

## Occasional Review

# Prospective study of aetiological factors in burning mouth syndrome

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### Abstract

**A prospective study of 150 consecutive patients with burning mouth syndrome and with a minimum follow up period of 18 months is reported. Factors related to dentures, to vitamin B complex deficiency, and to psychological abnormalities were found to be important, and undiagnosed diabetes mellitus, reduced salivary gland function, haematological deficiencies, candidal infection, parafunctional habits, and allergy might also play a part. Given a protocol for management which takes all these factors into account, some two thirds of patients can be cured or have their symptoms improved.**

### Introduction

Historically, burning mouth syndrome has evolved as a distinct clinical entity.<sup>1,6</sup> Its prevalence is uncertain, but it has been reported world wide. It has also been named glossopyrosis,<sup>7</sup> glossodynia,<sup>2</sup> and oral dysaesthesia.<sup>4</sup>

Burning of the oral mucosa occurs in various oral conditions, including erosive lichen planus and geographic tongue, but patients with burning mouth syndrome are a separate group. These patients have a normal oral mucosa on examination, in contrast to the other groups, and the burning is unremitting.<sup>1,2</sup> Patients complain either of burning on waking that persists throughout the day or of burning developing during the day which worsens as the day goes on.<sup>3,4</sup>

A review of published work showed no previous prospective studies of the condition so we set up a burning mouth clinic to try to establish the frequency of the various causes of burning mouth syndrome and its response to treatment. We paid attention to the known aetiological factors, which include problems with dentures,<sup>5,6,9</sup> parafunctional habits such as clenching and tongue thrusting,<sup>8,10</sup> haematological disorders,<sup>5,6,11</sup> vitamin B complex deficiencies,<sup>12</sup> candidal infection,<sup>11,13</sup> reduced salivary gland function,<sup>14</sup> the climacteric,<sup>2,5,6,15</sup> and undiagnosed diabetes.<sup>5,16</sup> Additional factors such as depression, anxiety, and cancerphobia were also evaluated.<sup>2,6,11,17</sup> Uncommon causes of a burning sensation, such as oesophageal reflux, were also considered, although in such cases the clinical course is atypical. In some patients evidence of acrylic allergy was also sought.<sup>18</sup>

### Patients and methods

We studied 150 consecutive patients who were referred to our departments over 16 months. All patients gave a history of the burning mouth syndrome. Some 131 were women and 19 were men, with a median age of 59. The source of referral was medical consultants (6%), general medical practitioners (22%), self (22%), and general dental practitioners (50%).

A detailed history was taken of duration of the condition, site affected, and pattern of burning. The severity and the response to treatment were assessed with a linear analogue scale.<sup>19</sup> The relation of the condition to wearing dentures, provision of dentures, or alterations to existing dentures, as well as parafunctional habits such as clenching and tongue thrusting, was established. A full medical and drug history was also taken, including symptoms of oesophageal reflux and of the climacteric such as night sweating and facial flushing. Patients were asked directly about cancerphobia, depression, and anxiety. Careful questioning in an unhurried atmosphere was necessary to elucidate causes of anxiety such as financial, housing, and domestic problems.

A complete routine extraoral and intraoral examination was performed. If dentures were worn their design and condition were assessed. In particular the relation between the vertical and horizontal components of the jaw and the denture base extension were assessed and the freeway space measured. The teeth were examined for faceting as an indicator of a parafunctional habit.<sup>9,10</sup> Inadequate retention of dentures was assessed as some patients mentioned that abnormal tongue activity was a habit they had developed to retain their upper denture.

### LABORATORY AND CLINICAL INVESTIGATIONS

The following investigations were undertaken.

*Haematological investigations* comprised full blood count, mean corpuscular volume, mean corpuscular haemoglobin, and corrected whole blood folate, serum ferritin, and vitamin B<sub>12</sub> concentrations. If an abnormal result was obtained the investigation was repeated at the next appointment.

*Biochemical investigations*—If the fasting blood glucose concentration was abnormal a glucose tolerance test was performed at the next appointment. Patients who had glucose investigations undertaken but in whom no initial abnormality could be detected thereafter had serial glucose estimations every six months to detect the development of diabetes. We also measured blood concentrations of vitamins B<sub>1</sub>, B<sub>2</sub>, and B<sub>6</sub> on a random sample of patients.<sup>12</sup>

*Salivary gland investigations*—Stimulated parotid salivary gland flow rates were performed with a Carlsson-Crittenden cup, stimulation being with 1 ml of 10% citric acid. The volume of saliva produced in 1 minute was then measured. A value below 0.5 ml/min was considered abnormal.<sup>20</sup>

*Candidal isolation*—A rinse technique was used to detect oral candidal and other bacterial species.<sup>21</sup> This technique allows measurement and identification of any candidal species present.

*Psychological investigations*—Every third patient (n=47) was asked to complete Cattell's 16PF questionnaire.<sup>22</sup> This has been used to analyse the psychological aspects of patients with oral complaints, including those related to wearing dentures.<sup>23</sup> All patients were asked in detail about possible sources of cancerphobia and depression. Direct questioning about cancerphobia was routine, as well as questioning about cancer (particularly head and neck cancer) among relatives, friends, and neighbours. Sources of anxiety such as financial, social, and marital problems were sought. It became clear that other sources of anxiety such as bereavement, housing

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problems, and domestic upheavals had also to be sought. Finally, direct questions about symptoms of endogenous and reactive depression were asked, which specifically included sleep pattern—for example, early morning waking or difficulty in getting to sleep.

**Other investigations**—Infrequently additional investigations were undertaken. In 11 patients acrylic allergy was investigated by patch testing. Three others were patch tested towards food related products because of an atypical history—that is, the burning was intermittent and affected the tongue, soft palate, and throat.

## Results of investigations and corrective treatment

### GENERAL CONSIDERATIONS

Figure 1 shows the site of the oral mucosa affected by the burning sensation. In most patients (60%) more than one site was affected, but in all of them the sensation was bilateral. We asked all patients about the severity, using a linear analogue scale of zero (no burning) to 10 (intolerable burning). The median initial score was 8 (fig 2). The same scale was used to assess clinical response to treatment. Successfully treated patients gave a score of either zero or 1-3, which they invariably described as "liveable with." Figure 2 shows the clinical response to treatment.

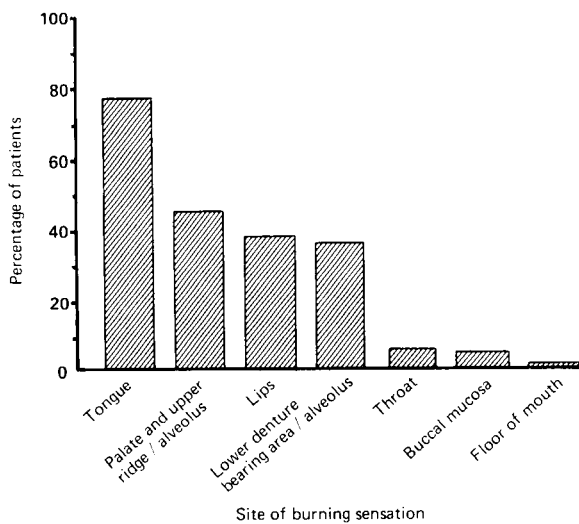


FIG 1—Histogram showing the site of burning as reported by patients.

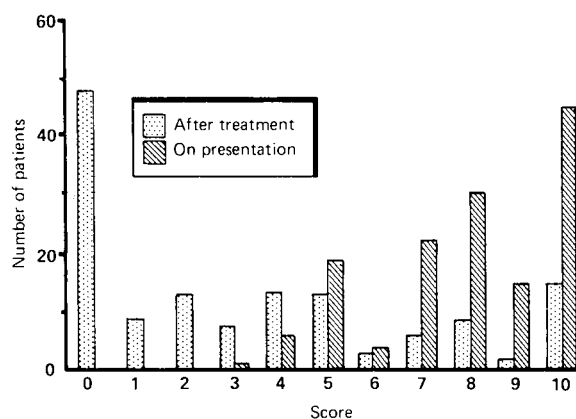


FIG 2—Score given by patients for burning mouth on presentation and score given after treatment. 0 to 10=no burning to intolerable burning.

### INDIVIDUAL FACTORS

**Dentures**—Some 95 of the patients were edentulous, and 87 wore complete upper and lower dentures; 34 had some teeth and wore dentures; 21 had all their teeth or some and were not wearing dentures. In 64 patients denture design was thought to be an important factor and in 28 the burning coincided

with the provision of dentures or additions or relines to their existing ones. Forty six patients had no change in symptoms on removing their dentures; nevertheless, on removal of one or both dentures symptoms were improved for 60 patients, totally alleviated in four, and made worse for six. Sixty four patients had new dentures constructed in an attempt to alleviate the burning. The most important design features were inadequate tongue space owing to faulty position of the teeth and lack of freeway space and inadequate base extension leading to overloading of the denture bearing tissues. When such features were present new dentures were constructed to a suitable design; this alleviated the burning in 33 of the 64 patients.

**Tongue thrusting** was present in nine patients, clenching and grinding in 21, and thrusting and clenching in one. Reinforcing the avoidance of clenching and tongue thrusting and modifying denture design or hypnotherapy helped in reducing the symptoms in 20 of these patients.

**Haematological factors**—Haematological deficiency was found in only 19 patients. Only one patient was anaemic, eight had low ferritin concentrations (3-12 ng/ml) and 12 had low vitamin B<sub>12</sub> concentrations (71-170 pg/ml). None had a low folic acid concentration and all had a normal mean corpuscular volume. Replacement treatment was undertaken after referral to a consultant physician. Patients were given ferrous sulphate 200 mg three times daily for three months or a six week course of 1000 µg cyanocobalamin. These restored all haematological indexes to normal and led to total alleviation of symptoms in eight and partial alleviation in five of the 19 patients with haematological deficiencies.

**Biochemical factors**—Eight patients had raised fasting blood glucose concentrations (6.5-17.7 mmol/l). Four of these had an abnormal glucose tolerance test result. Adequate control of diabetes was achieved in all cases and contributed to complete resolution of their oral symptoms. Four patients had known maturity onset diabetes, three being poorly controlled, with random blood glucose concentrations of 7.7 mmol/l, 14.2 mmol/l, and 14.7 mmol/l. One of these patients improved with vitamin B<sub>1</sub> and B<sub>6</sub> supplements, one with new complete dentures and avoidance of clenching, and the other was symptom free after being given a new partial upper denture. Two patients with a previously normal fasting blood glucose concentration developed overt maturity onset diabetes while under review at a later visit. Deficiencies of vitamins B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub>, or combinations of these vitamins were found in 26 of the 68 patients tested. Patients were given replacement treatment,<sup>12</sup> which abolished the symptoms in eight of the 26. Empirical treatment with vitamin B<sub>1</sub> plus B<sub>6</sub> was given to the remaining 82 patients, with relief of symptoms in a further 26. Hence vitamin B supplements alleviated symptoms in 34 of the 150 patients studied.

**Salivary gland factors**—Fifty one patients thought that they had inadequate saliva and suffered from some oral dryness. Twelve of these, and seven others as well, had stimulated parotid flow rates below 0.5 ml/min. Patients who considered dryness to be a factor in the burning were given artificial saliva substitute. Nineteen patients considered that their burning sensation was wholly or partly alleviated by this treatment.

**Candida isolation**—*Candida* species were isolated in two fifths of the patients. They were instructed in denture hygiene—namely, soaking dentures overnight in a hypochlorite solution. All also received topical antifungal treatment of amphotericin lozenges four times a day for 14 days. Repeat rinse cultures confirmed the absence of candida thereafter. About a seventh of the patients in whom *Candida* was isolated had burning symptoms reduced in response to antifungal treatment.

**Climacteric symptoms**—One hundred and four patients were postmenopausal, 19 were perimenopausal, and eight still had regular menstrual periods. Seventeen of the 19 perimenopausal patients had additional symptoms of the climacteric such as facial flushing and night sweats, but in only six of these were the symptoms of burning mouth syndrome eventually attributed solely to the climacteric.

**Reflux oesophagitis**—Five patients gave a history suggestive of reflux oesophagitis, generally of burning tongue on waking, but persistent in three patients and becoming worse throughout the day.

**Allergic factors**—Eleven patients were patch tested for allergies to polymethylmethacrylate and related materials because the burning sensation affected the denture bearing mucosa, and the results of all other investigations were negative. Two of these had positive patch tests to a 2% solution at 48 and 96 hours. In one patient substitution of vulcanite for acrylic dentures changed the symptoms only a little; the other patient was symptom free once the acrylic partial denture was replaced by a porcelain and gold alloy fixed pontic. Three other patients were also patch tested with food related products because their history was of intermittent burning of the tongue, soft palate, and throat. Sensitivity to (a) sorbic acid and propylene glycol, (b) benzoic acid, and (c) cinnamon was discovered on patch testing. Dietary advice abolished the symptoms in two of the three patients, and they have remained free of symptoms for the past 24 months.

**Psychological factors**—Some patients volunteered (though not always at the first appointment) that they thought anxiety and depression were factors in their condition. There were various reasons, such as concern over mortgage repayments and difficult home circumstances. Some 28 patients

had disabled or handicapped relatives, causing social isolation and increasing anxiety and tension within the home. Three patients had extremely adverse social circumstances and two of these lost their symptoms once they were rehoused. In some cases depression appeared reactive, usually owing to a recent family bereavement. In others there was no apparent reason for their depression, which could therefore be considered endogenous. At presentation 26 patients were taking tranquillisers, 48 sleeping tablets, and only nine antidepressants. We questioned 146 patients directly about a history of depressive illness; 43 said that they had been or were being treated for depression, although only five of these were taking antidepressant drugs on presentation. When depression was thought to be contributing appreciably to the symptoms dothiepin, a tricyclic antidepressant, was prescribed. This reduced symptoms in 27 patients, but dothiepin could often be withdrawn or reduced in dosage after other aetiological factors such as denture design had been attended to. Cancerophobia was an important factor in 28 patients; reassurance alone was often successful in alleviating the burning sensation, although sometimes several visits were required.

Given all known aetiological factors a third of patients were rendered symptom free and a fifth had only minimal symptoms—that is, scoring 1-3—after treatment. Without direct questioning and the use of an analogue scale these patients would otherwise also have been considered as cured since their symptoms were “liveable with.”

Of the remaining 67 patients, symptoms were improved in 21, forty three had no change, and three were worse.

## Discussion

This study illustrates the multifactorial origins of the burning mouth syndrome and the results support findings of a preponderance in women, particularly those aged over 50. It is imperative, however, to establish that patients are truly suffering from the syndrome, particularly that they have a normal mucosa on examination.

In considering aetiological factors much emphasis has been placed on the climacteric, but only a tenth of our patients had features of this, over three quarters of them being postmenopausal. Moreover, when other causes were considered, only six cases were thought to be due to the climacteric alone.

Problems with dentures are important in the syndrome, whether or not patients ascribe the onset of the condition to these. It is clinically helpful if patients find that removal of the denture alleviates their symptoms. A detailed analysis of denture design, with replacement if indicated, may help a large proportion of patients; in our study no fewer than 33 of the 64 patients who had replacement dentures were helped—that is, a quarter of all the patients who wore dentures. Parafunctional habits contribute to overloading of the denture bearing tissues. Attempts to reduce these habits entailed reinforcing avoidance of the habit or modifying the dentures. Occasionally hypnotherapy was used as an aid to relaxation.

Allergy was an infrequent cause of burning mouth syndrome since modifying the denture design often alleviated symptoms. Denture base materials such as nylon and polycarbonate for complete dentures are not readily available, and the poorer aesthetics of vulcanite means that even if allergy is proved an alternative to polymethylmethacrylate is hard to find. Therefore it is unwise to label a patient allergic to polymethylmethacrylate unless properly controlled skin patch testing has been undertaken, and even then its role in affecting the oral mucosa is uncertain.<sup>18</sup> Other allergies rarely cause the burning mouth syndrome, but two patients in our group with food sensitivity were cured by an exclusion diet. The site of burning and the high degree of day to day variability of these patients' symptoms were atypical which was why patch testing was undertaken.

Replacement therapy with iron and vitamin B<sub>12</sub> helped some of the patients. Again we emphasise the need to take all factors into account since, for example, the habit of clenching on a compromised oral mucosa may lead to symptoms, but both factors need attention if the condition is to be cured.

Other deficiencies of the vitamin B complex group were also identified. These occurred less often than reported, but no exclusions were applied to the present group,<sup>12</sup> and for technical reasons not all patients could be screened. The basis for the development of

these deficiencies is still not clear.<sup>24</sup> Our study shows the importance of recognising impaired glucose tolerance or undiagnosed diabetes mellitus. Patients had no classic symptoms of diabetes such as polyuria or polydipsia. Although only four of the 150 patients were affected, early diagnosis is important since half of all patients with maturity onset diabetes remain undiagnosed.<sup>25</sup> The sensitivity of the oral mucosa in highlighting systemic disorders is well illustrated in this group of patients. Although not all the symptoms were attributable to impaired glucose tolerance alone, there was an excellent response to control of the blood sugar concentration. In patients in whom the results of all investigations are negative and attempts at corrective treatment have failed regular repeat biochemical investigations are warranted to detect the late appearance of occult diabetes.

Despite a normal oral mucosa several patients had apparent salivary gland dysfunction as assessed by stimulated parotid flow rates. These patients had no other clinical signs of salivary gland dysfunction but appear to lie in the “grey area” between normal function and xerostomia, and more patients admit to dry mouth on questioning than volunteer it as a symptom. Nevertheless, saliva replacement treatment may be wholly or partially successful in alleviating burning mouth in about a tenth of patients.

There is good evidence for the oral carriage of candidal species in the general population,<sup>26</sup> and in our patients these were isolated in about a third. In three quarters of these the candidal count was greater than 100 colony forming units per ml, which is likely to be clinically important,<sup>27</sup> and in some antifungal treatment reduced the severity of complaints. The clinical importance of uncommon *Candida* species and other yeast organisms remains uncertain.

Uncommon causes of burning mouth syndrome such as reflux oesophagitis are mentioned in published work<sup>5</sup> but are rarely encountered in practice. A patient with classic symptoms of oesophageal reflux may give a history of a burning sensation of the oral mucosa present usually only on waking. Nevertheless, burning throughout the day was also a feature in our patients with possible reflux. In dentate patients palatal erosion of any remaining anterior teeth suggests the diagnosis,<sup>28</sup> but these individuals are best regarded as not having true burning mouth syndrome.

The psychological aspects of the condition have dominated previous publications. In clinical practice three main factors are important: anxiety, depression, and cancerophobia. No fewer than a fifth of our patients were responsible for caring for handicapped relatives, and the importance of such factors may be appreciated only if the initial interview is unhurried. The patients themselves often believe that the complaint signifies emotional instability. Attendance at many clinics, where nothing is found on examination, accentuates the problem, and these patients often say they have received unsympathetic hearing. An additional cause of concern may be that most patients have never heard of any other sufferers.

For the fifth or so of patients who are cancerophobic the presence of unremitting oral symptoms leads them to believe either that they already have cancer or that they are about to develop it. Repeated reassurance and direct questioning of their fears are important, and occasionally we have resorted to antidepressant treatment to break the vicious cycle. Some anxious patients readily become depressed, particularly if there is some additional adverse social circumstance such as a bereavement. Once again the initial prolonged interview often hinted at depression when they described social isolation, preoccupation with the oral complaint, sleep disorders, or a feeling of hopelessness. We found dothiepin (75 mg at night) very effective in relieving depression in these patients, and about a fifth of our patients were helped by such treatment after other aetiological factors were excluded and corrected.

## RECOMMENDATIONS

On the basis of these findings we propose the following treatment protocol for patients with burning mouth syndrome.

(1) Take time to determine details of the patient's complaint. Inquire tactfully into the home and social circumstances, and identify problems of stress, anxiety, or depression (psychological

forms may help). It is rare for the burning sensation to interfere with sleep, although a psychological problem may produce sleep disturbance, particularly early morning waking. Identify problems likely to precipitate anxiety or depression. Inquire about cancerophobia and ask directly about depression.

(2) Ask the patient to quantify their burning sensation on a scale of zero (no burning) to 10 (intolerable burning). This may need to be explained on several occasions, but it is the only guide available to assess the initial symptoms and the response to treatment.

(3) Measure the haemoglobin, ferritin, corrected whole blood folate, and vitamin B<sub>12</sub> concentrations. Further investigations to exclude an underlying cause should be undertaken before any replacement treatment.

(4) Measure the fasting blood glucose concentration, followed by a glucose tolerance test if indicated.

(5) Measure vitamin B<sub>1</sub>, B<sub>2</sub>, and B<sub>6</sub> concentrations. If this is not possible a replacement regimen of vitamin B<sub>1</sub>, 300 mg and vitamin B<sub>6</sub> 150 mg per day in divided doses for four weeks may be effective in deficient patients and may be tried.

(6) Assess salivary gland function by stimulated flow rates. Inquire whether the patient thinks the burning sensation and oral dryness are the same thing. If the answer is yes then even in the absence of quantification of saliva flow rate salivary replacement treatment may be effective.

(7) Quantify the oral carriage of *Candida* species by an oral rinse. If this is not possible then empirical antifungal treatment may be warranted.

(8) Inquire about the onset of the climacteric and the presence of menopausal symptoms, although hormone replacement treatment is ineffective in relieving the burning mouth syndrome. Fortunately, patients whose symptoms are attributable to the climacteric alone are usually only mildly affected.

(9) Obtain a specialist opinion about denture design, particularly if their removal eases symptoms. Features that contribute to overloading and tongue restriction are particularly important. Ask about parafunctional habits. Some patients retain their upper dentures inadequately and position their tongues to retain these, while in others tongue restriction or thrusting or jaw clenching are important.

It is our experience that patients with the burning mouth syndrome can be treated satisfactorily if a rational approach to management is adopted. The establishment of special clinics makes maximal use of the available resources and helps to prevent multiple attendances at various specialty clinics.

## Conclusions

This prospective study investigated aetiological factors in burning mouth syndrome in 150 patients with a minimum follow up period

of 18 months. On the basis of this study a protocol for the treatment of these patients is proposed which resulted in almost 70% of patients being cured or improved.

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## ANY QUESTIONS

*After a stroke several years ago a patient has developed the distressing symptom of severe unrelievable hunger. Tests have ruled out hyperinsulinism. Could damage to the satiety centre in the hypothalamus be the cause? Is there an effective treatment?*

The questioner does not state the age and sex of this patient or the time span between the stroke and the onset of hyperphagia. The Klein-Levine syndrome of hypersomnia and megaphagia characteristically occurs in young men and can follow a traumatic precipitant.<sup>1</sup> Bulimia nervosa—spree eating, not necessarily persistent hyperphagia—is probably psychogenically triggered and occurs mostly in women.<sup>2</sup> Other causes of increased appetite include depression, hyperthyroidism, Cushing's syndrome, diabetes mellitus, and moderate hyperglycaemia as well as hyperinsulinaemia.<sup>3</sup> The questioner is right to emphasise the importance of the satiety centre in the hypothalamus. Bilateral ventromedial hypothalamic lesions result in hyperinsulinaemia, which in turn produces hyperphagia and obesity.<sup>4</sup> Hyperphagia can, however, follow vagotomy, which prevents hyper-

insulinaemia.<sup>5</sup> Glucagon rather than insulin may be important in this respect. Although the hypothalamus is crucial to the regulatory process of food absorption, it does not operate alone. Frontal disinhibition, possibly after infarction, may be a factor; and destruction of parts of the limbic system may be associated with increased appetite and obesity.<sup>3</sup> I doubt if there is an effective treatment, but a further computed tomogram, additional endocrine tests, and treatment with thymoleptics may be worth doing.—E M R CRITCHLEY, consultant neurologist, Preston.

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