg alpha-lipoic acid once daily intravenously, 600 mg alpha-lipoic acid three times a day orally for six months, or a placebo in various sequences. Using the total symptom score as an outcome, the study found no significant difference between the alpha-lipoic acid group and the placebo group. In contrast, in BMS patients, there was one double-blind, randomized controlled study that involved 60 BMS patients who were given either alpha-lipoic acid or an inert control substance.

This study reported significant improvement in the alpha-lipoic acid group compared with placebo with the majority showing at least some improvement after two months. Finally, a three-treatment randomized, single-blind comparison study examined amisulpride (50 mg/day), paroxetine (20 mg/day) and sertraline (50 mg/day) over an eight-week period on 76 BMS patients. The study demonstrated beneficial effects on reducing BMS pain intensity for all three agents although amisulpride was the fastest acting of the three agents and no subject assigned to this agent stopped participation in the study. No serious
### Evidence Basis for Use

**RBCT shows that this agent is helpful for BMS.**

**No RBCT study performed so no data specific to BMS available.**

**One RBCT study showed that tramadol was ineffective for BMS.**

**No RBCT study performed so no data specific to BMS available. Obviously this is a powerful pain-relieving agent.**

**Only a single case report has reported it is helpful for BMS. No RBCT study performed to date.**

**One RBCT study showed that amisulpride was ineffective for BMS.**

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**Prognosis**

In spite of the many behavioral and medication-based treatments, the management of BMS is still not satisfactory, and there is no definitive cure, although help is provided with these methods. Untreated BMS represents a disorder with a very poor prognosis in terms of quality of life, and the patient’s lifestyle may worsen when psychological dysfunctions occur. Spontaneous remission of pain in BMS subjects has not been definitely demonstrated, the current treatments are palliative only, and while they may not be much better than a credible placebo treatment, few studies report relief without intervention.

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**References**


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adverse events were reported, and the incidence of side effects did not differ among the three groups. It is interesting to note that amisulpride is an antipsychotic that is disinhibitory at low doses (<10 mg/kg), with specific dopamine D2 and D3 receptor-blocking and little effect on other receptors. Unfortunately, this study had no placebo-control condition and amisulpride is not available in the United States.