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Aetiology, diagnosis and management of halitosis – a narrative review

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Abstract
Objectives
The present study aimed to present an overview of the aetiology of oral malodour and the diagnostic and treatment procedures.
Design
A comprehensive review of scientific literature (up to December 2021) was conducted using Medline and PubMed databases and Google Scholar, including checking reference lists of journal articles by hand-searching. Results are presented descriptively for halitosis's aetiology, diagnosis and clinical management.
Results
The origin of the foul odour problem is mainly due to intra-oral causes, while only a proportion of cases result from additional systemic problems. In some cases, the problem can be caused by co-existing oral and extraoral problems. Evidence suggests that the leading cause of intra-oral halitosis is the anaerobic microorganisms present in the tongue plaque. Less commonly, the foul odour is due to poor oral hygiene and periodontitis.
Conclusion
The origin of the foul odour problem is mainly due to intra-oral causes, while only a proportion of cases result from additional systemic problems. Dentists need to analyse and treat the oral problems that may be responsible for the patient's malodour, as well as inform the patient about the causes of the foul odour and oral hygiene procedures (flossing, tongue cleaning, selection and use of appropriate mouthwash and toothpaste). If the problem persists, they should know whom to refer the patient to for further diagnosis. It is reasonable to organise consultations on halitosis in a multidisciplinary setting - periodontists, otolaryngologists (ENT specialists), internal medicine specialists, gastroenterologists, psychiatrists, psychologists and others.

Keywords: halitosis; malodour; volatile sulphur compounds; mouthwashes; microbiota; periodontitis.

1. Introduction

Halitosis is a broad term for any unpleasant, unacceptable odour from the mouth, regardless of its cause. It is a combination of the Latin word *halitus* (breath) and the Greek term *osis* (pathology) (Bicak, 2018). In most patients, the odour comes directly from the oral environment. In some patients, it has a non-dental aetiology. Sometimes, the unpleasant odour is only perceived by the patient and is not perceptible objectively. The formation of volatile compounds in the human body is influenced by genetics, diet, stress and disease (Scully & Greenman, 2012).

1.1. Prevalence of oral malodour

Bad breath, like body odour, is a common complaint, often causing embarrassment and leading to social problems (De Geest et al., 2016; Seerangaiyan et al., 2017). It is estimated that 15-60% of the population has bad breath (Yokoyama et al., 2010; Bollen & Beikler, 2012; Seemann et al., 2016; Silva et al., 2018; Kumbargere Nagraj et al., 2019;). These differences may be due to the subjective perception of halitosis and cultural context (Rayman & Almas, 2008). The prevalence of bad breath is three times higher among men, and the risk is three times higher in people over 20 years of age than in children and adolescents (Nadanovsky et al., 2007).

1.2. Etiological classifications of halitosis

Classifications of halitosis based on the aetiology of fetor ex ore and showing the evolution of the term halitosis are those of Miyazaki et al. (1999), Tangerman & Winkel (2010) and Aydin & Harvey-Woodworth (2014).

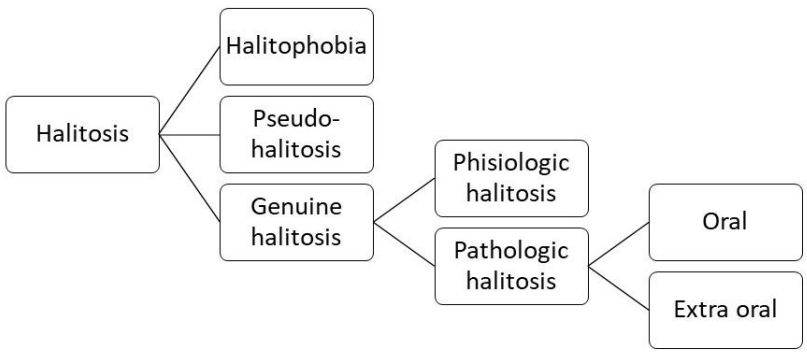

Fig.1. Classifications of halitosis according to Miyazaki et al. (1999)
Miyazaki et al. (1999) divided foul odour into real and delusional. Halitophobia and pseudohalitosis are conditions in which patients believe that their breath is smelly or stale, but this is not objectively verified (Pham, 2013). The social pressure of having fresh breath promotes these conditions. However, perceiving one's oral odour as unpleasant does not always reflect the actual clinical mouth odour (Rani et al., 2015; Tsuruta et al., 2017). It has been found that mainly male smokers perceive their oral odour as unpleasant (AlSadhan, 2016). Olfactory reference syndrome

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Abbreviations used: IOH – intra-oral halitosis; EOH – extra-oral halitosis; VSCs – volatile sulphur compounds; ENT – ear, nose and throat; CHX – chlorhexidine; CPC - cetylpyridinium chloride; RCTs - randomised controlled trials.

(ORS) is sometimes diagnosed. It is defined as a psychiatric condition characterised by a constant focus on body odour accompanied by shame, embarrassment, significant anxiety, avoidance and social isolation (Feusner et al.,2010; Begum & McKenna, 2011; Phillips & Menard, 2011; Greenberg et al., 2016). It falls within the spectrum of anxiety disorders, which include social anxiety syndrome.
Halitophobia is the fear that others will consider the patient's breath unpleasant. The patient also believes bad breath persists despite treatment (Scully & Greenman, 2012). Objectively verified oral malodour, so-called genuine halitosis, is divided into physiological and pathological malodour. Physiological bad breath is morning bad breath, passing shortly after waking up. Its occurrence is associated with reduced salivary secretion during the night, which increases the metabolic activity of microbes. No systemic disease or pathological condition can cause bad breath (Bicak, 2018).
Whereas intra- and extraoral causes are responsible for pathological oral malodour (Kapoor et al., 2016).
Extraoral halitosis (EOH) accounts for 5-10% of all halitosis. Causes of EOH include mainly respiratory and gastrointestinal diseases, metabolic disorders and medication (Kho et al., 1999; Hoshi et al., 2002; Tangerman & Winkel, 2007; Tangerman & Winkel, 2010; Longhini & Ferguson, 2011; Takeshita et al., 2012; Panov & Krasteva, 2012; Minh et al., 2012; Alkhouri et al., 2014; Anuradha et al., 2015; Magalhães et al., 2015; Barić et al., 2017; Pol et al., 2018). Transient bad breath can occur for exogenous reasons (e.g. drinking alcoholic beverages, smoking, and eating certain foods). Foods such as onions and garlic have a high sulphur content. Volatile sulphur compounds (VSCs) are perceptible as odour when exhaling from the lungs (Rosenberg & Cohen, 2007). Tobacco smoke contains VSCs and also predisposes to periodontitis. Alcohol consumption reduces saliva and causes bad breath (Rosenberg & Cohen, 2007).
According to De Geest et al. (2016) and Anbari et al. (2019), about 80-90% of pathological conditions in the oral cavity are intra-oral halitosis – IOH. The unpleasant odour is mainly caused by the putrefactive breakdown of endo or exogenous proteins and peptides by the oral microflora (Hampelska et al., 2020), mainly gram-negative anaerobic species, living on the posterior dorsal aspect of the tongue. In the absence of microorganisms, volatile odorous compounds cannot be formed. These microorganisms produce stinky, sulphur-containing gases - VSCs (Tangerman & Winkel, 2013). Other reeking compounds include aromatic compounds, amines, short-chain fatty or organic acids, alcohols, aliphatic compounds, aldehydes and ketones. The most critical VSCs are hydrogen sulphide, dimethyl sulphide, dimethyl disulfide and methyl mercaptan (Snel et al., 2011). VSCs can be toxic to human cells even at low concentrations. The oral bacteria most related to stinking are Actinomyces spp., Bacteroides spp., Dialister spp., Eubacterium spp., Eikenella, Fusobacterium sp., Leptotrichia spp., Peptostreptococcus spp., Porphyromonas spp., Prevotella spp., Selenomonas spp., Solthobacterium, Tan. Veillonella spp., Treponema (Scully & Greenman, 2012; Hampelska et al., 2020). Environmental factors are essential for the reproduction and growth of bacterial species (Hampelska et al., 2020). Oxygen reduction in saliva and plaque plays an important and complex role in developing oral malodour. As saliva secretion decreases, the number of bacteria and stinky breath in the mouth increases (Kleinberg et al., 2002).
The leading causes of bad breath are tongue biofilm, candidiasis, gum and periodontal disease, dental abscesses, cancer and reduced saliva secretion such as Sjogren's syndrome, radiotherapy (Hartley et al., 1996; Kazor et al., 2003; Davies & Epstein, 2010; Albuquerque et al., 2010; Scully & Greenman, 2012; Suzuki et al., 2016). Factors favouring bad breath include poor oral hygiene, fixed braces, mucous membranes irritation, stress, and menstrual cycle (Kawamoto et al., 2010; Calil et al., 2014; Nani et al., 2017).
There is a strong link between the number of bacteria on the tongue and oral malodour (Hartley et al., 1996; Van Tornout et al., 2013; Ye et al., 2014; Sara et al., 2016; Seerangaiyan et al., 2018). In people with healthy periodontal tissues and good oral hygiene, the leading cause of the oral odour is the posterior region of the back of the tongue. Tongue plaque may contain exfoliating epithelial cells, blood metabolites, food residues, and bacteria. The morphological structure of the tongue's papillary dorsum, especially the papillae's depth, influences the presence of a tongue biofilm. This structure provides a suitable anaerobic environment for bacterial growth, preventing the cleaning action of saliva in these areas (Sara et al., 2016). In both periodontal disease and healthy periodontal structures, bacteria colonise the dorsal tongue and periodontal pockets and play a significant role in forming VSCs (Bicak, 2018). In addition to specific bacterial species, specific physicochemical conditions favourable for the production of VSCs, i.e. adequate pH, oxygen partial pressure and oxidoreduction potential (Bollen & Beikler, 2012), are also necessary. The amino acids formed by the degradation of peptides contained in saliva are the main precursors of volatile compounds (Scully & Greenman, 2012; Bicak, 2018). Their metabolism leads to an increase in the concentration of nitrogenous compounds, increasing the pH of saliva. The resulting neutral or alkaline pH predisposes to halitosis (Yaegaki & Sanada, 1992).
Hydrogen sulphide and acetaldehyde are the odour agents responsible for carcinogenesis (Hampelska et al., 2020). A contributing factor to halitosis is stress. The catecholamines and cortisol produced during stress increase hydrogen sulphide production by the anaerobic bacteria colonising the gingival pockets (Calil et al., 2014).
Tangerman and Winkel's classification divided extraoral halitosis into bloodborne and non-bloodborne (figure 2) (Tangerman & Winkel, 2010).

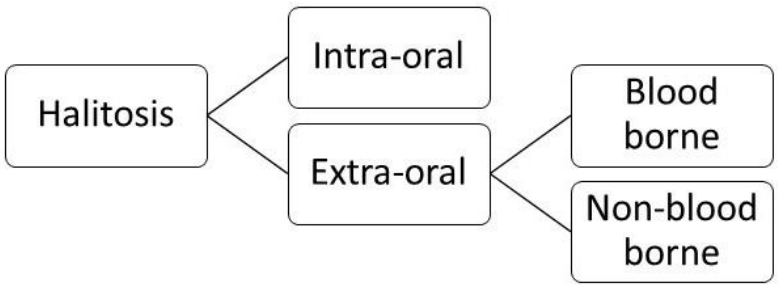

Fig. 2. Classifications of halitosis according to Tangerman & Winkel (2010).
Blood-borne halitosis originates in metabolic disorders, e.g. diabetes and kidney and liver diseases and is the result of certain drugs or foods. In these cases, odour-causing volatile compounds are carried into the oral cavity via blood vessels. The causes of non-blood-borne halitosis are diseases of the respiratory and digestive tracts.
Table 1 lists the causes of EOH (Tangerman & Winkel, 2010). Drugs that can cause extraoral foul breath are divided into ten groups: acid reducers, aminothiols, anticholinergics, antidepressants, antifungals, antihistamines and steroids, antispasmodics, chemotherapeutics, dietary supplements and sulphur compounds (Bicak, 2018:Mortazavi et al. 2020).

Extra-oral causes of halitosis	
Respiratory system	Antral malignancy; Bronchiectasis; Bronchitis; Cleft palate; Foreign bodies in the nose; Lung infection; Lung malignancy; Nasal malignancy; Pharyngeal malignancy; Sinusitis; Tonsillitis; Tonsillolitis
Gastrointestinal tract	Gastro-oesophageal reflux disease; Malignancy; Oesophageal diverticulum
Metabolic diseases (blood-borne)	Diabetes; Liver disease; Renal failure; Trimethylaminuria (fish odour syndrome); Dimethylglycinuria; Hypermethionineamia; Cystinosis
Drugs (blood-borne)	Amphetamines; Chemotherapy; Chloral hydrate; Dimethyl sulfoxide; Disulfiram; Nitrates and nitrites; Phenothiazines; Solvent abuse
Psychogenic causes	Depression; Hypochondriasis; Obsessive-compulsive disorder

Tab. 1. Extra-oral causes of halitosis according to Tangerman & Winkel (2010).

Aydin and Harvey-Woodworth concluded that previous definitions do not cover all possible causes of halitosis, nor do they draw a clear line between acceptable, physiological breath odour and pathological stink, nor do they distinguish normality (e.g. odour after eating garlic) from the disease (Aydin & Harvey-Woodworth, 2014). They assumed that anyone complaining of smelly breath, objective or subjective, should be considered a "halitosis patient". Evidence of objective stinky breath is information from the patient's relatives, the patient himself or objective halitometry. The absence of complaints from the patient's social environment, including family members, suggests that objective bad breath is not present. Furthermore, suppose there are no complaints from either the patients or their social environment. In that case, this usually means that there is no need for a diagnosis of stinky breath or treatment, even if halitometric measurements appear to indicate the presence of elevated VSCs. Stinky breath is almost always chronic, although it may occur sporadically. Some volatile foods have specific odours (e.g. garlic, onions) and can cause a short-lived stinky breath ('food odour'), as with some medications or poisoning. All are called temporary halitosis, and no further diagnosis or treatment is necessary. They, therefore, divided pathological stinky breath into five types: type 1 (oral), type 2 (airway), type 3 (gastro-oesophageal), type 4 (blood-borne) and type 5 (subjective) (figure 3).

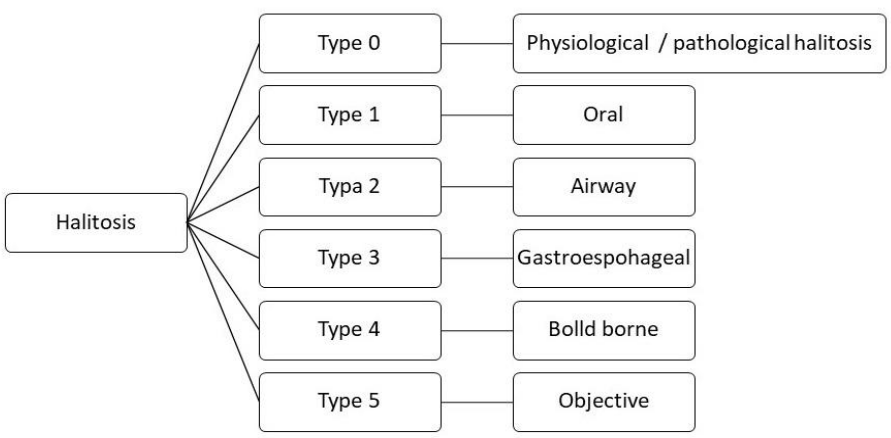

Fig. 3. Classification of halitosis according to Aydin & Harvey-Woodworth (2014).

They also distinguished oral malodour type 0 (physiological odour), a product of the mouth, respiratory tract, stomach and oesophagus, blood or is subjective. Types 1-5 represent different odour mechanisms that can occur in any combination at any time. Each type of halitosis (types 1 - 5) overlaps with a physiological odour (type 0). At any point, halitosis is the sum of all these source types and their respective physiological contribution. The relative contribution of these different physiological and pathological aetiologies is subject to interpersonal variation and can change within hours in the same person. Sometimes the level of one or more types may be so low as to give a negligible contribution to the overall ailment, or multiple factors may contribute to the same patient. This can be written as type 1 + 3, type 2 + 4, type 1 + 4 + 5 fetor ex ore etc. Each stinky ailment is potentially the sum of these types in any combination superimposed on type 0 (physiological odour) present in full health. This system allows for multiple diagnoses for the same patient, reflecting the multifactorial nature of the ailment. According to the authors, it represents the most accurate model for understanding bad breath and an efficient and logical basis for the clinical management of the condition (Aydin & Harvey-Woodworth, 2014). The new definition places less importance on organoleptic examination and a single halitometric reading and instead emphasises the patient's declarations and his/her social environment.

2. Diagnosis

In the diagnosis of halitosis, a detailed general medical, dental and oral history and a thorough physical examination - extraoral and intra-oral, including the condition of the teeth, periodontium and mucous membranes, as well as the state of oral hygiene - are essential (Seemann et al., 2014).

Research indicates that the dorsal surface of the tongue is the primary source of VSCs in the oral cavity (Yaegaki et al., 2002). It is, therefore, essential to assess the state of the tongue coating. The Winkel tongue coating index (WTCI) is used for this purpose, whereby plaque is assessed on six areas (A-F) of the dorsal surface of the tongue according to the following criteria: 0- no plaque, 1- thin plaque, 2- thick plaque (figure 4.) (Sanz et al., 2001; Winkel et al., 2003; Roldán et al., 2004).

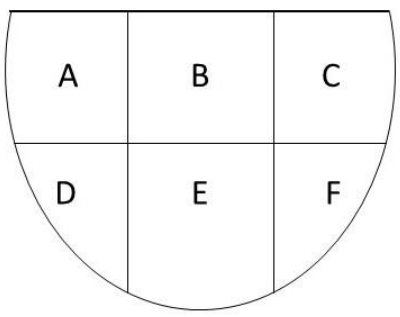

Fig. 4. Tongue Coating Index by Winkel et al. (2003).

The second most common source of VSCs in the oral cavity is the periodontium (Amou et al., 2014; Nalçacı et al., 2014). Therefore, it is essential to assess the condition of the gingiva, the periodontium and the state of oral hygiene. To differentiate, the authors practice supplementing the clinical examination with the organoleptic evaluation of plaque odour from the gingival pocket (pocket test) and plaque odour collected with a dental mirror from the posterior dorsal surface of the tongue (mirror test).

2.1. *Organoleptic examination*

The basic standard for the diagnosis of halitosis is an organoleptic examination. It is carried out even when other methods are available (Bollen & Beikler, 2012). Instructions on preparing for the organoleptic examination should be given to the patient before the visit to the fetor ex-ore specialist (Seemann et al., 2014).

The literature shows that a higher number of physicians performing the organoleptic test does not affect the evaluation quality because the test is not difficult but requires calibration (Greenman et al., 2014; Laleman et al., 2014). It is essential that the persons who assess halitosis have a good sense of smell, are not nicotine smokers and are calibrated, e.g. with a simple odour identification test (Sensonics Inc., Haddon Heights, NJ, USA). It is also recommended to perform regular self-calibration using own morning breath samples or instrumental measurements (Greenman et al., 2014).

The organoleptic evaluation should be carried out in the morning. For the measurement results to be reliable, the patient should be fasting, should not brush his/her teeth, use dental rinses or smoke on the day of the examination, should not clean his/her tongue for 24 hours, should not use deodorants on the day of the examination, should not be treated with antibiotics six up to 8 weeks before the examination.

The most straightforward organoleptic scale recommended for a dentist practitioner without experience is the scale for assessing breath from different distances shown in Table 2 (Bornstein et al., 2009; Greenman et al., 2014).

Distance malodour scale	
Grade 0	No malodour detected
Grade 1	Malodour is detected if the observer approaches a distance of about 10 cm to the mouth of the patient.
Grade 2	Malodour is detected if the observer approaches a distance of about 30 cm to the mouth of the patient.
Grade 4	Malodour is detected if the observer approaches a distance of about 100 cm to the mouth of the patient.

Tab. 2. Example of recommended organoleptic scale for the general dental practitioner according to Bornstein (2009).

For more experienced dentists, widely used are 6-point scales describing the intensity of the odour perceived from a fixed specific distance (Rosenberg, 1996; Murata et al., 2002), as shown in Table 3.

Organoleptic scoring scale	
Rose&McCulloch scale	Description
0	No detectable odour
1	Hardly detectable odour
2	Light odour
3	Moderate odour
4	Strong odour
5	Extremely strong odour

Tab. 3. Example for recommended organoleptic scale for the specialist according to Rosenberg (1996).

The test consists of the patient exhaling, preferably through a tube that prevents the air from diluting and having its smell assessed by the examiner. The organoleptic test at the first visit should always be carried out on oral and nasal air. This makes it possible to distinguish between nasal and blood-borne foul breath (Rosenberg, 1996). Organoleptic testing is a cheap test that does not require equipment. Its disadvantages are the subjectivity of the test and the need for calibration. However, an organoleptic examination is still considered the primary standard in the diagnosis of halitosis (Greenman et al., 2014).

2.2. Gas chromatography

A more objective method for diagnosing halitosis is analysing air samples using gas chromatography or halimeters - portable VSCs analysers (Bollen & Beikler, 2012). Instrumental VSCs detection is not mandatory for halitosis diagnosis. Gas chromatography enables the identification of chemical compounds present in exhaled air. This method makes it possible to determine the exact concentration of several hundred different compounds and determine their percentage composition. Despite its high sensitivity and specificity, conventional gas chromatography has entirely failed in everyday dental practice (Rosenberg, 1996). This method is non-invasive but requires well-trained diagnostic staff, and the test takes a long time and is expensive (Bollen & Beikler, 2012). It is more applicable as an examination method.

2.2.1. Portable gas analysers – halimeters

The use of portable gas analysers is recommended as a complementary organoleptic examination, a method for calibrating physicians, and a tool for building patient confidence, especially in patients with pseudo halitosis and halitophobia (Laleman et al., 2014). According to Laleman et al. (2014), three instruments are used in dental practices Halimetr (Interscan, Chatsworth, California, USA), Breathtron (Yoshida, Tokyo) and OralChroma (Abimedical, Miyamae-Ku Kawasaki-shi, Kanagawa, Japan).

Halimeter and Breathtron are electronic devices that detect some VSCs in exhaled air (Lenton et al., 2004). They are only used to assess EOH. They are not suitable for measuring blood-borne EOH. Both devices are small and very handy in dental surgery (Laleman, 2014).

OralChroma is a portable gas chromatograph that is simple to use, more efficient and, by limiting the target gases to three types [H2S, CH3SH and (CH3) 2S], less expensive than conventional gas chromatographs. The Halimeter measures the concentration of all VSCs in exhaled air.

Portable gas analysers have many advantages: they are easy to use and give fast reproducible results. Moreover, they are relatively inexpensive and can be operated by untrained personnel. The disadvantage is the limited variety of gases to be tested.

For collecting air for organoleptic and instrumental testing of malodour, Laleman et al. (2014) recommend different sampling methods (e.g. vacuum syringe method, sample bags).

Compared to an organoleptic examination, where the doctor/examiner directly sniffs the patient's exhaled air, this sampling technique offers the chance to obtain a more concentrated sample, allows cross-infection control, and ensures patient privacy (Seemann et al., 2014).

2.3. Indirect tests

Indirect tests are also available, such as:

- BANA Test -- indirect detection of Treponema denticola, Porphyromonas gingivalis and Tannerella forsythia and the volatile fatty acids they produce by determining the presence of fatty acid-metabolising enzymes in the BANA (benzoyl-DL-arginine-L-naphthylamide) test (Gülşen, 2012);
- Electronic nose/chemical sensor - in the presence of sulphide ions, an electrochemical voltage is generated, which is proportional to the perceived concentration of sulphides (Morita et al., 2001; Tanaka et al., 2004);
- Quantifying beta-galactosidase activity - Chromatographic discs for the assessment of beta-galactosidase activity – beta-galactosidase enzyme levels correlate with the malodour (van den Broek et al., 2007; Yoneda et al., 2010);

- Salivary incubation test - after several hours at 37 °C on an anaerobic medium, the tester evaluates the smell (van den Broek et al., 2007);
- Ammonia Detector - a pump that sucks in exhaled air after rinsing the mouth with urea and assesses the concentration of ammonia produced by bacteria (Amano et al., 2002; Takaesu et al., 2020);
- Ninhydrin Method - spectrophotometric method for the detection of low molecular weight amines and polyamines, which are formed by hydrolysis of peptide bonds in proteins by putrefactive bacteria and subsequent decarboxylation of the resulting amino acids (van den Broek et al., 2007);
- PCR - quantitative analysis of microorganisms producing VSCs from oral samples such as saliva, tongue plaque and subgingival plaque (Kamaraj et al., 2014; Kamaraj et al., 2014; Coffey et al., 2016);
- pH of oral saliva - a simple litmus strip test to assess the pH of saliva, Ph neutral or alkaline, not only predisposes to an increase in anaerobic bacteria but also enables greater production of VSCs (Yaegaki, & Sanada, 1992; Bollen & Beikler, 2012).

They are rarely performed due to their low specificity, indirect nature and the need for additional equipment

3. Management of intra-oral halitosis

3.1. Halitosis caused by oral reasons

As oral causes are related to microorganisms in the mouth, therapy consists of the following:

- patient education and supervision on oral hygiene (toothbrushing, flossing, tongue cleaning) (Wang & He, 2017),
- avoiding stimulants (tobacco, alcohol), products such as onions, garlic, cauliflower (van den Broek et al., 2007; Kapoor et al., 2011),
- the prevention and treatment of oral diseases through:
  - mechanical reduction of biofilm (Caygur et al., 2017),
  - chemical reduction of microorganisms (Rösing & Loesche, 2011),
  - binding of volatile gases (Rösing & Loesche, 2011),
  - masking unpleasant odours (Bradshaw et al., 2005),
- the use of probiotics (Burton et al., 2006; Liu et al., 2010; Iwamoto et al., 2010; Masdea et al., 2012; Yoo et al., 2019; Higuchi et al., 2019),
- in refractory cases, the use of Metronidazole (Hartley et al., 1999; Donaldson et al., 2005; Sayedi et al., 2015)
- dietary recommendations (Scully & Greenman, 2012),
- periodic odour checks (Bicak, 2018).

3.1.1. Mechanical biofilm reduction

The tongue is the largest biofilm reservoir, so thorough tongue cleaning is essential (Yaegaki et al., 2002). Cleaning the back of the tongue reduces the number of available nutrients available to microorganisms, which leads to improved odour (Bollen& Beikler, 2012). Home tongue cleaning should be performed regularly as part of your daily oral hygiene routine using a soft toothbrush or dedicated products (Ademovski et al., 2013; Saad et al., 2016; Laleman et al., 2018; Li et al., 2019; Acar et al., 2019). Stiff tongue scrapers are aggressive to the soft tissues, cause an overgrowth of the tongue papillae and do not bring benefits (Yaegaki et al., 2002; Outhouse, 2006; Erovic Ademovski et al., 2012). Since the most significant amount of coating is on the dorsal part of the tongue surface, this area should be cleaned carefully (Van der Sleen et al., 2010).
Cleaning the teeth and interdental spaces is also essential to fight plaque and oral microorganisms (Amou et al., 2014; Nalçacı et al., 2014; Bicak, 2018). Since periodontitis is one of the causes of oral odour, periodontitis must be treated. Simultaneous disinfection of the entire oral cavity, as described by Bollen et al., combining scaling and root planing in combination with chlorhexidine, produces a significant microbiological improvement for up to 2 months (Vandekerckhove et al., 1996; Bollen & Beikler, 2012). Mouth odour parameters are also improved (Vandekerckhove et al., 1996).

3.1.2. Chemical control of biofilms

Rinsing with chemical biofilm-reducing mouthwashes is common in treating oral malodour (Suzuki et al., 2019). The most commonly used antimicrobial ingredients in mouth rinses or toothpaste, with efficacy proven by many studies, are

- 0.12% - 0.2% chlorhexidine (CHX) (Rosenberg et al., 1992; Wigger-Alberti et al., 2010; Wilhelm et al., 2010; Berchier et al., 2010; Saad et al., 2011; Shetty et al., 2013; Yadav et al. 2015; Mendes et al., 2016; Sharma, et al., 2019);
- 0.1% chlorine dioxide (ClO2) (Frascella et al., 2000; Shinada et al., 2010; Shetty et al., 2013; Soares et al., 2013; Yadav et al., 2015);
- 0.05% cetylpyridinium chloride (CPC) (Wigger-Alberti et al., 2010; Wilhelm et al., 2010);
- triclosan (Raven et al., 1996; Feng et al., 2010; Mendes et al. 2016);
- amine fluoridede / tin fluoride: combination of AmF / SnF2 (Wigger-Alberti et al., 2010; Wilhelm et al., 2010; Feng et al., 2010; Sharma et al., 2019);
- 0.75% hydrogen peroxide (H2O2) (Veeresha et al., 2011; Dobler et al., 2020);
- essential oils (e.g. thymol, menthol, eucalyptol and methyl salicylate) (Feng et al., 2010);
- zinc ions, zinc (Zn) (Young et al., 2001; Wilhelm et al., 2010; Wigger-Alberti et al., 2010; Payne et al., 2011; Saad et al., 2011; Mendes et al., 2016).

Chemical neutralisation of oral malodour consists mainly of using active substances that react with VSCs or other compounds that cause halitosis to produce odourless compounds (Rösing & Loesche, 2011). Chemical compounds contained in toothpaste, mouthwashes and mouthwash can perform these functions. These products contain various oxidants and metal ions, e.g.:

- zinc ions (1% zinc acetate solution, zinc chloride, zinc citrate and zinc nitrate) (Young et al., 2001; Wilhelm et al., 2010; Wigger-Alberti et al., 2010; Feng et al., 2010; Payne et al., 2011; Saad et al., 2011; Mendes et al., 2016);
- sodium ions (van den Broek et al., 2007; Corteli et al., 2008);
- tin ions (van den Broek et al., 2007; Corteli et al., 2008);
- magnesium ions (Corteli et al., 2008; Basavaraj & Khuller, 2011);
- sodium bicarbonate (Roldán et al., 2003, Lourith & Kanlayavattanakul, 2010);
- hydrogen peroxide (H2O2) (Roldán et al., 2003; van den Broek et al., 2007).

Zinc ions have an inhibitory effect on the foul breath through sulfide binding and inhibition of the growth of VSCs-producing bacteria (Suzuki et al., 2018). In 5 randomised controlled trials (RCTs) on 293 patients. Compared to placebo, 0.05% chlorhexidine, 0.05% cetylpyridinium chloride, and mouthwash with 0.14% zinc lactate significantly reduced organoleptic properties but showed significantly more tongue staining and teeth (Sheng et al., 2005). The mechanism of action of zinc is to trap sulphur-containing gases (Young et al., 2001). Therefore, rinses containing 0.05% CHX, 0.05% CPC and 0.14% zinc lactate seem to be much more effective than CHX alone due to the effect of zinc. Zinc combined with CHX appears to have a synergistic effect, as Young et al. (2003) demonstrated.
Halitosis masking products contained in rinses, sprays, peppermint tablets, chewing gum, and herb-based preparations (e.g. tulsi extract) have only a limited and short-term masking effect (Pitts et al., 1983; Nagata et al., 2008; Akkaoui & Ennibi, 2017; Sharma et al., 2019). They mainly increase saliva production so that more soluble sulphur components are retained for a short time (Sterer & Rubinstein, 2006).
In cases of refractory halitosis, a 5-7 day treatment with metronidazole at a dose of 600-1000mg/day is used to reduce tongue microbiota and odour (Scully & Greenman, 2012; Sayedi et al., 2015).
Treatment with a metronidazole rinse also positively changes patients' periodontal status and breath odour. Topical application of the antibiotic reduces the systemic effects of its use (Southward & Bosy, 2013).

A systematic literature review of interventions for halitosis by Kumbargere Nagraj S. et al. was published in the Cochrane Library in 2019 (Kumbargere Nagraj et al., 2019). Results from 44 randomised controlled trials (RCTs) with 1809 participants divided into study and control groups were included. Different interventions were compared, which were classified as mechanical biofilm removal, chewing gums, systemic deodorisers, topical agents, toothpaste, mouthwashes, tablets and combined methods. Almost all studies described the short-term effects of the methods used. All groups showed low or very low efficacy of these methods in the treatment of halitosis. It was not possible to demonstrate the superiority of any of the methods. There is a need for well-designed RCTs examining long-term treatment effects to standardise interventions and preparation concentrations as indicated.

3.1.3. Probiotics, vaccines and other

Increasingly, probiotics (Bollen, & Beikler, 2012), Fusobacterium nucleatum vaccines (Liu et al., 2009; Liu et al., 2010), myric acid - a methionase inhibitor that inhibits VSCs production (Ito et al., 2010) and tea catechins that inhibit Phyromonas gingivalis and VSCs production are used in the treatment of halitosis (Xu et al., 2010; Singhal et al., 2017;).

Many studies have been conducted on probiotics' efficacy in halitosis treatment (Scully & Greenman, 2012). Probiotic treatments and vaccines are expected to be a new way to improve oral health (Suzuki et al., 2019). In order to replace the bacteria responsible for bad breath, preparations containing Streptococcus salivarius (K12) (Masdea et al., 2012), Lactobacillus salivarius (WB21) or Weissella cibaria (Burton et al., 2006; Iwamoto et al., 2010; Higuchi et al., 2019) are applied. Treatment aims to prevent the reappearance of unwanted bacteria, thereby reducing the recurrence of oral malodour over a more extended period (Burton et al., 2006). Furthermore, Weisella cibaria isolates have the ability of VSCs production both in vitro and in vivo (Kang et al., 2006).

The aggregation of F. nucleatum with other bacteria to form a plaque biofilm in the mouth causes bad breath. FomA, the major outer membrane protein of F. nucleatum, recruits other oral pathogenic bacteria, such as Porphyromonas gingivalis, in periodontal pockets. A halitosis vaccine directed against F. nucleatum FomA significantly abrogates the increased bacterial coaggregation, biofilms, VSCs production and gingivitis mediated by the interspecies interaction of F. nucleatum with P. gingivalis, suggesting FomA F. nucleatum to be a potential target for the development of vaccines or drugs against bacterial biofilm formation and associated pathogenesis (Liu et al., 2013).

Myric acid B inhibits H2S and pyruvate production by periodontal pathogens. Myric acid purified from Myrsine seguinii inhibited the production of methyl mercaptan (CH3SH) by Fusobacterium nucleatum (Ito et al., 2010).

3.1.4. Diet

Fasting and diets that reduce the number of calories or restrict nutrient groups (e.g. ketogenic diets, high protein diets) can lead to halitosis. When the body is no longer supplied with energy-providing carbohydrates, it first breaks down the glucose stored in the muscles and liver as glycogen. However, this does not last long. After a few hours, the body begins to break down its fat reserves and the metabolic products, ketones, give the breath its characteristic sweet and faint smell. This can also be observed in people who exercise intensely and do not consume enough carbohydrates (Kapoor et al., 2011). It is, therefore, crucial for the diet to be varied and metabolically balanced.

Another discussed aspect of human nutrition and halitosis is the food source for the anaerobic bacteria that cause bad breath. Most odorous compounds that cause bad breath are metabolic waste products produced by anaerobic bacteria that digest proteins. Degradation of salivary peptides leads to the formation of amino acids increases in pH, allowing the synthesis of VSCs (Yaegaki & Sanada, 1992; Scully & Greenman, 2012). This means that when we eat high-protein foods, the bacteria living in our mouths will also receive a substrate for metabolism. Its products are precisely volatile sulphur and nitrogen compounds. High-protein foods include meat, fish, seafood and, eggs, dairy products. High-protein diets that eliminate carbohydrates promote the production of volatile sulfur and nitrogen compounds. Therefore, patients with halitosis should have a balanced diet and beware of excess protein (Kapoor et al., 2011; Scully & Greenman, 2012; Kim et al., 2015; Bicak, 2018). In addition, the diet should be enriched with vegetables and fruits containing fibre. People who maintain a vegetarian or vegan diet have fewer chronic odour problems than those who consume protein-rich foods such as meat (Hartley et al., 1999; Mazur et al., 2020; Booth & Hurry, 2020).

It is important to remember that the mouth naturally contains proteins, such as dead epithelial cells or protein compounds found in saliva. It is, therefore, advisable to have the best possible oral hygiene and to drink plenty of water, especially after eating foods with a high protein content (Scully & Greenman, 2012; Kim et al., 2015).

Moreover, enriching the diet with green tea extract helps to effectively inhibit Porphyromonas gngivalis and the production of VSCs, thereby reducing malodour (Zeng et al., 2010; Xu et al., 2010; Singhal et al., 2017).

3.2. Management of other types of halitosis

Foul breath odour caused by extrinsic causes is eliminated by diagnosing and treating the underlying disease and cooperation with ENT specialists, pulmonologists, hepatologists, endocrinologists, and gastroenterologists. Experienced clinicians can identify psychogenic causes with high probability. These are usually suggested by obsessive behaviour, depression, anxiety in the form of phobias, paranoia, compulsive behaviour, and limited social interaction. These observations are not sufficient to make a diagnosis of pseudohalitosis. Pseudohalitosis and health phobia always require the exclusion of other causes, the patient's referral to a clinical psychologist or psychiatrist, and the involvement of the patient's relatives (Hayashi et al., 2010). The treatment of these patients is complicated and requires interdisciplinary collaboration. These patients often do not accept arguments and change doctors.

4. Summary

Despite extensive research into the causes of bad breath and its treatment methods, the problem is still very much alive. There are no clear diagnostic guidelines or treatment protocols. Foul breath, also known as "malodour" or "bad breath", is a common health problem affecting up to 60% of the population. The origin of the problem is mainly due to intra-oral causes, while only some cases result from additional systemic problems. This is why dentists should be the first medics to struggle with diagnosing this embarrassing problem. They must have a broad knowledge of the causes of the EOH and IOH as well as the treatment of oral causes of halitosis. A proper diagnosis makes it possible to manage this phenomenon. It is reasonable to organise consultations on halitosis in a multidisciplinary setting - periodontists, GPs, ENT specialists, internal medicine specialists, gastroenterologists, psychiatrists, psychologists and others.

Despite extensive research into the causes of bad breath and its treatment, the problem is still very relevant. In the 21st century, where not only the length but also the quality of life is a concern for medical professionals, halitosis’s prevalence can have serious social consequences leading to social exclusion and sometimes even depression. For this reason, research focusing on the causes of bad breath and long-term prevention methods is still very relevant and necessary to improve the quality of life of patients affected by halitosis.

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