

Periodontal diseases as a source of halitosis: a review of the evidence and treatment approaches for dentists and dental hygienists

SOPHIE DE GEEST, ISABELLE LALEMAN, WIM TEUGHEL, CHRISTEL DEKEYSER & MARC QUIRYNEN

Halitosis, fetor ex ore, fetor oralis and bad breath are terms that are frequently used to designate any noxious smell arising from the oral cavity when breathing or speaking. As the etiology of halitosis is rather complex, it is not uncommon for a variety of medical disciplines to be consulted by patients with halitosis. However, recent studies have confirmed that 80–90% of the causes of bad breath originate in the oral cavity, and thus the term ‘oral malodor’ can be applied (17, 55, 86). The most common spaces where halitosis originates are bacterial niches, such as the posterior tongue dorsum, periodontal tissue sites (including the gingival sulcus, pathological pockets and interdental spaces), defective dental restorations, deep carious lesions and poorly maintained dentures (17, 55, 86). Other pathological conditions from oral sources that can influence or provoke bad breath include xerostomia, dental abscesses, candidiasis, oral tumors, necrotizing periodontal diseases and pericoronitis (39).

Oral malodor is primarily caused by the microbial degradation of both sulfur-containing and nonsulfur-containing amino acids derived from proteins in exfoliated human epithelial cells and white blood cell debris, or present in plaque, saliva, blood and tongue coatings (84, 86). The most active bacteria in this process are *Porphyromonas gingivalis*, *Treponema denticola* and *Tannerella forsythia*, anaerobic gram-negative bacteria that also have been associated with periodontal disease (48). Volatile sulfur

compounds are generated by the putrefaction of sulfur-containing amino acids (i.e. cysteine, cystine and methionine). Other volatile organoleptic compounds, such as indole, skatole, amines and ammonia, are produced by the putrefaction of non-sulfur-containing amino acids (i.e. tryptophan, lysine and ornithine) (60). Studies have shown that volatile sulfur compounds are the major contributors to bad breath (60, 87). Hydrogen sulfide, methyl mercaptan and, to a lesser extent, dimethyl sulfide, represent 90% of the volatile sulfur compounds in bad breath (42, 60, 87).

When an intra-oral cause of bad breath can be ruled out, other sources of extra-oral origin must be taken into account. As extra-oral causes are responsible for only about 5–10% of all cases of halitosis, the prevalence of extra-oral causes should be considered as rather low (17, 55). Nonbloodborne halitosis includes infections of the lower respiratory tract and ear, nose and throat pathologies, such as tonsillitis, sinusitis or impaction of foreign objects (17, 55). Bloodborne halitosis can be an indication of serious systemic disorders, such as uncontrolled diabetes, liver cirrhosis, kidney insufficiency or trimethylaminuria (83). In this last systemic condition, the concentration of dimethyl sulfide is often very high. Through a rising concentration of certain metabolites, gases can escape via the lung alveoli. Similarly, consumption of particular foods and beverages (e.g. garlic, onions and alcohol) or dietary habits (e.g. protein-

rich alimentation or starvation) can cause a blood-borne and transient bad breath.

The most basic approach used to measure bad breath is organoleptic scoring. Following olfactory stimulation, human judges immediately evaluate samples of an individual's breath odor. Despite the subjective character of this method and the lack of reproducibility (both inter- and intra-examiner), this method remains the 'gold standard' because the human nose can distinguish the largest variety of different odors. To overcome the subjectivity of this technique, gas chromatography has been introduced (86). As these types of measuring approaches are very expensive, complex, time consuming and require well-trained staff, they are considered unsuitable for daily use. Currently, less expensive and simpler-to-use portable sulfide monitors (70) and portable gas chromatographs (e.g. Oral Chroma™) are available. These devices give quantitative and objective measures and correlate well with the organoleptic scoring.

Patients with periodontal disease often complain about bad breath. Several clinical studies have investigated a possible relationship between halitosis and the development of periodontal disease. Hypotheses that volatile sulfur compounds can be responsible for an accelerated destruction of periodontal tissues have been proposed. Furthermore, the morphology of periodontal pockets creates an ideal environment for sulfur-producing bacteria.

The aim of this review was to summarize and evaluate the literature available on halitosis/bad breath with the specific aim of determining if there is a relationship between chronic periodontal disease and oral malodor. If this relationship exists, how do we interpret it? Furthermore, the approaches for treatment of bad breath and an evaluation of these different approaches will be presented.

Relationship between oral malodor and periodontal diseases

For decades, researchers have been intrigued by the question of whether or not there is a relationship between periodontal disease and bad breath (Table 1). One of the first to describe a correlation between hydrogen sulfide production and the occurrence of inflamed periodontal pockets was Rizzo in 1967 (66). He demonstrated that the highest concentrations of hydrogen sulfide were present in the deepest pockets. Ten years later, Tonzetich (87) showed that the increase of volatile sulfur compounds in

mouth air correlated with the number and depth of periodontal pockets greater than 3 mm. By curettage and corrective periodontal surgery, these concentrations could be reduced. In 1991, Rosenberg et al. (68) published a study including 41 subjects with bad breath. A 30% increase of steady-state volatile sulfur compound values was observed in patients with one or more pockets of >5 mm. However, the correlation (Pearson correlation analysis) between the presence of these pockets and both the organoleptic and volatile sulfur compound scores was very weak. As only a small number of subjects showed severe pocket formation, no association could be found between the number of pockets and malodor scores. Yaegaki & Sanada (96) investigated the composition of oral air in 31 subjects, to evaluate if an increase in production of volatile sulfur compounds would occur in cases of periodontal disease. They demonstrated elevated concentrations of volatile sulfur compounds in subjects with probing depths of ≥ 4 mm, especially with concentrations of methyl mercaptan. It has been suggested that methyl mercaptan has a pronounced effect on the permeability of oral mucosa (42). Methyl mercaptan can be dimerized to dimethyl sulfide, and as sulfides are considered to be highly cytotoxic, methyl mercaptan can accelerate disease progression (96). Similarly, in the study of Yaegaki & Sanada (96), the methyl mercaptan/hydrogen sulfide ratio was much higher in patients with probing depths of ≥ 4 mm. Likewise, the volatile sulfur compound production and methyl mercaptan ratio increased proportionally with the bleeding index, the latter indicating a larger extent of periodontal inflammation. The increase of both volatile sulfur compound production and the methyl mercaptan ratio could be reduced by tongue cleaning in healthy subjects as well as in patients with periodontitis. It must be mentioned that the amount of tongue coating was much larger in the group with periodontal disease. In patients with periodontitis, the production of volatile sulfur compounds was estimated to be more than four times that of controls and the methyl mercaptan/hydrogen sulfide ratio was also higher. Yaegaki & Sanada (96) concluded that in patients with periodontitis, larger amounts of volatile sulfur compounds, and of methyl mercaptan in particular, were present in the oral cavity, with the tongue coating as the main source.

In 1994, Bosy and colleagues examined 127 subjects to investigate the correlation between oral malodor, periodontal parameters and trypsin-like activity of periodontal pathogens using the BANA test (8). After comparing halitosis in subjects with and without peri-

Table 1. Literature overview of articles analyzing an association between oral malodor and periodontal diseases

Authors, (year, reference number)	No. of study participants	Correlation	No correlation
Rizzo (1967) (66)		Inflamed pockets associated with hydrogen sulfide production	
Tonzetich (1978) (87)		Number and depth of pockets >3 mm associated with volatile sulfur compounds (mouth)	
Rosenberg et al. (1991) (68)	41	Probing pocket depth >5 mm weakly associated with organoleptic score and volatile sulfur compounds	
Yaegaki & Sanada (1992) (96)	31	Bleeding index and probing pocket depth associated with volatile sulfur compounds and methyl mercaptan/hydrogen sulfide ratio. Tongue coating score associated with volatile sulfur compounds and methyl mercaptan/hydrogen sulfide ratio	
Bosy et al. (1994) (8)	127	Organoleptic score (tongue) and organoleptic score (plaque) associated with volatile sulfur compounds. Floss odor associated with volatile sulfur compounds	Probing pocket depth, gingival index and plaque index not associated with organoleptic score and volatile sulfur compounds
Kozlovsky et al. (1994) (33)	52	Probing pocket depth associated with organoleptic score (mouth). Gingival index associated with organoleptic score (saliva).	BANA results not associated with volatile sulfur compounds
Miyazaki et al. (1995) (38)	2672	Community Periodontal Index for Treatment Needs associated with volatile sulfur compounds (in subjects >45 years of age). Tongue coating score associated with volatile sulfur compounds	
De Boever & Loesche (1995) (6)	55	Organoleptic score (tongue) and organoleptic score (mouth) associated with tongue coating score. BANA (tongue) associated with organoleptic score (mouth) and organoleptic score (tongue)	Periodontal parameters not associated with organoleptic score (mouth). BANA (tongue) not associated with volatile sulfur compounds
Ratcliff & Johnson (1999) (60)		Volatile sulfur compounds associated with evolution to gingivitis/periodontitis	
Söder et al. (2000) (78)	1681	Bad breath associated with periodontal disease. Periodontal disease + malodor: increasing severity of disease, higher percentage of probing pocket depth >5 mm. Bad breath associated with calculus index, plaque index and dental visits	
Morita & Wang (2001) (40)	81	Probing pocket depth associated with volatile sulfur compounds and organoleptic score (weak). Bleeding index associated with volatile sulfur compounds and organoleptic score. Sulcular sulfide levels (low and moderate sites) associated with volatile sulfur compounds and organoleptic score	

Table 1. (Continued)

Authors, (year, reference number)	No. of study participants	Correlation	No correlation
Morita & Wang (2001) (39)		Bad breath associated with periodontal disease	
Figueiredo et al. (2002) (19)	41	Volatile sulfur compounds associated with organoleptic score (in group with periodontal disease)	Volatile sulfur compounds not associated with organoleptic score (in group without periodontal disease)
Stamou et al. (2005) (79)	71	Organoleptic score (mouth) associated with volatile sulfur compounds	Gingival index, plaque index and probing pocket depth not associated with organoleptic score and volatile sulfur compounds
Liu et al. (2006) (35)	2000	Modified sulcus bleeding index, calculus index and probing pocket depth associated with organoleptic score and volatile sulfur compounds. Plaque index associated with organoleptic score. Tongue coating score associated with volatile sulfur compounds and organoleptic score	
Rosenberg (2006) (71)		Tongue coating as a major source of pocket odor from exposed interdental plaque (floss odor)	
Calil et al. (2009) (10)	72	Tongue coating score associated with volatile sulfur compounds	Age, bleeding on probing, number of sites with probing pocket depth >4 mm not associated with volatile sulfur compounds
Tsai et al. (2008) (89)	72	Organoleptic score and volatile sulfur compounds associated with tongue coating score	Probing pocket depth, gingival index, percentage probing pocket depth >5 mm and clinical attachment level not associated with organoleptic score and volatile sulfur compounds. Plaque index not associated with volatile sulfur compounds
Quirynen et al. (2009) (55)	2000	Tongue coating score and probing pocket depth associated with organoleptic score and volatile sulfur compounds	
Takeuchi et al. (2010) (82)	823	Organoleptic score associated with tongue coating score, volatile sulfur compounds, methyl mercaptan/hydrogen sulfide ratio, periodontal parameters	
Apatzidou et al. (2013) (4)	78	Tongue coating score associated with volatile sulfur compounds and organoleptic score. Patients with periodontal disease at higher risk for halitosis, and higher numbers of <i>Porphyromonas gingivalis</i> in tongue coating	

odontal disease, they concluded that there were no statistically significant differences between the groups for any of the parameters measured. The presence of pockets was not associated with organoleptic scores or the levels of volatile sulfur compounds. Plaque and gingivitis indices were not associated with volatile sulfur compound levels and were only weakly associated with organoleptic scores. Although the intensity of oral malodor was 19% less in periodontally healthy patients, it was concluded that oral malodor can be present in subjects without periodontitis. The authors emphasized the importance of the tongue dorsum as the main source of oral malodor (8). BANA-positive organisms, which have been associated with periodontal diseases, were also found in healthy gingival sites and on the tongue surface of both healthy subjects and patients with periodontitis. What must be highlighted is the observation that a statistically significant association was found between oral malodor and floss odor, suggesting that interproximal odor does not originate from periodontal pockets but from local interdental plaque, acting as an indirect link between periodontal infections and oral malodor (8). A study by Kozlovsky et al. (33), of 52 Israeli adults, used the BANA test to investigate a possible association with oral malodor. Samples were taken from four loci (i.e. shallow pocket, deep pocket, tongue dorsum and saliva). Statistically significant correlations were found between whole-mouth odor and mean probing depth, and between saliva odor and gingivitis index. The results from the BANA samples were not associated with the results from the sulfide monitor, indicating the presence of other independent volatile organic compounds (e.g. cadaverine) in oral malodor. It was concluded that the BANA test could be useful as an adjunctive test to volatile sulfide measurements (33). Miyazaki et al. (38) found statistically significant correlations between volatile sulfur compound values with both the periodontal condition and the tongue-coating status. They suggested that whether periodontal disease is currently active would be a better criterion for oral malodor than the actual presence of deep periodontal pockets. In addition, they assumed that oral malodor is mainly caused by tongue coating in young people and by a combination of periodontal diseases and tongue coating in the older generation.

Another study that refuted a possible association between oral malodor and periodontal parameters was conducted by De Boever & Loesche (6). Despite the comparatively small study population ($n = 55$), they did find a link with mouth air odor and both tongue odor and the presence and extent of the tongue coating. They also showed that the surface

characteristics of the tongue can be related to the nature of the tongue coating, and in patients with deep fissures, a greater amount of bacterial load could be harbored to create an environment that would be well protected against the flushing actions of saliva. A negative relationship was described between malodor and periodontal parameters. Specifically, as the number and depth of pockets increased, the mouth odor decreased. The BANA scores could be correlated with full-mouth and tongue odor, but not with volatile sulfur compound scores, confirming the findings of Kozlovsky et al. (33) that possible volatile organoleptic compounds in mouth air can be detected using the BANA test, but not with the sulfide monitor.

In a study of 1681 subjects, Söder et al. (78) confirmed that bad breath has a statistically significant association with oral hygiene and periodontal disease. Periodontitis patients with halitosis had a more severe periodontal disease, expressed as the percentage of pockets ≥ 5 mm. Morita & Wang (40) investigated a possible relationship between sulcular sulfide levels and oral malodor in patients with periodontitis. They found statistically significant correlations between bleeding index and both the organoleptic and volatile sulfur compound scores. Furthermore, they demonstrated significant correlation of sulcular sulfide levels with volatile sulfur compound scores at sites with low to moderate bone loss. They presumed that volatile sulfur compounds at sites with severe bone loss were not being released into the oral cavity because of the greater depth of the pockets, as they did not show a significant correlation between bone loss and oral malodor. Figureido et al. (19) looked for a possible association between a positive BANA test and clinical parameters, including oral malodor. Their results showed statistically significant correlations between volatile sulfur compounds and both gingivitis scores and BANA scores of subgingival plaque, but only in periodontitis patients (i.e. those with pockets of >3 mm). In the control group (i.e. individuals with pockets of <3 mm), no relationship between volatile sulfur compounds and BANA scores could be found. No significant correlation was found between volatile sulfur compound levels and organoleptic ratings in the periodontitis group; however, such a correlation was confirmed in the control group. Likewise in the control group, a significant correlation was found between probing depth and volatile sulfur compound levels.

Stamou et al. (79) reported no significant correlations between gingival index, plaque index and probing depth with malodor scores or volatile sulfur compound scores. This study supported the opinion

of Bosy et al. (8) that it is more likely that an indirect factor, such as floss odor, induced by interdental plaque, is responsible for the relationship between oral malodor and periodontal disease.

An extensive study carried out by Liu et al. (35), in 2000 Chinese individuals, found statistically significant correlations between volatile sulfur compounds and tongue coating, modified sulcus bleeding index, calculus index and pocket depths. In addition, Tsai et al. (89) described a significant correlation between tongue coating and organoleptic scores and the concentrations of volatile sulfur compounds. No relationship with periodontal parameters could be found. Calil et al. (10) proposed the tongue dorsum as the main cause for oral malodor, although a weak association between volatile sulfur compound and periodontal parameters could be shown.

Another large-scale study of 2000 patients with halitosis, conducted by Quirynen et al. (55), did reveal a significant correlation between probing pocket depths and both organoleptic scores and volatile sulfur compounds. However, in only a small number of patients, gingivitis or periodontitis could be indicated as the single cause of halitosis (3.8% and 7.4% respectively). The most frequent cause of halitosis was tongue coating (43.3%). Sometimes, a combination of tongue coatings and periodontal disease was seen in patients with oral malodor (18.2%). A study carried out by Takeuchi et al. (82), in 823 Japanese individuals, confirmed the association between periodontal disease and oral malodor. The more severe the oral malodor became, the higher the scores of hydrogen sulfide, methyl mercaptan, dimethyl sulfide, the methyl mercaptan/hydrogen sulfide ratio and the total volatile sulfur compound levels.

A recent study by Apatzidou et al. (4) investigated the association between oral malodor and periodontal disease in the general population. They found that oral malodor was more likely to occur in patients with gingivitis or periodontitis. However, the tongue surface remained the most important source of oral malodor, both in periodontally healthy subjects and in patients with gingivitis or periodontitis. It was shown that compared with periodontally healthy individuals, patients with periodontitis harbored greater amounts of *P. gingivalis* on their tongue dorsum. If the amount of *P. gingivalis* increased by three-fold, the subject was twice as likely to experience halitosis (4).

It is clear that there are a wide variety of opinions regarding the interaction between periodontal diseases and halitosis. Numerous arguments for and against this interaction have been proposed, which makes reaching a final conclusion difficult, especially in view

of the complex interactions of several factors. Further details of these arguments are presented below.

FOR: malodor is primarily caused by anaerobic gram-negative microorganisms

Among the cultivable oral bacteria, the three most active producers of hydrogen sulfide *in vitro* are *P. gingivalis*, *T. denticola* and *T. forsythia* (48). These anaerobic gram-negative microorganisms are associated with periodontal disease. Several studies have used a BANA test to investigate a possible relationship between the presence of these bacteria and the development of bad breath and periodontal diseases (6, 8, 33, 40). A significant association was confirmed in the majority of these studies (6, 8, 40). The potential contribution of the not-yet cultivable microorganisms to the production of hydrogen sulfide is unknown.

FOR: pockets are putrid

In infected circumstances, gingival crevicular fluid production markedly increases. Rizzo found a correlation between hydrogen sulfide production and pocket inflammation, using strips of filter paper that were impregnated with lead acetate (66). The highest concentrations of hydrogen sulfide were present in the deepest pockets. Studies have also shown that the pocket bleeding index is positively correlated with volatile sulfur compound levels and/or specifically methyl mercaptan production, suggesting that malodor increases in cases of periodontal inflammation (35, 38, 40, 78, 96).

FOR: volatile sulfur compounds are toxic to gingival tissues

Volatile sulfur compounds can be toxic at low concentrations and within short periods of time because they contain thiols (-SH groups) that can chemically interact with DNA and proteins (60). After incorporation into the cellular fraction of saliva, volatile sulfur compounds facilitate the entry of other bacterial enzymes and antigens, such as lipopolysaccharide (endotoxin), into the underlying lamina propria by altering the permeability of the epithelial lining (42, 87). Furthermore, the reaction of hydrogen sulfide with collagen can alter the protein structure, thereby rendering the periodontal ligament and bone collagen more susceptible to destruction by proteases (42). It has been shown that in cases of gingivitis and periodontitis, there is a decrease in the content of

acid-soluble and total collagen in the affected tissues (74). These findings suggest that increased production of volatile sulfur compounds may accelerate the progression of periodontal disease.

FOR: an increased putrefaction of salivary sediment appears in patients with periodontal diseases

Most of the volatile sulfur compounds in saliva are produced from the salivary sediment, which contains epithelial cells, leucocytes and microorganisms. During putrefaction, thiol and disulfide groups can become accessible for production of volatile sulfur compounds. As the saliva of individuals with periodontal disease contains higher total numbers and greater proportions of damaged epithelial cells and leucocytes, it is possible that patients with periodontal disease generate an objectionable odor more rapidly than those who do not (87).

AGAINST: periodontally healthy subjects can have halitosis

It is not surprising that even periodontally healthy patients can present with levels of bad breath. Every niche where food is retained is a possible source for putrefaction and production of volatile sulfur compounds (39). Bosy et al. (8) suggested that the oral malodor levels of patients with periodontitis are not different from those of periodontally healthy patients, which would imply that volatile sulfur compounds are unlikely to be indicative for the presence of periodontitis.

AGAINST: tongue coatings are the major cause of oral malodor

In a number of studies the tongue dorsum is considered as the principal source of volatile sulfur compound production, both in healthy and in periodontally affected patients (6, 8, 10, 89, 96). Tongue coatings contain desquamated epithelial cells, blood cells and bacteria, creating a perfect environment to nourish production of volatile sulfur compounds. Owing to its anatomy, the tongue dorsum has no self-cleaning surface. Because of its numerous depressions, bacteria can adhere to and grow on the surface and at the same time they are protected from the flushing action of saliva. Over time, an anaerobic environment is created by an increased thickness of tongue coating, and the colonization of certain microorganisms is favored. A study by De Boever

et al. (6) concluded that individuals with deep fissures had twice the total counts of bacteria, had significantly higher mouth-odor scores and emitted significantly more odor from their tongues. Tongue cleaning is more effective than brushing the teeth, which is why it has the highest priority in reducing oral malodor. By tongue cleaning, the levels of volatile sulfur compounds can be reduced by up to 75% (87). The formation of tongue coating is related to several factors, of which the level of oral hygiene is the strongest. Other parameters, such as smoking, periodontal status, saliva characteristics, dietary habits and use of a denture, may also contribute to the formation of tongue coatings (88).

FOR: the prevalence and contribution of tongue coatings are higher in patients with periodontitis

Patients with periodontal disease produce more tongue coatings than do subjects without periodontal disease (96). Moreover, it is estimated that volatile sulfur compound production from tongue coatings is four times greater in patients with periodontal disease than in periodontally healthy patients. The increase of the methyl mercaptan/hydrogen sulfide ratio in periodontally diseased vs. healthy subjects has been reported to be in particular more pronounced (31.3 vs. 1.0, $P < 0.01$) (96). After tongue cleaning, the production of total sulfur is decreased significantly, as is the mercaptan/hydrogen sulfide ratio (96). However, because of the high concentration of methyl mercaptan in periodontally diseased patients, it has been suggested that tongue coatings and plaque in periodontal pockets are important contributors to the total methyl mercaptan production in the oral cavity. Moreover, patients with periodontal disease harbor greater amounts of *P. gingivalis* on the tongue dorsum. The amount of *P. gingivalis* on the tongue dorsum of these patients was significantly associated with bad breath (4).

AGAINST: periodontal pockets are partially sealed, and the mass transfer of gases is low

In contrast to the argument that pockets are putrid, their contribution to oral malodor is negligible, for several reasons. As the periodontal pocket is considered a near-closed environment and the surface area of pockets is rather small, only a limited fraction of malodorous compounds can escape. A study by Morita & Wang (40) suggests that gases from deep

pockets are not even released into the oral cavity and will therefore not contribute to oral malodor. In a guest editorial, Rosenberg (71) concurred with the opinion of Bosy et al. (8), who suggested that the smell deriving from the interproximal spaces originates from interdental plaque rather than from periodontal pockets. In fact, in the study of Bosy et al. (8), oral malodor was related to floss odor, but not to periodontal parameters. This might be another useful argument to motivate patients to start cleaning in between their teeth.

AGAINST: tongue cleaning reduces volatile sulfur compound levels by more than 70%

Treating malodor starts with reducing the presence of anaerobes through oral-hygiene instruction and through both periodontal and general dental health-care. An early study demonstrated that tongue cleaning reduces volatile sulfur compound levels by up to 75%, whereas toothbrushing only can reduce volatile sulfur compound levels by 25% (87). This is why tongue cleaning has the greatest priority in the treatment of bad breath, and therefore tongue coating is considered as the main source of oral malodor. The importance of flossing in reducing oral malodor has been shown by Bosy et al. (8), as patients who floss will show less oral malodor than those who do not floss. In periodontally involved sites, reductions of volatile sulfur compound levels can be achieved after curettage and corrective surgery (87). Pham et al. (50) investigated oral malodor treatment options in patients with periodontal diseases and concluded that the most important improvement was achieved after periodontal treatment. Tongue cleaning alone was only successful in patients with gingivitis (50). Other than mechanical treatment options, additional reductions of volatile sulfur compound levels can be obtained by antibacterial agents such as chlorhexidine (8, 68). Other commercial mouthwashes, designed to reduce halitosis, often contain zinc components. Tonzetich (87) described a mouthwash which prevents oral malodor, contains zinc ions that have the capability to bind to thiol groups of enzymes, substrates and volatile sulfur compounds, and, in addition, inhibit the conversion of disulfide groups to thiols. The disadvantage of using such chemical agents is that no reductions in pocket depth and gingival inflammation are achieved, even though significant reductions in malodor and volatile sulfur compounds are observed (8). In addition, the agents in these mouthrinses cannot access deeper periodon-

tal pockets (79). A one-stage full-mouth disinfection (i.e. scaling and root planing of all pockets within 24 h plus irrigation of chlorhexidine in all intraoral niches and use of a chlorhexidine mouthwash during 2 months), as described by Quirynen et al. (56), can yield more rapid and additional reductions of organoleptic scores and improvement in periodontal parameters.

Treatment of halitosis

The treatment of oral malodor is based on a cause-related strategy. Oral malodor is engendered by microorganisms that cause metabolic degradation of sulfur-containing amino acids, present in available proteins, into malodorous gases. Treatment strategies can include: (i) masking the malodor; (ii) mechanical reduction of intraoral nutrients, substrates and microorganisms; (iii) chemical reduction of the oral microbial load; (iv) rendering malodorous gases nonvolatile; and (v) chemical degradation of the malodorous gases.

The general approach should be focused on reducing the bacterial load as well as the load of micronutrients by effective mechanical oral-hygiene procedures, including tongue scraping. Periodontal diseases should be treated and controlled. Oral rinses containing chlorhexidine and other ingredients may further reduce the oral malodor. If, after conscientious succession of these approaches, breath malodor persists and intraoral sources can be excluded, other (extraoral) sources of malodor, such as ear, nose and throat pathologies, lung diseases, gastrointestinal diseases and metabolic abnormalities (e.g. diabetes) should be investigated.

Masking the malodor

Masking agents are frequently used to cover halitosis, because of their instant relieving effect and commercial accessibility. Studies have shown, however, that the use of mouthrinses, sprays and lozenges containing volatiles with an agreeable odor only have a short-term effect (63, 65). Most common are mint-containing lozenges or other aromas present in rinses, which generally do not contain any antibacterial agents (16).

Another pathway used to mask the malodor is to increase the solubility of malodorous compounds in the saliva by stimulating the secretion of saliva because of the simple fact that larger saliva volumes allow increased amounts of volatile sulfur compounds to enter solution (30). This can be accom-

plished by ensuring a sufficient liquid intake or by using chewing gum, as chewing triggers the periodontal–parotid reflex.

Mechanical reduction of intraoral nutrients and microorganisms

The importance of tongue cleaning has already been emphasized because of the extensive accumulation of bacteria on the tongue dorsum (13, 72, 97). Previous investigations demonstrated that tongue cleaning reduces both the amount of coating (including bacterial nutrients) and the number of bacteria, and thereby effectively reduces oral malodor (6, 23, 24, 26, 59). Other reports indicate that the reduction of microbial load on the tongue after cleaning is negligible and that malodor reduction probably results partially from the reduction of bacterial nutrients (37, 54). Cleaning of the tongue can be carried out with a regular toothbrush, but in cases where a coating is established, a tongue scraper is preferred (46, 47). Tongue cleaning using a tongue scraper can reduce the volatile sulfur compound levels by up to 75% after 1 week (47). To prevent soft-tissue damage, scraping should be considered as gentle cleaning. As the posterior part of the tongue shows the greatest accumulation of coating (69), it is recommended to clean as far backwards as possible without injuring the circumvallate papillae. Tongue cleaning should be repeated until no more coating material can be removed (14). Gagging reflexes can be provoked, especially when using brushes (54), but practice will help to prevent this (12). It can also be helpful to pull out the tongue with a gauze pad. Tongue cleaning has the additional benefit of improving taste sensation (54, 95).

Toothbrushing and interdental cleaning are essential mechanical agents of dental plaque control. Both activities remove organisms and residual food particles that cause putrefaction. However, clinical studies have shown that the mechanical action of toothbrushing alone has no appreciable influence on the concentration of volatile sulfur compounds (81). Tonzetich & Ng (85) showed a short-term effect in bad breath reduction after brushing with a sodium monofluorophosphate-containing toothpaste. The effect was less than half of what was observed when combined with tongue brushing (30% and 73% reduction in volatile sulfur compounds, respectively).

In cases where chronic oral malodor appears with the presence of periodontitis, additional periodontal therapy is, of course, required (8, 15, 49, 96). A one-stage full-mouth disinfection, combining scaling and

root planing with the application of chlorhexidine, can reduce the organoleptic malodor levels by up to 90% (56). In a more recent study by the same authors, initial periodontal therapy alone had only a weak impact on the volatile sulfur compound levels, except when combined with a mouthrinse containing chlorhexidine (57).

Chewing gum may control bad breath temporarily because it triggers the salivary flow (63). The salivary flow by itself has, besides its antimicrobial effect, also a mechanical cleaning capability. Not surprisingly, subjects with an extremely low salivary flow rate have higher volatile sulfur compound levels and tongue coating scores than do those with normal saliva production (31). Waler (91) showed that chewing a gum without any active ingredient can result in a modest reduction of halitosis.

Chemical reduction of oral microbial load

Next to toothbrushing, mouth rinsing has become a common oral-hygiene practice (21). Every year, over 500 million dollars are spent in the USA on mouthwashes and sprays to combat halitosis. Formulations have been modified to carry antimicrobial and oxidizing agents in order to inhibit the process of oral malodor formation. The active ingredients usually include antimicrobial agents such as chlorhexidine, cetylpyridinium chloride, essential oils, chlorine dioxide, triclosan, amine fluoride/stannous fluoride, hydrogen peroxide and baking soda. Some of these agents have only a temporary effect on the total number of microorganisms in the oral cavity.

Chlorhexidine

Chlorhexidine is considered the most effective antiplaque and antigingivitis agent (1–3, 7, 29). Its antibacterial action can be explained by disruption of the bacterial cell membrane by the chlorhexidine molecules, increasing permeability and resulting in cell lysis and death (29, 34). Because of its strong antibacterial effects and superior substantivity in the oral cavity, chlorhexidine rinsing results in a significant reduction of volatile sulfur compound levels and organoleptic ratings (11, 67, 68, 80, 100).

Essential oils

A study evaluating the short-term effect (3 h) of a Listerine rinse (which contains essential oils), found Listerine to be only moderately effective against oral malodor ($\pm 25\%$ reduction vs. 10% for placebo, of volatile sulfur compounds at 30 min after rinsing)

and to cause a sustained reduction in the levels of odorogenic bacteria (51). Similar reductions in volatile sulfur compounds were found after rinsing for 4 days (11).

Two-phase oil–water rinse

Rosenberg et al. (67) designed a two-phase oil–water rinse containing cetylpyridinium chloride. The efficacy of oil–water–cetylpyridinium chloride formulations is thought to result from the adhesion of a high proportion of oral microorganisms to the oil droplets, which is further enhanced by the cetylpyridinium chloride. A twice-daily rinse with this product showed reductions in both volatile sulfur compound levels and organoleptic ratings. These reductions were superior to Listerine and significantly superior to a placebo (32, 67).

Triclosan

Triclosan, a broad-spectrum antibacterial agent, has been found to be effective against most oral bacteria and has a good compatibility with other compounds used for oral home care. A pilot study demonstrated that an experimental mouthrinse containing 0.15% triclosan and 0.84% zinc produced a stronger, and more prolonged, reduction in bad breath than a Listerine rinse (61). However, the anti-volatile sulfur compound effect of triclosan seems to be strongly dependent on the solubilizing agents (99). Flavoring oils or anionic detergents and copolymers are added to increase the oral retention and decrease the rate of release in toothpaste formulations containing triclosan. The effect of these toothpaste formulations in oral malodor has been illustrated in several studies (28, 44, 45, 75, 76). Significant reductions of the breath scores were observed after a single use, as well as after 1 week (28% and >50%, respectively), with similar effects on the volatile sulfur compound levels (57% reduction after 1 week).

Amine fluoride/Stannous fluoride

Stannous fluoride has been shown to be effective in the management of oral malodor as a component of a dentifrice for reducing both organoleptic scores and volatile sulfur compound levels (22). A superior short-term and overnight benefit of a stannous-containing dentifrice compared with a control dentifrice on morning bad breath has been recently demonstrated in a meta-analysis (18). The association of amine fluoride with stannous fluoride (amine fluoride/stannous fluoride) resulted in encouraging reductions of morning breath odor, even when oral hygiene was insufficient (53). Recently, new evidence supporting the use

of this amine fluoride/stannous fluoride rinse became available. The formulation showed short- and long-term effects on malodor indicators in patients with obvious malodor (16).

Hydrogen peroxide

Suarez et al. (81) demonstrated that rinsing with 3% hydrogen peroxide produced impressive reductions ($\pm 90\%$) in sulfur gases, which persisted for 8 h. However, side effects (including oral ulcerations) of the routine use of hydrogen peroxide mouthrinses have been reported (62). In addition, there is some concern about the potential carcinogenic effects of hydrogen peroxide (36, 41, 64, 92).

Oxidizing lozenges

Greenstein et al. (25) reported that sucking a lozenge with oxidizing properties can reduce tongue dorsum malodor for 3 h. This antimalodor effect may be caused by the activity of dehydroascorbic acid, which is generated by peroxide-mediated oxidation of ascorbate present in the lozenges.

Baking soda

Baking soda dentifrices have been shown to achieve a significant odor-reducing benefit for time periods up to 3 h (9, 43). The mechanisms by which baking soda inhibits oral malodor are related to its bactericidal effects (52).

Conversion of volatile sulfur compounds

Metal salt solutions

Some metal ions are efficient in capturing sulfur-containing gases. Zinc is an ion with two positive charges (Zn^{++}), which can bind to the twice-negatively loaded sulfur radicals and thus reduce the expression of the volatile sulfur compounds. The same applies for other metal ions, such as stannous, mercury and copper. Clinically, the comparative volatile sulfur compound inhibitory effect is $CuCl_2 > SnF_2 > ZnCl_2$. *In vitro*, the comparative inhibitory effect is $HgCl_2 = CuCl_2 = CdCl_2 > ZnCl_2 > SnF_2 > SnCl_2 > PbCl_2$ (98). Compared with other metal ions, zinc is relatively nontoxic, noncumulative, gives no visible discoloration and is one of the ingredients most commonly studied for the control of oral malodor (91, 98). Schmidt & Tarbet (73) reported that a rinse containing zinc chloride was remarkably more effective than a saline rinse (or no treatment) in reducing the levels of both volatile sulfur compounds

($\pm 80\%$ reduction) and organoleptic scores ($\pm 40\%$ reduction) for 3 h. Halita[®], a mouthrinse containing 0.05% chlorhexidine, 0.05% cetylpyridinium chloride and 0.14% zinc lactate, has been demonstrated to be more effective than a 0.2% chlorhexidine formulation in reducing the volatile sulfur compound levels and organoleptic ratings (58, 80). The effect of Halita[®] may result from the volatile sulfur compound conversion ability of zinc, besides its antimicrobial action. The combination of Zn⁺⁺ and chlorhexidine seems to act synergistically (100). The addition of zinc ions to a basic formulation containing amine fluoride and stannous fluoride caused a short- and long-term reduction of oral malodor indicators in volunteers with morning bad breath (93, 94) as well as in volunteers with obvious halitosis (16).

In a study by Hoshi & van Steenberghe (27), a zinc citrate/triclosan toothpaste applied to the tongue dorsum appeared to control morning breath malodor for 4 h. However, if the flavor oil was removed, the antimalodor efficacy of the active ingredients decreased. Another clinical study reported a reduction of up to 41% in volatile sulfur compound levels after 7 days' use of a dentifrice containing triclosan and a copolymer, but the benefit compared with a placebo was relatively small (17% reduction) (45). Similar reductions were also found in two other, more recent, studies (28, 44).

Chewing gum is often formulated with antibacterial agents, such as fluoride or chlorhexidine, helping to reduce oral malodor through both mechanical and chemical approaches. Tsunoda et al. (90) investigated the mode of action of chewing gum containing tea extracts. The chemical reaction between epigallocatechin, the main deodorizing agent among the tea catechins, and methyl mercaptan, resulted in a nonvolatile product. Waler (91) compared different concentrations of zinc in a chewing gum and found that retention of chewing gum, containing 2 mg of Zn⁺⁺ acetate, in the mouth for 5 min resulted in an immediate reduction in the volatile sulfur compound levels of up to 45%, but the long-term effect was not mentioned.

Chemical degradation of the malodorous gases

Chlorine dioxide

Chlorine dioxide and chlorite anion are powerful oxidizing agents that can combat bad breath by the oxidation of hydrogen sulfide and methyl mercaptan to nonmalodorous compounds. Through this oxidation, the precursor amino acids methionine and cysteine

are consumed (77). The chlorite anion has a strong bactericidal effect on odorogenic microorganisms (77). Studies have shown that the single use of a chlorine dioxide-containing oral rinse only slightly reduces mouth odor (20, 77). A recent study by Aung et al. (5) showed that a chlorine dioxide mouthwash reduced the levels of volatile sulfur compounds significantly and kept these volatile sulfur compound levels low during the study period of 4 weeks. In addition, tongue coatings were significantly reduced when using a chlorine dioxide mouthwash without tongue cleaning (5).

Conclusions

Halitosis is a complex phenomenon that is mainly a problem of oral origin. The oral origin of halitosis is supported by the observation that pathogenic oral bacteria are able to putrefy a variety of substrates, including plaque, food debris and epithelial cells, which are present in a variety of oral niches, but mostly on the tongue dorsum. The presence and amount of tongue coating is therefore crucial in oral malodor. On the other hand, the role of periodontal diseases has not been fully ruled out. Epidemiological data have shown that periodontal diseases can be an additional, but less important, cause of oral malodor as not all periodontally affected patients will have oral malodor, and periodontally healthy patients can present with malodor. In a small number of patients, gingivitis or periodontitis can be the single cause of halitosis. Several studies suggest that it is more likely that inflamed periodontal tissue (as measured by the bleeding index), rather than the depth of pockets, is related to the formation of volatile sulfur compounds. As interdental spaces become larger in periodontally affected patients, more food is impacted and putrefaction becomes prevalent. Moreover, patients with periodontitis harbor specific periodontal pathogens, which have been associated with oral malodor. It is a logical consequence that these organisms will settle on other surfaces where they can grow and multiply. Therefore, the tongue dorsum is an ideal environment for the generation of oral malodor. In addition, studies in patients with periodontitis have shown that with more tongue coating there is a greater prevalence of *P. gingivalis* and levels of volatile sulfur compounds.

Toxic volatile sulfur compounds are able to damage the periodontal tissues, creating even more loss of attachment. There is a mutual reinforcement of the loss of periodontal attachment and production of

volatile sulfur compounds, resulting in a vicious cycle. To break this cycle, an optimal oral hygiene regimen is required. The key message to patients is to clean the tongue surface regularly because this approach reduces the levels of volatile sulfur compounds by more than 70%. Additional reductions of volatile sulfur compound levels can be achieved by periodontal treatment and the use of mouthwashes.

Chlorhexidine remains the most efficient anti-plaque and anti-gingivitis agent. Other antimicrobial products that contain cetylpyridinium chloride, essential oils, chlorine dioxide, triclosan, amine fluoride/stannous fluoride, hydrogen peroxide, baking soda and metal ions (Zn⁺⁺) may also be effective anti-plaque and anti-gingivitis agents. Some of these agents only have a temporary effect on the total number of microorganisms in the oral cavity. Zn⁺⁺ and chlorhexidine seem to act synergistically. Chewing gum can reduce bad breath by increasing salivary flow and enhancing the solubility of malodorous compounds in the saliva. However, this effect is transient.

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