

## Halitosis: a review of associated factors and therapeutic approach

José Roberto Cortelli<sup>(a)</sup>  
Mônica Dourado Silva Barbosa<sup>(b)</sup>  
Miriam Ardigó Westphal<sup>(c)</sup>

<sup>(a)</sup>Vice-Provost of Research, University of Taubaté, Taubaté, SP, Brazil.

<sup>(b)</sup>Associate Professor, Department of Dentistry, School of Medicine and Public Health, the Sciences Development Foundation, Salvador, BA, Brazil.

<sup>(c)</sup>Assistant Professor of Periodontics, School of Dentistry, Federal University of Amazonas, Manaus, AM, Brazil.

**Abstract:** Halitosis or bad breath is an oral health condition characterized by unpleasant odors emanating consistently from the oral cavity. The origin of halitosis may be related both to systemic and oral conditions, but a large percentage of cases, about 85%, are generally related to an oral cause. Causes include certain foods, poor oral health care, improper cleaning of dentures, dry mouth, tobacco products and medical conditions. Oral causes are related to deep carious lesions, periodontal disease, oral infections, peri-implant disease, pericoronitis, mucosal ulcerations, impacted food or debris and, mainly, tongue coating. Thus, the aim of the present review was to describe the etiological factors, prevalence data and the therapeutic mechanical and chemical approaches related to halitosis. In general, halitosis most often results from the microbial degradation of oral organic substrates including volatile sulfur compounds (VSC). So far, there are few studies evaluating the prevalence of oral malodor in the world population. These studies reported rates ranging from 22% to more than 50%. The mechanical and chemical treatment of halitosis has been addressed by several studies in the past four decades. Many authors agree that the solution of halitosis problems must include the reduction of the intraoral bacterial load and/or the conversion of VSC to nonvolatile substrates. This could be achieved by therapy procedures that reduce the amount of microorganisms and substrates, especially on the tongue.

**Descriptors:** Halitosis/etiology; Halitosis/epidemiology; Halitosis/diagnosis; Halitosis/therapy; Mouthrinses/therapeutic use

**Corresponding author:**

José Roberto Cortelli  
Rua Visconde do Rio Branco, 210  
Taubaté - SP - Brazil  
CEP: 12020-040  
E-mail: jrcortelli@uol.com.br

Received for publication on May 27, 2008  
Accepted for publication on Jun 20, 2008

## Disclosures

This article was sponsored by an educational grant from Johnson & Johnson do Brasil Indústria e Comércio para Saúde Ltda.

## Introduction

Halitosis, *fetor oris*, oral malodor or bad breath are the general terms used to describe unpleasant breath emitted from a person's mouth regardless of whether the odorous substances in the breath originate from oral or non-oral sources.

Halitosis is an oral health condition characterized by consistently emanating odorous breath and may be caused by several agents including certain foods, poor oral health care, improper cleaning of dentures, decreased salivary flow rate, tobacco products or a medical condition. In 90% of cases, though, the causes of halitosis are located in the mouth and can be attributed to deep carious lesions, periodontal disease, oral infections, periimplant disease, pericoronitis, mucosal ulcerations, impacted food or debris, factors causing decreased salivary flow rate and, mainly, tongue coating.<sup>1</sup>

The tongue is a major site of oral malodor production, while periodontal disease and other factors seem to be only a fraction of the overall problem.<sup>2</sup> In addition, current social norms emphasize the importance of personal image and interpersonal relationships. Thus, halitosis may be an important factor in social communication and, therefore, may be the origin of concern not only for a possible health condition but also for frequent psychological alterations leading to social and personal isolation.<sup>3</sup> Although oral malodor or bad breath is an unpleasant condition experienced by most individuals, it typically results in transient discomfort.

At least 50% of the population suffer from chronic oral malodor and approximately half of these individuals experience a severe problem that creates personal discomfort and social embarrassment. The mouth air of chronic malodor sufferers is tainted with compounds such as hydrogen sulfide, methyl mercaptan and organic acids, which produce a stream of foul air that is gravely offensive to the people in their vicinity. Sufferers often make desperate attempts to mask their oral malodor with mints

and chewing gum, compulsive brushing, and repeatedly rinsing with mouthwashes.<sup>4</sup> Currently, three methods for measuring halitosis are available: (1) organoleptic measurement, (2) gas chromatography and (3) sulfide monitoring. Although the organoleptic measurement has many shortcomings it still is the golden standard method to assess halitosis.<sup>5</sup>

## Etiology

Although the source of oral malodor is located in the oral cavity in up to 90% of people with the condition and only a small percentage of cases may be due to non-oral causes, a serious underlying medical condition may warrant immediate referral to a physician.<sup>6</sup>

## Halitosis and the presence of oral microorganisms

The oral microorganisms most likely to cause oral malodor are Gram-negative bacteria species including *Treponema denticola*, *Porphyromonas gingivalis*, *Porphyromonas endodontalis*, *Prevotella intermedia*, *Bacteroides loescheii*, Enterobacteriaceae, *Tannerella forsythensis*, *Centipeda periodontii*, *Eikenella corrodens*, *Fusobacterium nucleatum*.<sup>7</sup>

However, no obvious association exists between halitosis and any specific bacterial infection, suggesting that bad breath reflects complex interactions between several oral bacterial species. The agents that give rise to oral malodor include especially the volatile sulfide compounds, diamines, and short chain fatty acids.<sup>8</sup>

The principal components of bad breath are volatile sulfide compounds (VSC), especially hydrogen sulfide (H<sub>2</sub>S), methyl mercaptan (CH<sub>3</sub>SH), and dimethylsulfide [(CH<sub>3</sub>)<sub>2</sub>S]<sup>10</sup> or compounds such as butyric acid, propionic acid, putrescine, and cadaverine.<sup>9</sup> These compounds result from the proteolytic degradation by predominantly anaerobic Gram-negative oral microorganisms of various sulfur-containing substrates in food debris, saliva, blood, and epithelial cells.<sup>10</sup> Substrates for volatile sulfide compounds production are sulfur-containing amino-acids such as cysteine, cystine and methionine present in saliva or gingival fluid.<sup>11</sup> Several microorganisms recovered from periodontal lesions of gingivitis and

periodontitis are related to produce large amounts of these volatile sulfur compounds.<sup>10</sup>

The bacterial interactions are most likely to occur in the gingival crevices and periodontal pockets, but oral malodor can also arise from the posterior dorsal tongue. As a consequence of its large and papillary surface area, the dorsum of the tongue can retain large amounts of desquamated cells, leucocytes, and microorganisms. Donaldson *et al.*<sup>12</sup> (2005), examining the microflora present on the tongue dorsum of subjects with and without halitosis, observed that the predominant species in test and control groups were *Veillonella sp.* and *Prevotella sp.* Greater species diversity was found in the halitosis samples compared with controls. The halitosis samples contained an increased incidence of unidentifiable Gram-negative rods, Gram-positive rods and Gram-negative coccobacilli. The authors stated that there was no obvious association between halitosis and any specific bacterial genus. The increased species diversity found in halitosis samples suggests that halitosis may be the result of complex interactions between several bacterial species. The role of uncultivable bacteria may also be important in contributing to this process. The same group, later<sup>13</sup> using molecular identification of bacteria on the tongue dorsum of subjects with and without halitosis, observed that the predominant species found in the control samples were Lysobacter-type species, *Streptococcus salivarius*, *Veillonella dispar*, unidentified oral bacterium, *Actinomyces odontolyticus*, *Atopobium parvulum* and *Veillonella atypica*. In the halitosis samples, Lysobacter-type species, *S. salivarius*, *Prevotella melaninogenica*, unidentified oral bacterium, *Prevotella veroralis* and *Prevotella pallens* were the most commonly found species. For the control samples, 13-16 (4.7-5.8%) of 276 clones represented uncultured species, whereas in the halitosis samples, this proportion increased to 6.5-9.6% (36-53 of 553 clones). In the control samples, 22 (8.0%) of 276 clones represented potentially novel phylotypes, and in the halitosis samples, this figure was 39 (7.1%) of 553 clones. They concluded that the microflora associated with the tongue dorsum is complex in both the control and the halitosis groups, but several key species predominate in both groups.

## Prevalence of halitosis

There are few studies evaluating the prevalence of oral malodor in the general population, with reported rates ranging from 22% to more than 50%. In addition, approximately 50% of adults and elderly individuals emit socially unacceptable breath, related to physiological causes, upon arising in the morning.<sup>14</sup> Moreover, there are no universally accepted standard criteria, objective or subjective, that define a halitosis patient.<sup>15</sup>

Up to 50% of the U.S. population reports that their own “bad breath” has concerned them during some point in the course of their lifetime. Half of this group is indeed likely to have an ongoing sporadic or a chronic breath malodor problem.<sup>16</sup>

A study performed by Miyazaki *et al.*<sup>17</sup> (1995) examining oral malodor in 2,672 individuals aged 18 to 64 years observed that there were no significant differences in the VSC between males and females in any age group. In each age group, the measured values of oral malodor were highest in the late morning group (58.6 ppb in average), followed by the late afternoon group (52.1 ppb), while lowest values were shown in the early afternoon group (39.4 ppb). Significant correlation was observed only between VSC values and periodontal conditions and tongue coating status. The results also suggest that oral malodor might be caused mainly by tongue coating in the younger generation and by periodontal diseases together with tongue coating in older cohorts in the general population. Age was not a risk factor for increasing VSC.

Liu *et al.*<sup>18</sup> (2006) examined the prevalence of halitosis in the Chinese population and assessed the relationships between halitosis and oral health, social and behavioral factors. These authors observed that the prevalence of halitosis was 27.5% according to the organoleptic score. The level of volatile sulfur compounds (VSCs) in mouth air was significantly lower in males and in some of the age groups after lunch. And, the amount of tongue coating played the most important role in increasing VSCs concentration in mouth air, followed by periodontal status and plaque index values. DMFT, social, and behavioral factors did not contribute to halitosis. They concluded that tongue coating score, modified sul-

cus bleeding index and calculus index were factors significantly related to oral malodor in this study.

Interestingly, Al-Ansari *et al.*<sup>19</sup> (2006) assessed the prevalence and factors associated with self-reported halitosis in 1,551 Kuwaiti patients. The prevalence of self-reported halitosis was 23.3%. Use of the toothbrush less than once daily was the factor most strongly associated with self-perceived halitosis. Other factors significantly associated with self-perceived halitosis included current or past smoking, female gender, being 30 years of age or older, having high school education or less, history of chronic sinusitis or gastrointestinal disorders, never using miswak (a natural toothbrush made from the twigs of the *Salvadora persica* tree), and never using dental floss. They concluded that inadequate oral hygiene practices were the factors most strongly associated with self-reported oral malodor in this sample of Kuwaiti patients. Other factors with significant associations included history of gastrointestinal tract disorders, chronic sinusitis, older age, female gender, and lower education levels.

## Therapeutic approach to manage oral halitosis

Successful treatment of halitosis depends on a correct diagnosis and the implementation of a cause-related therapy.<sup>20</sup> After a positive diagnosis for oral halitosis has been made, the treatment plan is implemented, which comprises elimination of the causative agent and improvement of the oral health status.<sup>21</sup> Although the multiple possible etiologies include oral and non-oral causes, the majority of breath malodor cases originate from the oral cavity. Briefly, the treatment of oral malodor can therefore be focused on the reduction of the intraoral bacterial load and/or the conversion of VSC to nonvolatile substrates.

Miyazaki *et al.*<sup>22</sup> (1999) established the recommended examination for halitosis and a classification of halitosis with corresponding treatment needs. Accordingly, different treatment needs (TN) have been described for the various diagnostic categories. The responsibility for the treatment of physiologic halitosis (TN-1), oral pathologic halitosis (TN-1 and TN-2), and pseudo-halitosis (TN-1 and TN-4)

resides on dental practitioners. However, extra-oral pathologic halitosis (TN-3) and halitophobia (TN-5) should be managed by a physician or medical specialist and a psychiatrist or psychological specialist. Table 1 describes the 5 different categories of treatment needs according to diagnosis (Miyazaki *et al.*<sup>22</sup>, 1999).

The management of halitosis starts by taking a detailed history of the condition, duration, severity, and impact on the patient's everyday life. Examination involves clinical, radiographic, and special tests. The contributing medical conditions, once identified, are referred for treatment accordingly. Clinical examination checks the patient's oral hygiene, caries, and periodontal status; plaque retention factors are also recorded. Radiographic examination should look for evidence of dental caries, alveolar bone defects, and defective restorations.<sup>21</sup> Special tests are performed to detect the foul-smelling VSCs along with the associated bacteria. The results collected can be used to confirm the diagnosis and to monitor the treatment progress. There are many diagnostic techniques among which are organoleptic measurement, gas chromatography, and halimeter examination.<sup>23,24,25,26</sup>

Since malodor originating from the mouth is due to the metabolic degradation of available proteinaceous substrates to malodorous gases by certain oral microorganisms, oral malodor can be ameliorated through: (1) Reduction of bacterial load, (2) reduction of nutrient availability, (3) conversion of VSC to nonvolatiles and (4) masking the malodor.<sup>1,20,27</sup>

**Table 1** - Treatment needs (TN) for breath malodor divided in 5 categories.

| Category | Description  |
|----------|--|
| TN-1     | Explanation of halitosis and instructions for oral hygiene (support and reinforcement of a patient's own self-care for further improvement of his/her oral hygiene). |
| TN-2     | Oral prophylaxis, professional cleaning and treatment of oral diseases, especially periodontal diseases.   |
| TN-3     | Referral to a physician or medical specialist.   |
| TN-4     | Explanation of examination data, further professional instruction, education and reassurance.  |
| TN-5     | Referral to a clinical psychologist, psychiatrist or other psychological specialist.   |

## Reduction in total load of oral microorganisms and or bacterial nutrients in the oral cavity

### Mechanical approach

Several studies have implicated the dorsum of the tongue as the primary source of VSC, both in periodontally diseased and healthy individuals.<sup>1,28,29,30,31,32</sup> Researchers have been able to find positive correlations between tongue coating status (amount and or presence) and the different parameters directly related with oral malodor. In this scenario, the tongue becomes the most important microenvironment to study and to target in the prevention and treatment of oral halitosis and also as a potential reservoir for periodontal pathogens.

The papillary structure of the dorsum represents a unique ecological niche in the oral cavity, offering a large surface area that favors the accumulation of oral debris and microorganisms. The morphology of the dorsum of the tongue provides additional irregularities such as fissures, grooves and depapillated areas that may serve as retention areas for harboring bacteria.<sup>1,29,33,34</sup>

The development of a predominant anaerobic microbiota associated with tongue coating has been considered an ideal microenvironment to produce malodorous compounds, and therefore different authors have tried to assess the relationship between the morphology of the tongue and the severity of oral halitosis.<sup>35,36</sup>

Numerous studies have found a relationship between the mechanical removal of tongue coating and the reduction of both organoleptic scores and VSC levels, including reduction in methyl mercaptan levels and the methyl mercaptan/hydrogen sulfide ratio, in both healthy and periodontitis patients, with or without halitosis.<sup>20,21,31,37</sup>

Mechanical reduction of malodor and of the intraoral bacterial count may be achieved by disrupting the tongue biofilm, thus decreasing the production of VSCs and other volatile organic compounds.<sup>32,34,38</sup>

Various available instruments can be applied to the tongue, and by gentle pressure the majority of the tongue coating can be scraped off.<sup>38</sup> Brushing the dorsum of the tongue with toothpaste was more

effective than brushing the teeth. The duration of these effects varies from 15 to 100 min and depends on the device used to remove the coating, i.e., toothbrush or tongue scraper, lasting longer for tongue scrapers than for toothbrushes.<sup>39</sup> The percentage of VSC reduction has been related to the different devices used, ranging from 33% with a toothbrush, to 42% with a specially designed tongue cleaner; and also to the periodontal health status, being higher for halitosis patients without periodontal disease (51.8%) than for periodontitis patients (49%).<sup>33</sup>

Other studies found a relationship between tongue cleaning and the reduction of both organoleptic scores and levels of volatile sulphur-containing compounds.<sup>40,41</sup> In patients with high levels of oral malodor, a regular toothbrush was statistically significantly less effective in tongue cleaning than a device that brushed and scraped, or a scraper. Because of the limited duration of the effect, efficacy remained questionable.<sup>41</sup> Scraping the tongue after cysteine challenge testing reduced halitosis only modestly, but brushing the tongue dorsum was remarkably effective.<sup>42</sup> Two weeks of tongue brushing or scraping by a group of patients free of periodontitis resulted in negligible reductions in bacteria on the tongue, whereas the amount of tongue coating decreased significantly. Therefore, tongue cleaning seems to reduce the substrates for putrefaction, rather than the bacterial load.<sup>43</sup>

In addition, mechanical cleaning of teeth, such as brushing the teeth and flossing reduced the amount of oral bacteria and substrates, thereby presumably reducing oral malodor.<sup>44</sup> Interdental cleaning and tooth brushing are essential mechanical means of oral hygiene. This home care removes residual food particles and organisms that cause putrefaction.<sup>27</sup> However, according to Faveri *et al.*<sup>32</sup> (2006), interdental flossing has no added value with regard to reducing morning bad breath. Clinical studies revealed that brushing the teeth exclusively was not very effective in reducing oral malodor scores.<sup>42,45</sup> A combination of tooth and tongue brushing or tooth brushing alone have a beneficial effect on bad breath for up to 1 h (73% and 30% reductions in VSC, respectively).<sup>27</sup>

In subjects free of caries, periodontal disease



and tongue coating, brushing the teeth exclusively had no appreciable influence on the concentration of volatile sulfur containing compounds in morning breath, when compared with no brushing and rinsing the mouth with water.<sup>40</sup> Since periodontitis can be a factor in chronic oral malodor,<sup>1,27</sup> professional periodontal treatment is mandatory. Thus, initial periodontal therapy in moderate periodontitis patients can be expected to improve breath odor parameters by reducing the number of periodontopathogens.<sup>11,46</sup>

### Chemical approach

The goal of any antimicrobial treatment would be to reduce the proteolytic, anaerobic flora found on the tongue surface. Treatment procedure should include a debridement component, such as the use of a tongue scraper, possibly in combination with an antimicrobial mouthrinse.

Mouthrinses with antimicrobial properties can reduce oral malodor by reducing the number of microorganisms chemically. Often used active ingredients in these products are chlorhexidine (CHX), essential oils (EOs), triclosan and cetylpyridinium chloride (CPC). Mouthrinses can also reduce halitosis by chemically neutralizing odor compounds, including VSCs. Often used active ingredients of these products are metal ions and oxidizing agents.

### Chlorhexidine

CHX gluconate is a cationic bis-biguanide, with a very broad antimicrobial spectrum. The American Dental Association has approved its use. Being the most studied antimicrobial agent in the treatment of gingivitis, it has also been tested for its efficacy in the treatment of oral halitosis. Results from a case-series study in halitosis patients suggested a significant effect of CHX rinsing and tongue brushing after 1 week of treatment.<sup>47,48</sup> In several studies, a 0.2% CHX mouthrinse produced significant reductions in volatile sulfur-containing compound levels and in organoleptic scores.<sup>49,50</sup> Similar results with 0.12% CHX-(di)gluconate were reported in combination with teeth and tongue brushing.<sup>47,48</sup>

Due to its substantivity, the anti-VSC effect of the 0.2% solution is satisfactory after 1 h but, more

importantly, it shows a tendency to improve at 2 h and 3 h.<sup>51</sup> A commercial product containing 0.12% CHX-gluconate has been demonstrated as an effective anti-VSC product, and showed kinetics similar to that of the 0.2% CHX solution.<sup>42</sup> Although only moderately effective against VSC production, the lower CHX concentration maintains its effect for over 3 h.

Although being considered the gold standard mouthrinse for halitosis treatment, CHX has undesirable side effects. The safety of an effective agent that might be used repeatedly needs to be established. Ninety of 101 patients who used the 0.2% CHX rinse for 1 week responded to a questionnaire concerning adverse reactions.<sup>47</sup> Eighty-eight percent of the patients had at least one complaint, with 59% experiencing a change in the taste of food and 25% experiencing a burning sensation at the tip of the tongue. About 4% of the subjects reported sloughing of the tissues or gingival pain, which would be a more serious concern. As this was reported after only 1 week of unsupervised usage, one might expect even more problems if the patients were using this agent for a longer time period. An agent is needed that approaches the clinical efficacy of CHX but with better safety and comfort features.

### Essential oils

Essential oils, including hydro-alcohol solutions of thymol, menthol, eucalyptol, and methyl salicylate, have been used in mouthwashes to prevent periodontal disease. Anti-plaque and anti-gingivitis activity has been demonstrated in several studies [for details see a meta-analysis published by Gunsolley<sup>52</sup> (2006)].

An EO mouthrinse was able to reduce the offensive gases present in morning bad breath as measured by a sulfide monitor,<sup>50</sup> a result that is in agreement with those of a previous short-term study,<sup>53</sup> in which the results indicated a reduction of the organoleptic scores by EOs, which caused a sustained reduction in the plaque odorigenic bacteria, unlike the placebo. An argument was made that the re-odorization was important to the overall activity of the product only for about 30 min after treatment and, at post-treatment times of 60-180 min, the anti-odor

activity of the product was due to its anti-microbial action.<sup>53</sup> That conclusion became the basis for the premise that anti-VSC agents would succeed if they had an antimicrobial component.

Rinsing with an EOs mouthrinse can have long-lasting effects in reducing anaerobic bacteria overall as well as Gram-negative anaerobes and VSC producing bacteria. The significant reductions in numbers of these bacteria produced by the EO mouthrinse, both in plaque and on the dorsum of the tongue, can play a key role in explaining the EO mouthrinse's effectiveness in reducing supragingival plaque and gingivitis as well as its effectiveness in controlling intrinsic oral malodor throughout the test period of 14 days.<sup>54</sup>

### Triclosan

The clinical experiments performed by Young *et al.*<sup>55</sup> (2002) showed that mouth-rinsing with triclosan solubilized in sodium lauryl sulfate, propylene glycol and water gave a marked and long-lasting anti-VSC effect. It cannot be excluded that sodium lauryl sulfate contributed to the observed anti-VSC effect. However, the *in vitro* experiments described by the authors support the contention that triclosan exhibits an anti-VSC effect *per se*.

In the Carvalho *et al.*<sup>50</sup> (2004) investigation, plaque formation was not always directly associated with VSC measurements, since the triclosan and CPC mouthrinses were more effective in reducing bad breath than in reducing supragingival plaque accumulation. Therefore, it could be postulated that the superior reducing effect of these specific mouthrinses on bad breath may be related primarily to their efficacy in reducing the load of VSC-related microorganisms and oral debris in the whole mouth niches rather than only in supragingival plaque reduction.

### Cetylpyridinium chloride

Quaternary ammonium compounds, such as benzalkonium and cetylpyridinium chloride, inhibit bacterial growth, but reviews concluded that the results were modest for plaque and equivocal for gingivitis. A CPC rinse used in a 6-week pre-brushing study failed to confer any adjunctive benefit to oral

hygiene and gingival health compared to a control rinse.<sup>56</sup>

Although there is still debate over the action of cationic antiseptics in the oral cavity, what is clear is the lack of substantivity of cetylpyridinium chloride. This is highlighted by a persistence of antimicrobial activity of CPC in the mouth of only 3 h, which compares poorly with the greater than 12-hour action of CHX.<sup>57</sup> A more frequent use of CPC could improve plaque inhibition, but is likely to lead to compliance problems. Some studies also demonstrated that the CPC mouthrinse presented the lowest impact in reducing VSCs of morning breath when compared with other products.<sup>50,51</sup> This fact could be supported by the observation that this quaternary ammonium compound agent is not substantive enough to promote an essential antibacterial activity.<sup>49</sup>

### Zinc

Metals such as zinc, sodium, tin and magnesium are thought to interact with sulfur. The mechanism proposed is that metal ions oxidize the thiol groups in the precursors of volatile sulfur-containing compounds.<sup>58</sup>

Morning breath odor can be successfully reduced by the sole use of an amine fluoride-stannous fluoride-containing mouthrinse twice daily, which significantly reduces the bacterial load in the saliva and retards the *de novo* plaque formation.<sup>59</sup> Unfortunately, both cupric and stannous ions have the potential to discolor teeth, either as a result of sulfide formation on the teeth after extended periods of use or due to the precipitation of dietary chromogen. Nonetheless, cupric chloride is the most effective metal solution for inhibiting hydrogen sulfide production at 1, 2 and 3 h after rinsing.<sup>60</sup> Zinc is the metal ion of choice with this purpose because of its low toxicity and its other favorable properties, such as not causing dental staining. It is known that zinc ions possessing anti-VSC effects have affinity for sulfur, forming sulfides with low solubility.

Oral products containing zinc are also effective in reducing or inhibiting oral malodor. In a study conducted by Young *et al.*<sup>51</sup> (2003), a 1% zinc acetate solution had excellent anti-VSC effect throughout the test period of 3 h, although the metallic taste

experienced at this concentration is a little unpleasant (as experienced by the test panel). This problem may be overcome in commercial products by masking with other ingredients.

### Chlorine dioxide

Experimentally, the use of chlorine dioxide associated with chlorite anion has been shown to result in oxidative consumption of amino acids like cysteine and methionine, which are precursors of VSCs.<sup>61</sup> Thus, clinical use of this mouthrinse can be expected to reduce oral malodor by reducing concentrations of VSCs. Chlorine dioxide, a strong oxidizing agent, consumes oral substrates containing cysteine and methionine, thus preventing the production of VSCs.

A study evaluated the effect of a commercially available chlorine dioxide mouthrinse on VSCs levels in a panel of healthy subjects.<sup>61</sup> The results of that investigation demonstrated a beneficial effect of a chlorine dioxide mouthrinse on VSC control in the morning breath of healthy subjects when compared with its own placebo. Previous studies have shown the positive effects of chlorine dioxide on the inhibition of VSC formation<sup>61</sup> which is in agreement with those results.

A higher success rate has been reported following the use of an intraoral liquid-air spray device and an ultrasonic intraoral dental cleaner modified to deliver a 20 ppm molecular chlorine dioxide irrigant to the hard and soft tissues of the mouth.<sup>62</sup> The subjects of the study were instructed as to how to floss their teeth, to clean the posterior third of the tongue with a tongue blade and to rinse with a proprietary chlorine dioxide mouthrinse. Seventy eight percent of 1,343 individuals responded “yes” to a questionnaire that asked “Do you feel there has been a significant improvement in your breath odor problem?” and only 4% responded “No”. Both this result and that of the Belgian clinic<sup>62</sup> indicate that subjects with malodor can benefit from the existing treatment modalities.

## Effective combination of agents

### Chlorhexidine and zinc

A CHX and zinc mouthrinse had a strong effect on volatile sulfur-containing compounds and was

effective for at least 9 hours. Control rinses with CHX or zinc alone had a moderate and strong effect for 1 hour, but this effect diminished with time, respectively, fast and slightly.<sup>51</sup>

### Cetylpyridinium and zinc ions

A CPC and zinc mouthrinse had a good synergistic effect on volatile sulfur-containing compounds levels after 1 hour, but minimally above the effect of zinc alone.<sup>51</sup>

### Chlorhexidine, cetylpyridinium chloride and zinc-lactate

Chlorhexidine is still the gold standard mouthrinse, but it does have some side effects. Due to these disadvantages, new formulations have been developed. Since CHX and CPC are both antimicrobial agents, it seems reasonable to assume that the new marketed mouthwash that contains CHX and CPC acts by reducing the number of VSC-producing bacteria on the dorsum of the tongue. Moreover, zinc-lactate, besides its antimicrobial activity, may reduce VSC scores by transforming them into insoluble compounds. Two dual-center, double-blind, placebo-controlled studies demonstrated that a new mouthwash containing CHX (0.05%), CPC (0.05%) and zinc-lactate (0.14%) is effective in the treatment of oral halitosis.<sup>29,63</sup> The one adverse effect of the active mouthwash was staining of the dorsum of the tongue.

Some studies have indicated a synergistic action between CHX and cetylpyridine.<sup>11,64</sup> Their data illustrate that the replacement of alcohol in a CHX formulation by CPC does not change the antimicrobial activity of the mouthrinse, even though the CHX concentration is reduced to 0.05%.<sup>11</sup> A 0.12% CHX and 0.05% cetylpyridinium solution was compared to a 0.05% CHX, 0.05% CPC and 0.14% zinc-lactate solution, and to other 3 different commercial mouthrinses with CHX.<sup>64</sup> Formulations combining CHX and CPC achieved the best results, both in terms of anti-microbial activity and anti-halitosis efficacy. Conversely, a formulation combining CHX with NaF showed significantly lower anti-halitosis and anti-microbial efficacy.



## Conclusions

The present review described the etiological factors related to halitosis, including prevalence data, and the mechanical and chemical therapeutic approaches. Tongue biofilm seems to be directly involved in the production of oral halitosis and may have an important role in the success of periodon-

titis therapy since it is a potential reservoir for periodontal pathogens. It is clear that a successful treatment of halitosis involves an appropriate diagnosis, professional therapy, mechanical plaque control, including tooth brushing and tongue cleaning, possibly combined with the use of an effective antimicrobial mouthrinse.

## References

1. van den Broek AM, Feenstra L, de Baat C. A review of the current literature on management of halitosis. *Oral Dis*. 2008;14(1):30-9. Review
2. Rosenberg M. Bad breath and periodontal disease: how related are they? *J Clin Periodontol*. 2006;33(1):29-30.
3. Sanz M, Roldán S, Herrera D. Fundamentals of Breath Malodour. *J Contemp Dent Pract*. 2001 Nov 15;2(4):1-17.
4. Bosa A. Oral malodor: philosophical and practical aspects. *J Can Dent Assoc*. 1997;63(3):196-201. Review
5. Greenman J, Duffield J, Spencer P, Rosenberg M, Corry D, Saad S *et al*. Study on the organoleptic intensity scale for measuring oral malodor. *J Dent Res*. 2004;83(1):81-5.
6. Ayers KMS, Colquhoun AUK. Halitosis: causes, diagnosis, and treatment. *New Zeal Dent J*. 1998;94:156-60.
7. Awano S, Gohara K, Kurihara E, Ansai T, Takehara T. The relationship between the presence of periodontopathogenic bacteria in saliva and halitosis. *Int Dent J*. 2002;52 Suppl 3:212-6.
8. Porter SR, Scully C. Oral malodour (halitosis). *BMJ*. 2006;23;333(7569):632-5. Review.
9. Goldberg S, Kozlovsky A, Gordon D, Gelernter I, Sintov A, Rosenberg M. Cadaverine as a putative component of oral malodor. *J Dent Res*. 1994;73(6):1168-72.
10. Tonzetich J. Production and origin of oral malodor: a review of mechanisms and methods of analysis. *J Periodontol*. 1977;48(1):13-20.
11. Quirynen M, Zhao H, Soers C, Dekeyser C, Pauwels M, Coucke W *et al*. The impact of periodontal therapy and the adjunctive effect of antiseptics on breath odor-related outcome variables: a double-blind randomized study. *J Periodontol*. 2005;76(5):705-12.
12. Donaldson A, McKenzie D, Riggio M, Hodge P, Rolph H, Flanagan A *et al*. Microbiological culture analysis of the tongue anaerobic microflora in subjects with and without halitosis. *Oral Dis*. 2005;11 Suppl 1:61-3.
13. Riggio MP, Lennon A, Rolph HJ, Hodge PJ, Donaldson A, Maxwell AJ *et al*. Molecular identification of bacteria on the tongue dorsum of subjects with and without halitosis. *Oral Dis*. 2008;14(3):251-8.
14. Rosenberg M. Bad breath: research perspectives. Ramat Aviv: Ramot Publishing-Tel Aviv University Press; 1997.
15. Newman MG. The role of periodontitis in oral malodour: clinical perspectives. *In*: van Steenberghe D, Rosenberg M, eds. *Bad Breath: A multidisciplinary approach*. Leuven: Leuven University Press; 1996. p. 3-14.
16. Lee SS, Zhang W, Li Y. Halitosis update: a review of causes, diagnoses, and treatments. *J Calif Dent Assoc*. 2007;35(4):258-60, 262, 264-8. Review.
17. Miyazaki H, Sakao S, Katoh Y, Takehara T. Correlation between volatile sulphur compounds and certain oral health measurements in the general population. *J Periodontol*. 1995;66(8):679-84.
18. Liu XN, Shinada K, Chen XC, Zhang BX, Yaegaki K, Kawaguchi Y. Oral malodor-related parameters in the Chinese general population. *J Clin Periodontol*. 2006;33:31-6.
19. Al-Ansari JM, Boodai H, Al-Sumait N, Al-Khabbaz AK, Al-Shammari KF, Salako N. Factors associated with self-reported halitosis in Kuwaiti patients. *J Dent*. 2006;34(7):444-9.
20. Yaegaki K, Coil JM. Examination, Classification, and Treatment of Halitosis; Clinical Perspectives. *J Can Dent Assoc*. 2000;66:257-6. Review.
21. Lee PP, Mak WY, Newsome P. The aetiology and treatment of oral halitosis: an update. *Hong Kong Med J*. 2004;10(6):414-8.
22. Miyazaki H, Arao M, Okamura K, Kawaguchi Y, Toyofuku A, Hoshi K *et al*. [Tentative classification of halitosis and its treatment needs] [Article in Japanese]. *Niigata Dent J*. 1999;32:7-11.
23. Morita M, Wang HL. Relationship between sulcular sulfide level and oral malodor in subjects with periodontal disease. *J Periodontol*. 2001;72(1):79-84.
24. Tanaka M, Yamamoto Y, Kuboniwa M, Nonaka A, Nishida N, Maeda K *et al*. Contribution of periodontal pathogens on tongue dorsa analyzed with real-time PCR to oral malodor. *Microbes Infect*. 2004;6(12):1078-83.
25. Peruzzo DC, Jandiroba PFCB, Nogueira Filho GR. Use of 0.1% chlorine dioxide to inhibit the formation of morning volatile sulphur compounds (VSC). *Braz Oral Res*. 2007;21(1):70-4.
26. Ueno M, Shinada K, Yanagisawa T, Mori C, Yokoyama S, Furukawa S *et al*. Clinical oral malodor measurement with a portable sulfide monitor. *Oral Dis*. 2008;14:264-9.

27. Quirynen M, Zhao H, van Steenberghe D. Review of the treatment strategies for oral malodour. *Clin Oral Investig*. 2002 Mar;6(1):1-10. Review.
28. Yaegaki K, Sanada K. Volatile sulfur compounds in mouth air from clinically healthy subjects and patients with periodontal disease. *J Periodontol Res*. 1992;27:233-8.
29. Roldán S, Winkel EG, Herrera D, Sanz M, Van Winkelhoff AJ. The effects of a new mouthrinse containing chlorhexidine, cetylpyridinium chloride and zinc lactate on the microflora of oral halitosis patients: a dual-centre, double-blind placebo-controlled study. *J Clin Periodontol*. 2003;30(5):427-34.
30. Roldán S, Herrera D, O'Connor A, González I, Sanz M. A combined therapeutic approach to manage oral halitosis: a 3-month prospective case series. *J Periodontol*. 2005;76(6):1025-33.
31. Farrell S, Baker RA, Somogyi-Mann M, Witt JJ, Gerlach RW. Oral malodor reduction by a combination of chemotherapeutic and mechanical treatments. *Clin Oral Investig*. 2006;10(2):157-63.
32. Faveri M, Hayacibara MF, Pupio GC, Cury JA, Tsuzuki CO, Hayacibara RM. A cross-over study on the effect of various therapeutic approaches to morning breath odour. *J Clin Periodontol*. 2006;33(8):555-60.
33. Roldán S, Herrera D, Sanz M. Biofilms and the tongue: therapeutic approaches for the control of halitosis. *Clin Oral Investig*. 2003;7:189-97.
34. Krespi YP, Shrimel MG, Kacker A. The relationship between oral malodor and volatile sulfur compound-producing bacteria. *Otolaryngol Head Neck Surg*. 2006;135(5):671-6.
35. De Boever EH, Uzeda M, Loesche WJ. Role of tongue surface characteristics and tongue flora in halitosis. *J Dent Res*. 1995;74:127.
36. Mantilla Gómez S, Danser MM, Sipos PM, Rowshani B, van der Velden U, van der Weijden GA. Tongue coating and salivary bacterial counts in healthy/gingivitis subjects and periodontitis patients. *J Clin Periodontol*. 2001;28:970-8.
37. Loesche WJ, Kazor C. Microbiology and treatment of halitosis. *Periodontol 2000*. 2002;28:256-79.
38. Yaegaki K, Coil JM, Kamemizu T, Miyazaki H. Tongue brushing and mouth rinsing as basic treatment measures for halitosis. *Int Dent J*. 2002;52 Suppl 3:192-6.
39. Kaizu T, Tsunoda M, Aoki H, Kimura K. Analysis of volatile sulphur compounds in mouth air by gas chromatography. *Bull Tokyo Dent Coll*. 1978;19:43-52.
40. Suarez FL, Furne JK, Springfield J, Levitt MD. Morning breath odor: influence of treatments on sulfur gases. *J Dent Res*. 2000;79:1773-7.
41. Seemann R, Kison A, Mozghan B, Zimmer S. Effectiveness of mechanical tongue cleaning on oral levels of volatile sulfur compounds. *J Am Dent Assoc*. 2001;132:1263-7.
42. Kleinberg I, Codipilly DM. Cystein challenge testing: a powerful tool for examining oral malodour process and treatments *in vivo*. *Int Dent J*. 2002;52(3):221-8.
43. Quirynen M, Avontroodt P, Soers C, Zhao H, Pauwels M, Steenberghe D. Impact of tongue cleansers on microbial load and taste. *J Clin Periodontol*. 2004;31(7):506-10.
44. Tanaka M, Anguri H, Nishida N, Ojima M, Nagata H, Shizukuishi S. Reliability of clinical parameters for predicting the outcome of oral malodor treatment. *J Dent Res*. 2003;82:518-22.
45. Yaegaki K, Sanada K. Biochemical and clinical factors influencing oral malodor in periodontal patients. *J Periodontol*. 1992;63:783-9.
46. Tsai CC, Chou HH, Wu TL, Yang YH, Ho KY, Wu YM *et al*. The levels of volatile sulfur compounds in mouth air from patients with chronic periodontitis. *J Periodontol Res*. 2008;43:186-93.
47. Bosy A, Kulkarni GV, Rosenberg M, McCulloch CA. Relationship of oral malodor to periodontitis: evidence of independence in discrete subpopulations. *J Periodontol*. 1994;65(1):37-46.
48. De Boever EH, Loesche WJ. Assessing the contribution of anaerobic microflora of the tongue to oral malodor. *J Am Dent Assoc*. 1995;126(10):1384-93.
49. van Steenberghe D, Avontroodt P, Peeters W, Pauwels M, Coucke W, Lijnen A *et al*. Effect of different mouthrinses on morning breath. *J Periodontol*. 2001;72(9):1183-91.
50. Carvalho MD, Tabchoury CM, Cury JA, Toledo S, Nogueira-Filho GR. Impact of mouthrinses on morning bad breath in healthy subjects. *J Clin Periodontol*. 2004;31:85-90.
51. Young A, Jonski G, Rölla G. Inhibition of orally produced volatile sulfur compounds by zinc, chlorhexidine or cetylpyridinium chloride – effect of concentration. *Eur J Oral Sci*. 2003;111:400-4.
52. Gunsolley JC. A meta-analysis of six-month studies of antiplaque and antigingivitis agents. *J Am Dent Assoc*. 2006 Dec;137(12):1649-57. Review.
53. Pitts G, Brogdon C, Hu L, Masurat T, Pianotti R, Schumann P. Mechanism of action of an antiseptic, anti-odor mouthwash. *J Dent Res*. 1983;62(6):738-42.
54. Fine DH, Furgang D, Sinatra K, Charles C, McGuire A, Kumar LD. *In vivo* antimicrobial effectiveness of an essential oil-containing mouth rinse 12 h after a single use and 14 days' use. *J Clin Periodontol*. 2005;32:335-40.
55. Young A, Jonski G, Rölla G. A study of triclosan and its solubilizers as inhibitors of oral malodour. *J Clin Periodontol*. 2002;29:1078-81.
56. Moran J, Addy M. The effects of a cetylpyridinium chloride prebrushing rinse as an adjunct to oral hygiene and gingival health. *J Periodontol*. 1991;62:562-4.
57. Roberts WR, Addy M. Comparison of the *in vivo* and *in vitro* antibacterial properties of antiseptic mouthrinses containing chlorhexidine, alexidine, cetyl pyridinium chloride and hexetidine. Relevance to mode of action. *J Clin Periodontol*. 1981;8:295-310.

58. Ng W, Tonzetich J. Effect of hydrogen sulphide and methyl mercaptan on the permeability of oral mucosa J Dent Res. 1984;63:994-7.
59. Quirynen M, Avontroodt P, Soers C, Zhao H, Pauwels M, Coucke W *et al*. The efficacy of amine fluoride/stannous fluoride in the suppression of morning breath odour. J Clin Periodontol. 2002;29:944-54.
60. Young A, Jonski G, Rölla G, Wåler SM. Effects of metal salts on the oral production of volatile sulfur-containing compounds (VSC). J Clin Periodontol. 2001;28:776-81.
61. Frascella J, Gilbert R, Fernandez P. Odour reduction potential of a chlorine dioxide mouthrinse. J Clin Dent. 1998;9(2):39-42.
62. Richter JL. Diagnosis and treatment of halitosis. Compendium Contin Educ Dent. 1996;17:370-2, 374-6 passim; quiz 388.
63. Winkel EG, Roldán S, Van Winkelhoff AJ, Herrera D, Sanz M. Clinical effects of a new mouthrinse containing chlorhexidine, cetylpyridinium chloride and zinc-lactate on oral halitosis. A dual-center, double-blind placebo-controlled study. J Clin Periodontol. 2003;30:300-6.
64. Roldán S, Herrera D, Santa-Cruz I, O'Connor A, González I, Sanz M. Comparative effects of different chlorhexidine mouth-rinse formulations on volatile sulphur compounds and salivary bacterial counts. J Clin Periodontol. 2004;31:1128-34.