## **Review Article**

# Oral malodor: A review of etiology and pathogenesis

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### **ABSTRACT**

Oral malodor or halitosis is a condition characterized by unpleasant odors emanating from the oral cavity. The aim of the present review is to classify and explain the etiology and pathogenesis of oral malodor. Volatile sulfur compounds (VSCs) that result from bacterial breakdown of protein are considered to be the main culprits for this foul odor. The etiology of oral malodor can be attributed to both systemic and oral conditions. However, nearly 85% of the cases originate from mouth due to tongue coating (especially posterior third of the dorsal surface), periodontal disease, poor oral hygiene, infections, ulcerations, food debris, dry mouth and faulty restorations. Bad breath can be caused by systemic disorders such as upper and lower respiratory tract infections; hepatic, pancreatic, and nephritic insufficiencies; trimethylaminuria and some medications. In addition, there are very few instances where patients suffer from pseudohalitosis or halitophobia.

Key words: Benzoyl-DL-arginine-napthylamide, gas chromatography, halitosis, oral malodor, organoleptic, volatile sulfur compounds

### INTRODUCTION

Do you mind if I sit back a little? Because your breath is very bad.

Donald Trump

Bad breath is a source of embarrassment in social circles. A person having bad breath could be a subject of mockery and may therefore suffer from emotional and psychological distress. In spite of its unfortunate consequences, it has received more attention in fiction than in the scientific literature. Malodor is the scientific term for bad breath and has its origin from Latin ("malus," bad, evil + "odorem, odor," smell, scent)<sup>[1]</sup> and defined as a distinctive smell that is offensively unpleasant. *Oral malodor* is perceptibly

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unpleasant or offensive odors emanating from the mouth while exhaling during breathing and *per se* does not imply any particular cause or source.<sup>[2]</sup>

Halitosis is a medical term, first coined by the Listerine Company in 1921, to describe oral malodor or bad breath (in fact Listerine was first formulated by Lister in 1879 as a surgical antiseptic and then by Dr. Joseph Lawrence and Jordan Wheat Lambert in 1879. It was given to dentists for oral care in 1895 and became the first over-the-counter mouthwash sold in the United States in 1914).<sup>[3]</sup> Oral halitosis is the specific term used to define halitosis with an origin within the oral cavity.

Etymologically, halitosis is actually a combination of the Latin "halitus", for breath and related to "halare", to breathe and the Greek suffix "osis" to describe a medical condition. Though literally, it means a condition of breath, it is generally understood to mean offensive breath.<sup>[1]</sup>

Other synonyms for this malodorous condition include: *Foetor oris* (Latin "foetere," to stink + "oris," oral cavity), *ozostomia* (Greek "*ozein*", to smell + "*stoma*", mouth), *bromopnoea* (Greek "*bromos*," stench + "*pnein*," to breathe), *stomatodysodia* (Greek "*stoma*," mouth + "*dys*," bad + "*odoia*," condition of odor), bad breath, foul breath and breath malodor. [2,4]

However, according to some, though these are detected from the mouth, the terms are not synonymous. Ozostomia refers to a putrid smell that is derived from the upper respiratory tract whereas stomatodysodia indicates foul breath originating from local areas in the lower respiratory tract, particularly below the caryna from the bronchi, bronchioles and alveoli, or other contiguous parts of the lung, e.g., pleura. [5]

### **CLASSIFICATION OF HALITOSIS**

Oral malodor can be classified according to its duration as temporary (exogenous) or persistent (endogenous).<sup>[6]</sup> Temporary malodors are caused by certain foods (e.g., garlic) or drinks for transient period after consumption and that will only last 24-72 h. These external substances when ingested get absorbed into the circulatory system and release of odors through breathing and saliva. The best way to control this type of malodor is to refrain from ingesting and avoiding the offending substances.<sup>[7]</sup> On the other hand, persistent or endogenous malodor is primarily due to proteolytic, anaerobic, Gramnegative bacteria which cause protein digestion and produce several fetid substances that is, volatile sulfur compounds (VSCs), primarily hydrogen sulfide (H<sub>2</sub>S) and methyl mercaptan.[8]

According to its etiology, oral malodor can be classified<sup>[9-12]</sup> as [Figure 1]:

- Genuine halitosis: Obvious malodor with intensity which is beyond socially acceptable level.
  - Physiologic: Malodor that originates in the oral cavity and not caused by any specific disease or pathologic condition. The main source of origin is likely to be dorsum of the tongue.
  - Pathologic, oral: Halitosis caused by disease or pathologic processes related to the oral cavity.
  - Pathologic, extra-oral: Malodor caused by disease or pathologic processes related to nasal, paranasal and/or laryngeal regions.

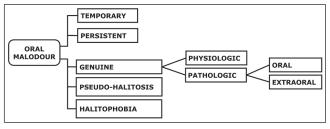


Figure 1: Classification of oral malodor

- Pseudohalitosis: There is no obvious malodor perceived by others, but the patient believes that he or she has oral malodor.
- Halitophobia: Patient complains of malodor which is not perceived by others. Halitophobia is characterized by a patient's persistent belief that he or she has halitosis despite reassurance, treatment and counseling.

Pseudohalitosis can be treated by dental practitioners, but halitophobic patients must be referred to psychological specialists. Moreover, studies have shown that 20% of subjects diagnosed with genuine halitosis were considered to be provisionally neurotic and patients with physiologic halitosis showed significantly higher symptoms of depression than those with oral pathologic halitosis.<sup>[13]</sup>

# AETIOPATHOGENESIS OF ORAL MALODOUR

One of the common myths about oral malodor is that it originates in the stomach, which is seldom the case. The esophagus, which connects the stomach with the mouth, is not an open tube and is normally collapsed,<sup>[14]</sup> thereby, preventing odorous gases to escape from the stomach to the mouth.

Although several extraoral sites and systemic conditions have been implicated in the source of oral malodor, in 80-90% of cases the site of origin is oral cavity. [4,15] In a recent study of 2000 patients who visited a multidisciplinary bad breath clinic in Leuven, Belgium, an oral cause was found in nearly 76% of the patients, especially tongue coating (43%), gingivitis/periodontitis (11%) or a combination of the two (18%). Pseudo-halitosis/halitophobia was diagnosed in 16% of the cases; and ENT/extra-oral causes were found in 4% of the patients. [16] Table 1 presents the list of possible etiological factors responsible for oral malodor.

The cause of bad breath is most likely to originate from the dorsoposterior region of the tongue, even in individuals who maintain excellent oral hygiene, good dentition and a healthy periodontium.<sup>[17]</sup>

The irregular and deeply fissured posterior dorsum of the tongue provides favorable conditions to support bacterial growth and not surprisingly, harbors the

#### **TABLE 1: CAUSES OF ORAL MALODOR**

Genuine

Physiologic

Diet – vegetables such as onions, garlic,

radishes, turnips and leeks

Beverages such as tea and coffee

Alcohol-based wine, brandy, whisky, liqueurs and beer

Dairy products that contain protein

Dehydration, starvation, constipation, diarrhea

**Pathologic** 

Local oral

Tongue coating (poor oral hygiene)

Gingivitis-ANUG, acute herpetic gingivostomatitis

Periodontitis

Xerostomia (e.g. from drugs, Sjögren's

syndrome, radiotherapy, chemotherapy)

Pericoronitis

Candidiasis

Oral sepsis

Oral cancer

Bone diseases — dry socket, osteomyelitis, osteonecrosis

Debris under dental appliances (e.g., dentures,

removable orthodontic appliances, bridges)

Extraoral (nonoral systemic conditions)

**ENT** 

Postnasal drip

Tonsillitis, tonsilloliths

Rhinitis, rhinoliths

Sinusitis, antral malignancy

Nasal polyps, carbuncle, carcinoma

Nasal obstruction/foreign bodies

Other systemic factors

 $\label{lem:lemma$ 

bronchial carcinoma, pulmonary infarcts and its sequelae

Renal - renal failure, uremia

Hepatic - cirrhosis, gall bladder dysfunction, hepatic failure

Renal failure

 ${\sf Carcinomas}\ ({\sf various}\ {\sf types}) - {\sf bronchial}\ {\sf carcinoma}$ 

Diabetic ketoacidosis — acetone breath

of uncontrolled diabetes

Trimethylaminuria — fish odor syndrome

 ${\sf Gastro-intestinal-esophageal\ reflux,\ pyloric\ stenosis,}$ 

hiatal hernia, malabsorption syndrome, enteric infection

Other systemic conditions - dehydration, starvation, Sjögren's syndrome, leukemias and other blood dyscrasias

Medications — antihistamines/decongestants, antidepressants,

anxiolytics, anticholinergics, antipsychotics etc

Halitophobia

Pseudo-halitosis

Idiopathic

ANUG = Acute necrotizing ulcerative gingivitis

highest amounts of anaerobic bacteria that could explain for being the most common location for oral halitosis.<sup>[18]</sup>

There is change in focus from individual bacteria to complex biofilms, which thrive in these niches such as the posterior dorsum of the tongue, gingival sulcus, periodontal pockets and tonsillar tissue.<sup>[7,19,20]</sup> Persons with periodontitis and gingivitis, are known to be more malodorous.<sup>[21,22]</sup> Other factors of the mouth that contribute to halitosis include imperfect dental restorations, food impactions and abscesses.<sup>[23]</sup> Dentures are another important cause of oral malodor, particularly if they are worn overnight.<sup>[24]</sup> Usually, the odor has a somewhat sweet, but unpleasant character and is readily identifiable, particularly if the dentures are placed in a plastic bag and smelled after several minutes.<sup>[25]</sup> Following tongue care maintenance and overnight removal of dentures, patients' oral malodor levels decrease significantly.<sup>[24]</sup>

Oral malodor is related to the salivary flow. Bad breath levels during the day are inversely related to salivary flow.[26] Xerostomia or dry mouth is considered to be a major contributory factor in the production of oral malodor because reduced salivary flow weakens the normal cleansing mechanism of the mouth and predisposes the oral flora toward the Gram-negative organisms responsible for the malodor.[27,28] In fact, the so-called called morning breath is considered to be oral malodor caused by reduced salivary flow during sleep. [29] Salivary flow is lowest overnight, due to fasting and insufficient water intake, leading to an increase in halitosis intensity. Conversely, mastication increases saliva flow, with concomitant cleansing of the oral cavity and reduction in malodor.[30] Understandably, medications that reduce salivary flow abet halitosis.

However, not all agree with the view that dry mouth is linked to the production of oral malodor. Koshimune *et al.*<sup>[31]</sup> did not find significant correlation between the level of VSCs and salivary flow rate. However, subjects with extremely low resting salivary flow rates had significantly higher methyl mercaptan (CH<sub>3</sub>SH) and H<sub>2</sub>S concentrations and tongue-coating scores than those with higher resting salivary flow rates. It has been suggested that a reduction of reduced salivary flow might influence the production of tongue coating and the periodontal health and that oral malodor was caused by the interaction of multiple risk factors.<sup>[32]</sup>

A wide range of nonoral causes also been reported to cause halitosis which include ear-nose-throat (ENT) infections, ulcerations and tumors in the respiratory or gastrointestinal tract, certain systemic diseases,

metabolic disorders and carcinomas.<sup>[33]</sup> Nasal malodor (rhinohalitosis) may be indicative of either nasal infection or a problem affecting airflow associated with thick mucus secretions. Patients with excessive postnasal drip are more prone to bad breath, though it may not be indicative of any frank nasal infection or other nasal pathology. Although postnasal drip might not smell initially, its subsequent putrefaction by abundant flora at the posterior tongue renders it malodorous.<sup>[25]</sup>

As a compounding factor, persons with sinus conditions often breathe through their mouths secondary to nasal congestion. The drying effect of mouth-breathing creates an environment that promotes bad breath. This may be further compounded by the anticholinergic effect of antihistamines many sinus sufferers take.<sup>[7]</sup> Dilated and deep tonsillar crypts may also contain tonsilloliths (soft, fetid stones, usually several millimeters in diameter, rough-edged and white or yellowish in color) which themselves have a foul odor, particularly when pressed.<sup>[25]</sup>

The most likely pathogenesis of halitosis is microbial putrefaction of food debris, defoliated epithelial

# TABLE 2: BACTERIA ASSOCIATED WITH ORAL MALODOR

Actinomyces species Aggregatibacter Atopobium parvulum actinomycetemcomitans Bacteroides forysthus (formerly Actinobacillus Campylobacter rectus actinomycetemcomitans) Dialister species Bacteroides (Bacteroides) Eikenella corrodens loescheii Enterobacteriaceae Centipedia periodontii Eubacterium limosum Desulfovibrio species Fusobacterium nucleatum Eubacterium sulci Granulicatella elegens Firmicutes species Peptosteptococcus anaerobius Fusobacterium periodonticum Porphyromonas endodontalis Micros prevotti Prevotella intermedia Peptostreptococcus micros Prevotella loescheii Porphyromonas gingivalis Solobacterium moorei Prevotella (Bacteroides) Staphylococcus warneri melaninogenica Veillonella species Selenomonas artermidis Vibrio species Tannerella forsythia (formerly Bacteriodes forsythus) Treponema denticola Unidentified oral bacterium

cells, saliva and blood. [18,34] Figure 2 schematically represents the etiopathogenesis of oral malodor.

### MICROBIOLOGY OF ORAL HALITOSIS

It is generally believed that halitosis reflects putrefaction by anaerobic, Gram-negative bacteria. [35,36] These microorganisms digest proteins from food residues, cells and other saliva debris into amino acids. This is followed by further cleavage of certain amino acids to bad-smelling by-products of bacterial metabolism, predominantly VSCs (H<sub>2</sub>S, CH<sub>3</sub>SH and dimethyl sulfide [CH<sub>3</sub>]<sub>2</sub>S), organic acids (butyric acid), aromatic compounds (indole, skatole) and amines (putrescine, cadaverine). [36,37] Table 2 lists the various bacterial species associated with oral malodor and Table 3 enumerates various bacteria responsible for production of VSCs.

The general view is that halitosis reflects complex interactions between several oral, mostly anaerobic, Gram-negative bacteria, and no specific bacterial strain is responsible for the condition.<sup>[18,34]</sup>

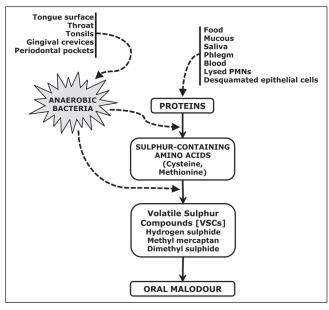


Figure 2: Flow chart depicting etiopathogenesis of oral malodor

### TABLE 3: BACTERIOLOGY OF VSCS PRODUCTION IN ORAL MALODOR

H <sub>2</sub> S from cysteine	CH <sub>3</sub> SH from methionine	H <sub>2</sub> S from serum	CH <sub>3</sub> SH from serum
Peptosteptococcus anaerobius	Fusobacterium nucleatum	Prevotella intermedia	Porphyromonas gingivalis
Micros prevotti	Fusobacterium periodonticum	Prevotella loescheii	(BANA positive)
Eubacterium limosum	Eubacterium spp.	Porphyromonas	Treponema denticola
Bacteroides spp.	Bacteroides spp.	Gingivalis (BANA positive)	(BANA positive)
Centipedia periodontii		Treponema denticola	Porphyromonas
Selenomonas artermidis		(BANA positive)	endodontalis

VSCs = Volatile sulfur compounds, BANA = Benzoyl-DL-arginine-naphthylamide

Studies have shown that five common bacteria are responsible for oral malodor in saliva and lingual dorsum, namely Porphyromonas gingivalis, Tanerella forsythia, Fusobacterium nucleatum, Prevotella intermedia, and Treponema denticola.[38,39] However, Haraszthy et al.[40] showed that Solobacterium moorei (a Gram-positive bacterium originally isolated from human faeces and that has been associated with bacteremia, septicemia and refractory cases of endodontic infections) was present in all subjects with halitosis, but not in any control subjects. Other bacterial isolates found only in the halitosis group were Granulicatella elegens, Eubacterium species, Firmicutes species, Porphyromonas species, Staphylococcus warneri, Dialister species, and P. intermedia. Of 4,088 isolates and phylotypes identified from the 13 subjects, 32 species including 13 noncultivable species were found only in subjects with halitosis. Studies have shown that essentially all odor production is a result of Gram-negative bacterial metabolism and that the Gram-positive bacteria contribute very little odor.[41]

### CHEMISTRY OF HALITOSIS

It is generally accepted that oral malodor is the result of a mixture of gases and foul-smelling substances into the breath which include VSCs, especially H<sub>2</sub>S, CH<sub>2</sub>SH and (CH<sub>2</sub>)<sub>2</sub>S, organic acids (butyric acid), aromatic compounds (indole, skatole) and amines (putrescine, cadaverine). [5,12,29,42] The amounts of VSCs and CH<sub>2</sub>SH/H<sub>2</sub>S ratio in mouth air from patients with periodontal involvement were reported to be eight times greater than those of control subjects. [43] While H<sub>2</sub>S is associated with those patients who are periodontally healthy, CH,SH is associated with those who have periodontal disease. [20] VSCs not only create malodor, but also aid in progression of periodontal infections by increasing mucosa permeability, which allows more bacteria and endotoxin invasion. Moreover, these compounds impede wound healing by interfering with collagen and protein synthesis, and suppressing DNA synthesis. [43-45] Table 4[46] lists various volatile organic compounds (VOCs) that may be present oral malodor, and Table 5<sup>[33,47,48]</sup> provides the etiology of halitosis and the related compounds. Table 6<sup>[6,49]</sup> correlates the smell with the chemicals responsible.

Volatile sulfur compounds are likely to result from bacterial metabolism of amino acids in food debris,

TABLE 4: LIST OF VOC PRESENT IN ORAL MALODOR

Category	Chemical
Sulfur compounds	Hydrogen sulfide-H <sub>2</sub> S
	Methylmercaptan-CH <sub>3</sub> SH
	Methanthiol
	Allyl mercaptan
	Dimethyl sulfide-(CH <sub>3</sub> ) <sub>2</sub> S
	Dimethyl disulfide
	Dimethyl trisulfide
Short chain fatty acids	Propionic acid
	Butyric acid
	Valeric acid
	Isocaproic acid
	Capric acid
	2-and 3-ethyl butyric acid
	Lauric acid
	Myristic acid
Polyamines	Cadaverine
	Putrescine
Alcohols	1-propoxy-2-propanol
Phenyl compounds	Indole
	Skatole
	Pyridine
Alkanines	2-methyl-propane
Ketones	
Nitrogen-containing compounds	Urea, ammonia

VOCs = Volatile organic compounds

TABLE 5: ETIOLOGY OF ORAL MALODOR
AND RELATED COMPOUNDS

AND RELATED COMPOUNDS			
Cause	Specific compounds		
Oral malodor	Hydrogen sulfide, methyl mercaptan, dimethyl sulfide and dimethyl disulfide		
Diabetes mellitus — weight reduction	Acetone, other ketones		
Uremia — kidney failure	Dimethylamine, trimethylamine, ammonia		
Liver diseases	Dimethyl sulfide, ethanethiol, C2-C5 aliphatic acids (acetic acid, proprionic acid), butyric acid, isobutyric acid, and isovaleric acid		
Lung carcinoma	Acetone, 2-butanone, <i>n</i> -propanol, aniline, and <i>o</i> -toluidine		
Upper respiratory/ oropharyngeal carcinoma	C2-C8 normal and branched organic acids Trimethylaminuria Trimethylamine		
Food: garlic/onions	Allyl methyl sulfide		
Other potential compounds	Indole, skatole, cadaverine, putrescine, carbon disulfide, and dimethyl selenide		

desquamated cells from oral mucosa, and leukocytes that accumulate in the oral cavity. [29,41,42] It appears that the tongue coating and the periodontal pocket are the main sources of VSC production, which is evidenced by the fact that an increase in the amount of tongue coating and the number of periodontal pockets significantly correlates with an increase in

TABLE 6: ORAL MALODOR SMELL AND RELATED COMPOUNDS

Compound	Smell
Hydrogen sulfide (H <sub>2</sub> S)	Rotten eggs
Methyl mercaptan (CH <sub>3</sub> SH)	Feces
Skatole	Feces
Cadaverine	Corpses (cadaver)
Dimethyl sulfide (CH <sub>3</sub> ) <sub>2</sub> S	Rotten cabbage
Putrescine	Decaying meat
Indole	Small quantity in perfumes, smelly in large amounts
Isovaleric acid	Sweaty feet

the concentration of VSCs in mouth air. [20,37,43,49] It has been suggested that the primary sources of volatile sulfur production are the benzoyl-DL-arginine-naphthylamide-hydrolyzing pathogens in the substrates. [50] Elevated concentrations of VSC frequently occur in mouth air from stressed patients without oral disease, but only a few studies have directly addressed the issue of emotional disorders and halitosis development. [51] A recent review by Yaegaki [52] has highlighted the role of these VSCs in production of periodontal diseases and their carcinogenic potential.

### **CONCLUSION**

Oral malodor is not uncommon and usually of oral origin, and rarely from the gastrointestinal tract or due to other systemic disorders. The posterior tongue dorsum is the most frequently overlooked source of oral malodor. The main causes of foul odor are VSCs produced by anaerobic Gram-negative bacteria in various niches of the oral cavity though other VOCs can also be produced. It is imperative to understand he etiology and pathogenesis of oral malodor to manage it.

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