Halitosis – a common medical and social problem. A review on pathology, diagnosis and treatment

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Abstract

Bad breath is a condition that has health and social implications. This paper provides a comprehensive review of the classification of halitosis, it's etiology, it's prevalence, diagnosis and treatment strategies for the condition. Halitosis is affecting about 25-30% of world's population. It includes categories of genuine halitosis, pseudo-halitosis and halitophobia. It is believed that in 80-90% of cases halitosis origins in the oral cavity and the most common causes are : gingival pathologies, caries and poor oral hygiene. Extra-oral sources of halitosis are responsible for 10-20% of all cases and are caused by poor diet, alcohol abuse, tobacco smoking, certain drugs and diseases of other parts of digestive tract as well as some systemic conditions. Diagnostics of halitosis includes subjective methods (examiner's sense of smell) and objective methods (instrumental analysis). Simple, subjective examination is considered a "golden standard" in clinical practice. In case of pathological halitosis identifying the direct cause of halitosis is essential. After excluding, or after successful treatment, of all oral pathologies, in case of remaining fetor ex ore identification and treatment of halitosis often requires multidisciplinary approach. Many unknowns remain in causes and mechanisms of halitosis. It can significantly impair quality of life, social interactions, lead directly to depression, low self-esteem or other mood disorders, therefore it is important to properly identify, treat and continue research on halitosis. (Acta gastroenterol. belg., **2012**, 75, **300-309**).

Key words : Halitosis, epidemiology, etiology, microbiological aspects, diagnosis, treatment.

Introduction

The term "halitosis" derives from latin and greek languages, where *halitus* means smell and *osis* refers to a chronic pathology. Unpleasant smell from oral cavity is also known as *fetor ex ore, oral malodor* or simply *bad breath*. It is a widely spread phenomenon affecting about 25-30% of world's population (1,2,3). Exact prevalence remains unknown, as some authors calculate that up to 50-60% of world's population may suffer from halitosis (4,5,6,7,8,9).

A simple classification was reported by Miyazaki *et al*. in 1999. The classification of halitosis includes categories of genuine halitosis, pseudo-halitosis and halitophobia. Genuine halitosis is subclassified as primary physiologic halitosis or pathologic halitosis.

Primary physiological halitosis usually occurs in the morning, right after awakening. It is caused by diminished production of saliva during the night hours, and leads to drying of oral cavity mucosa (10).

Primary pathological halitosis is described as unacceptable oral malodor (11) and may be caused by various different factors. Depending on origin of the causes, bad breath can be classified as *oral* or *extra-oral* halitosis. It is believed that in 80-90% of cases halitosis origins in the oral cavity (4,12,13,14,15,16). Most common causes of oral halitosis are : gingival pathologies, caries and poor oral hygiene. Extra-oral sources of halitosis are responsible for 10-20% of all cases (7,13) and are caused by poor diet, alcohol abuse, tobacco smoking, certain drugs and diseases (especially diseases of digestive tract and airways – see table 1). It is believed that in primary halitosis patient cannot smell his own odor coming out of his oral cavity. The reason for this is possible adaptation to the odor (3) and difference in the flow of inhaled and exhaled air. Inhaled air flows vertically through the nasal cavity, while exhaled air flows horizontally – thus possibility to smell own breath is very limited. If oral malodour does not exist but the patient believes that he or she has oral malodour, the diagnosis would be pseudo- halitosis. If, after treatment for either genuine halitosis or pseudohalitosis, the patient still believes that he or she has halitosis, the diagnosis would be halitophobia.

Causes of halitosis

Halitosis is caused when certain substances can be detected in exhaled air (17) – usually various volatile sulfur compounds (VSCs) (3,18). In 90% of cases these are : methyl mercaptan, hydrogen sulphide and dimethyl sulfide (19,20). These products of bacterial metabolism are created during proteolytic processes. Main substrates are cysteine, methionine, lysine and tryptophan (21,22, 23,24). Main source of above mentioned AA are food remains, epithelial cells, dead leucocytes and bacterial cells, but halitosis can be also caused by residuals on the base of the tongue, plaque, post nasal drip, blood and even mucins from saliva (10,19,25,26,27,28). Proteolysis in the oral cavity is a physiological process present in patients with and without halitosis. It may be modified by numerous factors such as : diminished pro-

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Table 1. — **Aetiology of halitosis (Quirynen *et al.* ; Authors' modification)**

1. Oral halitosis (80-90%) includes ENT causes of halitosis (5-8%)	1. Tongue coating 2. Gingvitis 3. Periodontitis 4. Xerostomia 5. Teeth diseases 6. Candidosis 7. Tonsillitis 8. Rhinosinusitis 9. Nose obstruction
2. Extra-oral halitosis (10-20%)	1. Gastrointestinal problems 2. Trimetyloaminuremia 3. Other rare diseases 4. Drugs 5. Hormonal disorders 6. Diet
3. Halitophobia, pseudo-halitosis (unknown)	

duction of saliva or inflammation of oral mucosa (3,10,18). Gaseous sulfur compounds are toxic for gingival and periodontal tissues and may result in destruction of epithelial cells. Increased permeability of protective barriers intensifies the flow of prostaglandins and other inflammatory cells (29). Calenic *et al*. (30) confirmed that hydrogen sulfide participates in the process of apoptosis of human fibroblasts isolated from gingival tissue as an initiator of mitochondrial path of fibroblasts decomposition.

Compounds responsible for oral malodor can produce various smell sensations. Methyl mercaptan is believed to be the substance with the most unpleasant odor (31, 32) comparable to faeces. The odor of hydrogen sulphide reminds of rotten eggs, while dimethyl sulfide smells like rotten cabbage (33,34,35,36). It has been shown, that methyl mercaptan (as well as hydrogen sulfide to some extent) are responsible for oral halitosis, while dimethyl sulphide is more typical for extra-oral halitosis (37). In this second case – foul smelling substances are absorbed by blood and transported to the lungs, where they are exhaled. Exhaled air contains also mixture of other secondary substances responsible for malodor (38). These substances are : putrescine and cadaverine (responsible of foul odor of decaying meat and corpses) and short-chained fatty acids, such as butyric acid, propionic acid, valeric and isovaleric acids (smell comparable to sweaty feet). Phenyl compounds : indole, piridine and skatole (responsible for odor of faeces) (3,33,34,35,36). Nitrogen compounds (ammonia, urea) are responsible for odor of urine. Other substances responsible for malodor are alcohols (ie. 1-propoxy-2-propanol), alkanines (isopropane) and ketones (24).

Microbiological findings in halitosis

Many bacteria capable of producing volatile sulfuric compounds (VSCs) were identified. Most potent producers of these compounds are Gram-negative anaerobic bacteria (22,23,25,35,39,40). Oral cavity can be colonized by over 700 different bacterial species (19) and even greater variety was identified in patients with halitosis (41,42). Largest concentrations of bacteria capable of producing sulfuric compounds can be found on the base of the tongue and in the plaque where they form bacterial biofilms (19,20,22,40,43). Most common species found in biofilm of the tongue base are : *Veillonella, Prevotella, Actinomyces, Fuscobacterium, Peptostreptococcus* (19,20,41,44). They are present in patients with and without halitosis (20,41,45). This means that not presence but increased number of these pathogens (and related increase in the amounts of produced sulfuric gases) is responsible for halitosis (20,41,42). Bacteria found only in patients with halitosis are among others : *Solobacterium moorei, Granulicatella elegens, Eubacterium spp, Prophyromonas spp, Dialister spp*. (39). *In vitro* research allowed to identify main producers of sulfuric compounds : *Bacteriodes forsythus, Fuscobacterium nucleatum, Fuscobacterium peridonticum, Atopobium parvulum, Prevotella intermedia, Porphyromonas gingvinalis, Treponema denticola, Tanarella forysthenis, Solobacterium moorei, Eubacterium sulci, Selenomonas spp., Peptosterptococcus spp*. (3,5,19,22,24,31,46,47).

Fuscobacterium nucleatum, Fuscobacterium periodonticum, Eubacterium spp,, Bacteriodes spp. are able to produce methyl mercaptan from methionine. *Selenomonas artermidis, Eubacterium limosum, Peptostreptococcus anaerobicus, Centipedia peridontii, M.prevotii, Bacteriodes spp*. produce hydrogen sulfide from cysteine. *Treponema denticola, Porphyromonas gingvinalis, Porphyromonas endodontalis* produce methyl mercaptan from blood serum and *Prevotella intermedia, Prevotella loescheii, Porphyromonas gingvinalis, Treponema denticola* can produce hydrogen sulfide from blood serum (22,24,28).

Bacteria that are able to produce volatile sulfur compounds are also found in plaque. Their presence was confirmed in patients with mild as well as severe forms of halitosis (18,19,28,46,48). There is a correlation between the number of bacterial colonies in plaque's biofilm that are able to produce sulfuric compounds and the severity of halitosis (48). Some pathogens identified in plaque are able to produce also short-chained fatty acids (SCFA) –

Table 2. — **Characteristic smells in subjective diagnosis of halitosis**

Smell	Compound	Type of halitosis	Example of condition
Faeces	Methyl mercaptan (CH_3SH)	Mainly oral halitosis Extraoral halitosis	Periodontal diseasesl ; xerostomia/ low salivary flow
	Scatole	Mainly oral halitosis Extraoral halitosis.	Periodontal diseases ; tongue coating ; diet
Rotten egg	Hydrogen sulfid (H_2S)	Mainly oral halitosis Extraoral halitosis	Peridontal diseases ; xerostomia/ low salivary flo
Cadaver	Cadaverine	Mainly oral halitosis. Extraoral halitosis.	Periodontal diseases ; diet ; xerostomia/ low salivary flow
Sweaty feet	Isovaleric acid	Mainly oral halitosis Extraoral halitosis	Tongue coating ; diet
Decaying meat	Putrescine	Oral and extraoral halitosis.	Diet ; xerostomia/low salivary flow
Rotten cabbage	Dimethyl sulphide (CH_3)2S	Mainly extraoral halitosis.	Tertiary lues
Rotten fish	Trimethylamine (TMA)	Extraoral halitosis	Trimethylaminuria (TMAU, *fish odor syndrome)*
Urine	Nitrogen-containg compounds : urea, ammonia.	Extraoral halitosis	Systemic diseases : renal failure, cirrhosis of the liver
Sweet fresh apples	Ketones (aceton)	Extraoral halitosis	Systemic diseases : diabetes mellitus, ketoacidosis,
Squashed bedbug	Unknown	Extraoral halitosis	Ozena

usually butyric and valeric acids – but also putrescine and skatole (25,28,46).

Correlations between *Helicobacter pylori* (Hp) and halitosis were a subject of research in recent years. The first reports linking Hp and halitosis were described by Marshall *et al*. in 1985 (49). In the recent years few studies on large populations of Hp carriers with dyspeptic symptoms and halitosis were conducted. Eradication of Hp resulted in permanent elimination of malodor (50,51,52,53). It is believed that oral cavity is the second largest (after the stomach) reservoir of Hp (54,55,56). Hp was identified in dental plaque in the 1990s (57). The mechanism responsible for halitosis is not yet fully understood. Suzuki *et al*. (58) observed increased numbers of bacteria capable of producing sulfuric compounds in Hp carriers with and without periodontitis. Authors suggest indirect mechanism – Hp can aggravate inflammation. It is also known that Hp can produce ammonia from urea. Amount of ammonia produced by Hp in hyperammonemia depends on numerous factors. Liver functions seems to be the most important, since hyperammonemia is only present in case of hepatic cirrhosis (59). The breakthrough in research between Hp and halitosis came with finding that these bacteria are also able to produce methyl mercaptan and hydrogen sulfide (60,61).

Besides typical anaerobic also some facultatively-anaerobic bacteria from Enterobacteriaceae (*Klebsiella pneumoniae, Klebsiella oxytoca* i *Enterobacter cloacae*) are known to produce VSCs, cadaverine and putrescine (44). Their presence was confirmed on the base of the tongue, saliva and gingival pockets.

Gram-negative bacteria are primarily responsible for halitosis, however most available proteins in oral cavity are glycoproteins (62). Therefore Gram-positive bacteria producing galactosidases are essential in development of halitosis (63,64). Gram-positive bacteria deliver proteins that Gram-negative pathogens can later process into VSCs. Galactosidases are mainly produced by *Streptococcus salivarius*. Also highest amounts of sulfuric gases were registered with simultaneous incubation of *Streptococcus salivarius and Porphyromonas gingivinalis* in comparison to *Porphyromonas gingivinalis* alone (23).

Bacteriological studies also confirm that Gram-positive cocci are the dominant species on the base of the tongue (65,66). 12-40% of oral flora is *Streptococcus salivarius* (5,19,41). Harszthy *et al*. identified it in all subjects with and without halitosis. However their numbers appeared to be higher in patients suffering from malodor when compared to subjects without halitosis (19).

Diet, lifestyle, medications – exogenous (transient) halitosis

Food is an important factor in development of halitosis, especially high-protein and high-carbohydrate diets (3). Aminoacids containing sulfur are released during decomposition of foods rich in sugars and proteins. They are later metabolized by bacteria capable of producing volatile sulfur compounds. It is believed that fats can also contribute to development of halitosis (67). Halitosis is only partially caused by sulfuric compounds

released during the processes of decomposition of food remains. Sulfuric gases exhaled from the lungs are also important. In 1999 Suarez *et al*. (68) showed a gas chromatography tracing of sulfur-containing gases released from raw garlic. Gases identified were hydrogen sulfide, methanethinol, allyl mercaptan, allyl methyl sulfide-AMS and allyl disulfide. Becker and Hills showed that fat-rich diet increases frequency of relaxation of lower esophageal sphincter (LES), both in healthy adults and in patients with gastro-esophageal reflux disease (GERD) what further increases the risk and severity of halitosis (68,69). Nitrogen compounds present in tobacco smoke are responsible for lowering LES tension and therefore increase number of reflux incidents. Rosenberg *et al*. (2007) proved that obesity is an important risk factor of halitosis (70). Obesity predisposes to GERD and contributes to sleep disorders (snoring, OSAS) which lead to dryness of oral mucosa (47).

Malodor present after consumption of alcoholic beverages is caused not only by presence of acetaldehyde (metabolite of ethanol) in exhaled air, but also by relaxation of lower esophageal sphincter and dryness of oral mucosa (71). Tobacco smoke contains sulfuric compounds that are inhaled directly to the lungs during smoking and partially absorbed to bloodstream (they can be exhaled even after few hours). Smoking contributes to dryness of oral mucosa what aggravates halitosis (3).

Halitosis can also be caused by certain drugs and medications. The mechanism is usually related to dryness of oral mucosa. The medications strongly related with development of halitosis are : antihistamines, antidepressants, diuretics, antiparkinson drugs, anticonvulsives, antipsychotic medications (benzodiazepines, phenothiazine, MAO inhibitors, tranquilizers and sedatives) and medications that reduce appetite and prevent vomiting (3). Also certain vitamins (B-group), oils and arsenic compounds are excreted with sweat, urine and exhaled air and can contribute to malodor.

Halitosis that is a direct result of lifestyle factors (diet, alcohol and smoking) is also called temporary halitosis. The endogenic (true) halitosis can be a result of various diseases of digestive and respiratory tracts and sometimes other medical conditions.

Halitosis in digestive tract diseases

Oral halitosis

A healthy adult produces about 1,5 liters of saliva every day. At night the amount of produced saliva is significantly lower than during the day. Diminished production of saliva is also present in many salivary gland disorders, diabetes, renal insufficiency or hyperthyroidism. It may also be a result of dehydration, intense physical activity, infection, increased temperature, external conditions (heat, low humidity), insufficient exposition to sunlight or as a result of prescribed medications. Proteases responsible for decomposition of foods are activated extra-orally, when pH of saliva increases (72). Similar processes that contribute to physiological (morning) halitosis is also observed during decomposition of saliva at night. In the research of Koshimune, in patients with diminished production of saliva, higher concentrations of methyl mercaptan and hydrogen sulfide was observed together with thicker layer of bacterial coating on the tongue when compared to patients with normal amounts of produced saliva (73). About 80-90% of all cases of halitosis is oral halitosis – usually caused by specific bacterial flora on the dorsal parts of the tongue (19).

Insufficient (or lacking) oral hygiene is a very common cause of halitosis.

Periodontitis is another important cause of halitosis. The main predisposing factor is plaque (74) that gathers due to interactions of oral bacteria and hosts tissues (75). Unpleasant odor is caused by VSCs produced by bacteria colonizing the plaque. Numerous toxins, enzymes and organic acids release from bacterial biofilm directly cause hosts response – which leads to gingival inflammations (19,24,74).

Caries is another important cause of halitosis. Pathogenes responsible for development of caries also participate in formation of plaque. They can initiate caries by production of acids (mainly lactic acid) during metabolism of sugars. Acidic environment increases demineralization of enamel and proteolytic destruction of teeth (76).

Extraoral halitosis

Extraoral halitosis – caused by diseases of other parts of digestive tract – are not common and contribute to less than 5% of all cases of halitosis. Gastroenterological causes of malodor are GERD and Hp infection (77). Extra esophageal reflux (EER) – often together with Hp – may reach pharynx, oral cavity, nasopharynx, nasal cavity, paranasal sinuses, Eustachian tube, tympanic cavity, larynx and even trachea and bronchi (gaseous reflux) (78,79). EER may also initiate or contribute to development of periodontitis (80,81).

Halitosis may also be caused by esophageal diverticulosis. In about 70% of such cases Zenker's diverticulum is diagnosed. Prevalence of this anomaly in world's population is about 2:100000 – therefore it is not a common cause of halitosis (82). Fetor ex ore may be also caused by trauma – destruction and necrosis of esophageal walls leads to secondary bacterial infection. Such problems are often observed after chemical burns of esophagus. Esophageal cancers may also result in malodor, especially in advanced stages during tumor's necrosis and blocked passage of foods to the stomach. Controversies arise whether or not diseases of lower parts of digestive tract (below gastro-esophageal junction) can cause halitosis. Fetor ex ore may be present during regurgitations, vomiting or during LES disorders (10). Malodor may be caused by cancers localized in cardia ventriculi. Crohn's disease can also present with halitosis in rare cases when

ulcerous changes are localized in oral cavity and are prone to bacterial infestation (83).

Halitosis in diseases of airways

Upper airways

Nasal congestion is another important cause of halitosis. Breathing through the mouth leads to dryness on oral mucosa and makes it harder to properly clean the oral cavity. The discharge residing in nose and paranasal sinuses for prolonged period of time is often colonized by bacteria. Infected, purulent discharge leads to post-nasal drip and results in malodor. Deformations of nasal septum and lateral nasal wall are most common acquired pathologies. Congenital disorders – such as palatal cleft or cleft lip – are less common (1 per 650-750 alive newborns) (84). Unilateral, long lasting, purulent nasal discharge – especially in children – can be a result of a foreign body in nasal cavities. Organic foreign bodies undergo decomposition processes and aggravate fetor ex ore. Nasal congestions – and therefore halitosis – may also be caused by acute and chronic infections. About 80% of acute infection of the nose and paranasal sinuses are caused by viruses (85). Chronic, hypertrophic or atrophic rhinitis all lead to impairment of nasal breathing and secretory functions of nasal mucosa. One example of chronic atrophic rhinitis is ozena. The most spectacular symptom is extremely unpleasant odor, often compared to the smell of squashed bedbug (86). Thick, purulent, glue-like discharge is present in nasal cavities. In advanced stages of the disease grayish layer of dried discharge can cover whole nasal mucosa. Etiology is not fully understood, but often Gram-negative *Klebsiella ozenae* is found in bacterial swabs.

Bacterial infections of sinusal mucus lead to development of purulent sinusitis. Aerobic and anaerobic bacteria known to produce VSCs can be identified in acute and chronic (87,88).

Necrosis of granulation tissues is another cause of halitosis. Bacterial infestations of necrotic tissues further increase *fetor ox ore*. Examples of infectious chronic granulomatous condition of the nose are tuberculosis, syphilis or scleroma. Decomposition of syphilitic lesions leads to massive ulceration with accompanying halitosis (fetor comparable to rotten cabbage) (86). Chronic non-infectious granulomatous condition of the nose is also observed in some autoimmunological diseases : Wegener's disease, Churg-Strauss syndrome, SLE or sarcoidosis. Non-infections rhinitis is caused by allergies in about 70% of cases (89). Other non-infections causes include vasomotoric, hormonal and iatrogenic rhinitis.

Tumors of nasal cavity and paranasal sinuses lead to impairment of nasal breathing and prevents proper ventilation of sinuses. It also predisposes to secondary bacterial infections, what aggravates the malodor (72).

Pharynx is located at the intersection (junction) of airways and digestive tract. Inflammatory processes may lead to destruction of pharyngeal epithelium. Amino-acids and peptides present in hosts tissues become substrates for bacteria capable of producing sulfuric gases.

Congenital nasopharyngeal pathologies can lead to halitosis. Foreign bodies in nasopharynx are a direct cause of nasal congestions (particular example : posterior nasal packing). Inflammation of lymphatic tissues (adenoiditis) is usually caused by bacteria typically found in upper airways (90). Purulent, foul smelling discharge can drip to nasopharynx, for example in acute and chronic middle ear infections (84,91). Infection of Tornwald's cysts may cause nasopharyngeal abscess (92). Benign and malignant tumors often cause malodor due to obstruction, destruction of surrounding tissues, necrosis and secondary bacterial infections.

In the oral part of the pharynx, between pharyngeal arches palatine tonsils are located. One gram of residues found in tonsillar crypts can contain 10^8 bacteria (with a ration of anaerobic to aerobic as high as 10:1) (72). During infections the number of bacteria increases significantly. Most common cause of acute tonsillitis in children and in adults are viruses (70-90%). Bacterial infections are much less common (10-30%) (72,93). Streptococcal infections of tonsils can lead to local complications (peritonsillar abscess) which are accompanied by malodor – usually much stronger than during primary disease (72,93). Microbiological examinations show, that 50% of complications of pharyngeal anginas are caused by anaerobic bacteria, 25% are caused by aerobic beta-*haemolyticus gr. A Streptococcus* and in the remaining 25% mixed bacterial flora is identified (72).

Anginas with superficial (aphtosis, thrush) or deep ulcerations (Plaut-Vincent's angina, mononucleosis) are less common. In Plaut-Vincent's angina *Spirochaeta denticolata* and *Bacillus fusiformis* are identified, but it is highly probable that other anaerobic bacteria also play an important role.

Sometimes chronic tonsillitis is mentioned as possible cause of halitosis (72,93,94,95). Frączkowska *et al*. found that 40% of pathogens in chronic tonsillitis were streptococci, 40% – *Staphylococcus aureus* and in remaining 20% *Candida spp*. were found (96). Radosz-Komoniewska *et al*. have demonstrated microbiological analysis of tonsillar smears taken from 158 patients with chronic purulent tonsillitis. Every time in about 30% of cases beta-haemolyticus streptococci were identified (97). Sometimes patients report formation of white or yellow, hard and foul smelling so called tonsillar stones that are an important source of halitosis (95, 98,99). Microbiological examination of tonsillar stones shown presence of anaerobic bacteria able to produce sulfuric gases (100). Inflammation of lymphatic tissue with ulcerations, and cancers can manifest with halitosis.

Fetor ex ore can be caused by conditions originating locally in pharynx or be transferred from other parts of respiratory and/or digestive tracts. Fungal infections manifest with halitosis. Acute submucosal inflammations, abscesses, erysipelas, can all be accompanied with

malodor. Halitosis in acute purulent laryngeal perichondritis usually develops due to complications of trauma or radiotherapy. Actinomycosis is typically connected with other infections of cervical tissues. Purulent discharge (when it appears) usually contains characteristic yellow papule (72).

Lower airways

Disruptions of physiological transport of mucus (for example in tobacco smokers) allows for easier bacterial infections of lower airways. Halitosis appears in such diseases as bronchitis (with accompanying necrosis and destruction of tissues), pulmonary abscesses or infected cysts (72,101). Fetor is also present in cancers of lower airways.

Halitosis in other systemic diseases

Some systemic diseases can also manifest with halitosis (3,10,101,102). *Fetor ex ore* is caused by disturbances in urea cycle, as a result of hepatic insufficiency. Ammonia present in exhaled air is sometimes described as *fetor hepaticus* due to its characteristic sweet odor (10). Also higher level of endotoxins in blood serum is observed (mercaptans, fatty acids, phenols). All these substances, when exhaled, contribute to halitosis (24). Van de Velde examined composition of exhaled air in 52 patients with hepatic cirrhosis using gas chromatography-mass spectrometry (GCMS). Authors have shown that dimethyl sulfide is responsible for fetor hepaticus (103).

Fetor ex ore comparable to the smell of rotten fish is often found in trimethylaminuria (TMAU, *fish odor syndrome*) (3,101,102,104). This is a rare metabolic disorder that causes trimethylamine to build up. It is released in the person's sweat, urine, and breath, giving off a strong, fishy odor.

Halitosis can be caused by chronic renal insufficiency (3,101,102). Products of protein metabolism accumulate in blood (82). Uremic toxins like : hippuric acids, guanidynoacetic acid and glycoproteins are probably responsible for characteristic odor. Ketonemia is another source of halitosis. It is usually present in poorly controlled diabetes or during starvation (3,101,102). It results in ketonemia, ketonuria and presence of ammonia in exhaled air.

Diagnosis of halitosis

Simple, subjective examination is considered a "golden standard" in clinical practice (12). It is a quick method that allows for initial localization of causes of halitosis. Smell of air exhaled from patient's mouth is compared to air exhaled through patient's nose with his mouth closed. If the fetor can be smelled only when the air is breathed through the mouth, the most probable source of halitosis is located in oral cavity or pharynx. If the odor is more significant when exhaling through the nose, then halitosis most probably originates in the nasal cavity, nasopharynx or paranasal sinuses. If odor's intensity from mouth and nose is comparable, a disease of lower airways, digestive tract or other systemic disease must be considered. It may also be a result of patient's diet or habits (Table 1).

Rosenberg's six-point scale is commonly used to describe intensity of halitosis (105,106,107). Patients breathes out air to a tube and the air is smelled by the examiner. Patients should not receive any antibiotics at least for 21 days prior to examination, avoid garlic, onions and other spicy foods for at least 48 hours before examination and also avoid using perfumes and deodorants for 24 hours prior to the examination. It is also recommended not to brush teeth, do not eat and/or drink, use breath fresheners and not smoke for 12 hours before the examination. The examiner should not drink tea, coffee, fruit juices at least few hours before examination. He should also be a non-smoker (or at least he should avoid smoking for at least few hours before examination). To increase credibility, the tests should be repeated for 2-3 consecutive days (108,109).

Objective confirmation of halitosis nowadays is based on detection of VSCs in exhaled air. Halimetric examination measures their total concentration in exhaled air, but does not identify particular chemical substances. Halimeters are highly sensitive for hydrogen sulfide, but not for methyl mercaptan, cadaverine, indoles nor skatoles (108). Therefore a lot of false negative results. Acetone, ethanol and methanol in exhaled air can on the other hand produce false positive results.

Fresh kiss is a small, portable device that operates on the same principles as halimeter – it measures concentration of VSCs and carbohydrates in exhaled air (48). A simple and quick way to assess intensity of malodor is Halitox-test. It allows identification of VSCs and polyamids (cadaverine, putrescine).

Accurate analysis of exhaled air (qualitative and quantitative) can be only obtained during GCMS analysis. Due to complex procedures and it's relatively high costs GCMS is not routinely used in clinical practice. Current research focuses on developing tests for halitosis based on incubation of patients saliva. Quirynen *et al*. reported that there is a positive correlation between saliva tests, organoleptic examination and instrumental tests (110). It is also possible to measure concentrations of ammonia in exhaled air (111,112).

Identification of bacteria responsible for halitosis is another, recent and accurate method of diagnosis. Identification of pathogens include polymerase chain reaction tests (PCR), dark-field microscopy (Treponema spp.) or using BANA-test (113).

In the diagnostic standard provided by the authors (Fig. 1) patients with typical smell sensations (like fish-odor) are excluded.

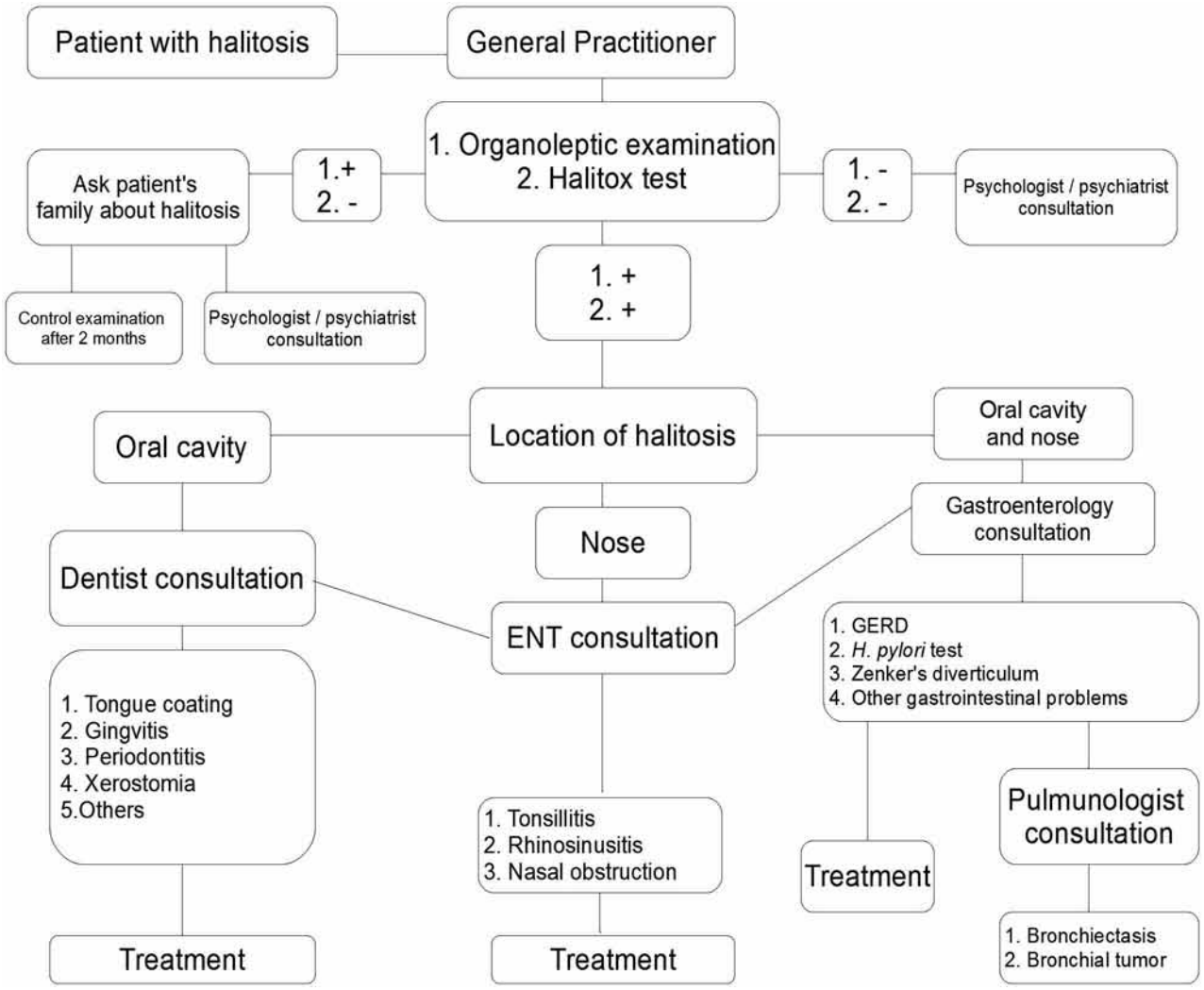

Fig. 1 – Suggested algorithm for the investigation of halitosis

Treatment of halitosis

Miyazaki *et al*. presented therapeutic standards for patients suffering from halitosis (114). Patients with oral halitosis should be treated by dentists. Patients with extraoral halitosis should be referred to GPs and later to appropriate specialists. Patients with halitophobia should be treated by GP, psychologists or psychiatrists. Oral hygiene usually prevents or limits malodor in patients with physiological halitosis. Proper adjustment of dental prostheses prevents accumulation of food remains in oral cavity and thus prevents halitosis. Most common cause of physiological halitosis is coating on the posterior dorsal part of the tongue. It contains epithelial cells, blood cells and bacteria. Over 100 bacteria producing sulfuric compounds may adhere to a single epithelial cell. In such cases cleaning of posterior part of the tongue with special brushes seems to be a good idea. However some scientist have shown that brushing the base of the tongue increases the risk of carcinogenesis (115,116). Most common cause of oral halitosis are periodontitis and caries. Proper sanitation of oral cavity is therefore the fundamental treatment. Popular breath-fresheners used today were already used by ancient Greeks. Citizens of Crete produced breath refreshing candies from *Cistus creticus* over 2000 years ago. Other popular breath fresheners include parsley in Italy, cloves in Iraq, cinnamon in Brazil, guava peels in Thailand, anise seeds (*lat. Pimpinella anisum)* in Far East (3). Also magnolia extracts or other essential oils are mentioned (117). Chewing gum or mint candies may also serve a temporary relief. All the above mentioned "treatments" only mask the fetor.

Lodhia *et al*. in 2008 conducted a research and shown that after drinking a cup of green tea, concentration of methanethiol in exhaled air diminished significantly (118). Popular mouth washing fluids containing chlorhexidine and zinc are effective in reducing the

malodor, however they may cause teeth stains, allergic reactions and often have unpleasant taste. Zinc participates in oxidation of thiol groups and therefore reduces the amount of sulfuric compounds in exhaled air up to 45% (119). Sterer *et al*. proposed new solution for fighting halitosis in 2005 (120). Authors showed that the exposure of mixed salivary microflora to blue light caused a reduction in malodor production concomitant with a selective inhibitory effect on the population of Gram-negative oral bacteria. These results suggest that light exposure might have clinical applications for the treatment of oral malodor.

In patients with halitosis lifestyle factors (proper diet, tobacco smoking, alcohol consumption) are important. Limiting the amount of consumed fats, proteins or alcoholic beverages significantly reduces *fetor ex ore* (47,67,121). Probably malodor can be also reduced by lowering patient's BMI. Rosenberg et. al suggested that body mass index (BMI) is predictive for bad breath, independent of alcohol consumption. Obesity is related to sleep apnea problems that may cause dry mouth, which presents a risk for bad breath (69).

Patients with pseudohalitosis, when presented with proper explanations, often understand their condition and require no further treatment. If multiple convincing is not effective, such patient can be diagnosed with halitophobia (108). Halitophobia can be also diagnosed in patients, who still claim to suffer from halitosis, despite confirmed, successful treatment of the underlying cause of halitosis. Such patients require proper psychological counseling or even psychiatric treatment.

Research on halitosis is currently conducted in many academic centers. Most important findings in the recent years include identification of *Streptococcus salivarius* in oral and Hp in extraoral halitosis. Still many unknowns remain in causes and mechanisms of this unpleasant pathology. Halitosis has a great impact on individual's life. It can significantly impair social interactions, lead directly to depression, low self-esteem or other mood disorders.

Conclusions and prospect for further research

Halitosis is an important symptom. It is mostly caused by oral disorders but it can be also the first manifestation of a many systemic diseases. Bad breath is a common medical and social problem. Proper treatment is important for the patients, their relatives and co-workers. Further research on diagnostic methods and treatment is therefore essential.

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