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Extra-oral Halitosis

Universidade Fernando Pessoa

Faculdade de Ciências da Saúde

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ABSTRACT

Halitosis affects around 25% of the whole population and has a large social and economic impact. For the majority of patients suffering from bad breath, it causes embarrassment and affects their social communication and life. Dentists and periodontologists are the first-line professionals to be challenged with this problem, so they should be aware of the origin, the detection and the treatment of this pathology. But halitosis can be indicative of underlying diseases, requiring a multidisciplinary team approach. Depending on the place where it is originated, halitosis can be divided into intra-oral and extra-oral, whose treatment is much more complicated than for intra-oral halitosis.

In this work, the origins of extra-oral halitosis were addressed, as well as the responsible sulfur compounds. Distinctive methods of detection of halitosis were focused and their advantages and disadvantages were highlighted. Gas differentiation methods as an auxiliary tool were emphasized in the diagnosis of halitosis type and, therefore, in its specific treatment. At last, different methods of treatment of extra-oral halitosis have been approached, from masking the bad breath to more invasive treatments.

Keywords: “halitosis”; “extra-oral”; “periodontology”; “sulfur compounds”; “dimethyl sulphide”; “microbiology”.

RESUMO

A halitose afeta aproximadamente 25% da população e tem um grande impacto social e económico. Para a maioria dos pacientes que sofrem de halitose, a patologia causa constrangimento e afeta a sua comunicação oral e qualidade de vida. Os médicos dentistas e periodontologistas são os primeiros profissionais a serem confrontados com este problema, pelo que devem dominar a deteção, diagnóstico e tratamento desta patologia. Mas a halitose pode ser indicativa de doenças mascaradas, sendo necessária a abordagem de uma equipa multidisciplinar. Dependendo do local de origem, a halitose pode ser dividida em intraoral ou extraoral, sendo o tratamento mais complicado na extraoral que na primeira.

Neste trabalho foram abordadas as diversas origens da halitose extraoral, assim como os compostos sulfurados responsáveis. Distintos métodos de deteção da halitose foram focados e evidenciados as suas vantagens e desvantagens. Foram salientados métodos de diferenciação gasosa como ferramenta de auxílio no diagnóstico do tipo de halitose e, consequentemente, no seu tratamento específico. Por último, foram discriminados métodos de tratamento da halitose extraoral, desde técnicas para disfarçar o mau hálito até tratamentos mais invasivos.

Palavras-chave: "halitose"; "extraoral"; "periodontologia"; "compostos sulfurados"; "dimetilsulfureto"; "microbiologia".

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LIST OF ABBREVIATIONS

AMS – Allyl methyl sulphide

CT – Computed tomography

DMS – Dimethyl sulphide

ENT – Ears, nose and throat

GC – Gas chromatography

GERD – Gastroesophageal reflux disease

H_2S – Hydrogen sulphide

MM – Methyl mercaptan

VSCs – Volatile sulphur compounds

I. INTRODUCTION

Bad breath is still a large but underestimated taboo. Halitosis affects around 25% of the whole population and has a large social and economic impact. A public investigation in 2005 in the Netherlands (Vandekerckhove, 2009), showed that halitosis was one of the one hundred biggest human overall exasperations. For the majority of patients suffering from bad breath, it causes embarrassment and affects their social communication and life. Dentists and periodontologists are the first-line professionals to be challenged with this problem, so they should be aware of the origin, the detection and the treatment of this pathology. But halitosis can be indicative of underlying diseases, requiring a multidisciplinary team approach: dentists, periodontologists, ear-nose-throat surgeons and specialists in family medicine, internal medicine and psychiatry need to be updated in this field (Aylikci, 2013).

There is lack of scientific data about this problematic and several reasons explain this. First, there is the difference in cultural and racial appreciation of odours, for patients as well as for investigators. Second, there is absence of uniformity in evaluation methods, both for organoleptical and for mechanical measurements (Rayman, 2008).

Large variety of data suggest that there are large shortcomings in the methodology of the overall research projects concerning halitosis (Vandekerckhove, 2009). A standardized evaluation protocol for halitosis studies is needed to compare epidemiological data. Therefore, a mechanical detection method should be selected as a golden standard for bad breath research.

1.1. Materials and methods

PubMed, Medline and B-on databases were electronically researched, from January to June 2017, for scientific articles, preferably of the last five years. The following keywords

were used, jointly or individually: halitosis, microbiology, periodontology, extra-oral, sulfur compounds, dimethyl sulphide. Additionally, manual search of articles was made.

II. DEVELOPMENT

2.1. Origin

Depending on the place where it is originated, halitosis can be divided into intra-oral (85%) and extra-oral (15%), whose treatment is much more complicated than for intra-oral halitosis.

Extra-oral halitosis might be a manifestation of a serious disease. It is therefore of utmost importance to differentiate between intra-oral and extra-oral halitosis (Calil, 2009). Extra-oral halitosis can be subdivided into non-blood borne and blood-borne (Saito, 2012).

2.2. Clinical differentiation between intra-oral and extra-oral halitosis

In almost all the cases, differentiation between intra-oral and extra-oral halitosis can be easily done by examining mouth as well as nose breath. Patients with intra-oral halitosis only have bad breath from the mouth but not from the nose. All patients with extra-oral blood-borne halitosis have bad breath from both the mouth and the nose, because of the presence of odorous volatile compounds in alveolar air. Nearly all patients with extra-oral non-blood-borne halitosis also have bad breath from both the mouth and the nose, except those patients in whom the origin of bad breath is situated in upper respiratory tract above the throat, e.g. in the nose. The later patients only have bad breath from the nose and not from the mouth (Quirynen, 2009).

2.3. Gas differentiation in halitosis

Regarding to odour type, bad breath can be roughly subdivided into three different types, namely breath with fruity odour, breath with an ammoniacal or urine-like odour and breath with sulphurous or faecal odour. The fruity odour is caused by the presence of acetone and is most often smelled in diabetics. The ammoniacal or urine-like odour is caused by the presence of ammonia and other amines (dimethyl amine, trimethyl amine), in uraemia (Tanaka, 2004). Microbial degradation in the oral cavity is the main cause of oral malodour. Due to this process, volatile sulphur compounds (VSCs) are produced, which give a faecal odour. The most important among these VSCs are hydrogen sulphide (H_2S), methyl mercaptan (CH_3SH) (MM) and dimethyl sulphide ($(CH_3)_2S$) (DMS) (Figure A.1). These VSCs are mainly produced by gram-negative anaerobic oral bacteria. Other molecules involved in this bacterial degradation process are diamines (indole and skatole) and polyamines (cadaverine and putrescine). They seem to play a less important role in bad breath, mainly because oral pH does not favour their volatilization (Krespi, 2006).

MM and, to a lesser extent, H_2S are the main contributors to intra-oral halitosis. These compounds immediately react with whole blood within seconds, resulting in irreversible binding and oxidation, preventing their transportation from the blood into alveolar air and thus into breath. That is not true for DMS, the prevailing VSC in extra-oral halitosis. DMS is a neutral molecule which is stable in the blood and can be transported by it from the gut into alveolar air and breath. This stability is responsible for the difficulty to remove DMS from blood. Then, DMS is a systemic and an oral volatile compound (Morita, 2001).

Investigation using an analytical technique to identify the volatile odorous compounds associated with the odour is highly important, in order to diagnose the cause and to find a possible treatment. In fact, breath analysis might become a good substitute for blood measurements when dealing with volatile organic compounds (Faveri, 2006). Identification of the odorant and simulation of the breath samples by producing experimental gas mixtures with the same concentration of the odorant is important for establishing a causative relation (Saito, 2012).

2.4. Extra-oral non-blood-borne halitosis

i. Ears, nose and throat

Maximally two thirds of the extra-oral malodour cases originate from the ears, nose and throat (ENT) region. Foreign bodies in the nose can become a hub for bacterial degradation and hence produce a striking odour to the breath. The purulent discharge from the paranasal sinuses gets collected at the dorsum of the tongue resulting in halitosis. Atrophic rhinitis is caused by *Klebsiella ozenae*, which inhibits the self-cleaning property of nasal mucosa. Carcinoma of the larynx, nasopharyngeal abscess, acute pharyngitis and sinusitis and lower respiratory tract diseases such as bronchiectasis, chronic bronchitis, lung abscess, asthma, cystic fibrosis, interstitial lung diseases, and pneumonia, have as well been known to cause halitosis (Aylikci, 2013).

Acute tonsillitis is the most important ENT origin of halitosis. Mostly, infections with streptococci play a role, but also viral infections (e.g. mononucleosis infections) are possible. In the case of chronic tonsillitis, the elimination of the deep crypts, which harbour exfoliated cells, debris and bacteria, is important. Patients can be instructed to perform a proper hygiene by squeezing the debris out of the cryptic tonsils. Alternatively, a tonsillectomy is recommended when oral hygiene measures do not result in improvement of the breath (Lanza, 2004).

Bacterial sinusitis develops mostly from acute viral sinusitis. *Streptococcus pneumonia* and *Haemophilus influenza* are the main responsible bacteria. On radiological or computed tomography (CT) images, fading is perceived. When purulent mucous is produced, a typical odour appears (Lanza, 2004).

ii. Oesophagus and pulmonary pathology

When a Zenker's diverticulum is present, a chronic unpleasant odour appears. The incidence of this phenomenon is less than 0.1%. Also, bleeding of the oesophagus can cause a musty odour. Symptomatically, coughing, postnasal drip, pyrosis, irritations and ulcerations of the oesophagus and halitosis will be detected. When the diagnosis is missed, carcinomatous deterioration can occur (Stoeckli, 2002).

2.5. Extra-oral blood-borne halitosis

i. Stomach and intestine

In a study where 94 patients had halitosis, 54 of those had gastrointestinal pathology, suggesting that gastrointestinal problems are one of the common extra-oral causes of halitosis. Gastrointestinal causes like gastroesophageal reflux disease (GERD), gastric and peptic ulcers, *Helicobacter pylori*, congenital bronchoesophageal fistula, gastric cancer, hiatus hernia, pyloric stenosis, enteric infections, dysgeusia, duodenal obstruction, and steatorrhea are some of the sources of pathological mouth odour (Kinberg, 2010).

A faecal mouth odour may be also detectable in cases of intestinal obstruction (Kinberg, 2010).

ii. Metabolic disorders

Renal failure, and cirrhosis are associated with high blood urea nitrogen levels and low salivation flow rates, leading to halitosis. Peritoneal dialysis decreases the problem.

Also, pancreatic insufficiencies can cause oral bad odours (Keles, 2011).

Diabetic ketoacidosis leads to a typical breath odour, so type 2 diabetes patients exhibit a typical sweet and fruity odour (Van Steenberge, 2009).

Several metabolic disorders like trimethylaminuria cause a specific fishy odour and may lead to halitosis. This genetic disease is the largest cause of undiagnosed body odour. Trimethylaminuria is a disorder in which the volatile, fish-smelling compound, trimethylamine accumulates and is excreted in the urine, but it is also found in the sweat and breath. Trimethylamine is formed by bacteria in the mammalian gut from reduction of compounds. Primary trimethylaminuria sufferers have an inherited enzyme deficiency where trimethylamine is not efficiently converted to the non-odorous trimethylamine-N-oxide in the liver. Diagnosis of trimethylaminuria requires the measurement of trimethylamine and trimethylamine-N-oxide in urine. The symptoms of trimethylaminuria can be improved by changes in the diet to avoid precursors of trimethylamine, which are found in high concentrations in marine fish. Treatment with antibiotics to control bacteria in the gut, or activated charcoal to sequester trimethylamine, may also be beneficial (Mackay, 2011).

In hypermethioninemia the body produces a peculiar odour which resembles boiled cabbage and is emanated through sweat, breath and urine (Mudd, 1995).

Also, some hereditary disorders can influence the breath: tyrosinemia is the most important example, which manifest cabbage odour (Van den Velde, 2008).

Cysteamine usage in patients with nephropathic cystinosis resulted in extra-oral blood-borne halitosis due to formation of DMS, an unwanted by-product, out of cysteamine (Gahl, 1995).

Elevated levels of DMS can also be found in apparently healthy patients, in which no systemic disease is detected. The elevation of DMS in these patients is likely due to a hitherto unknown metabolic disorder (Sigler, 2009).

iii. Hepatology and endocrinology

The fetor hepaticus in patients with liver cirrhosis is caused by DMS, which originates from the gut. Extensive shunting of portal blood around the liver in cirrhosis results in elevated DMS concentration in systemic blood. Liver failure inhibits the detoxification of the whole body, causing unpleasant odours (Van Den Velde, 2008).

In severe hepatologic problems, a liver transplantation can be necessary. In less life-threatening situations, liver dialysis can be sufficient to treat the problems. In more simple pathology, cortisone therapy and a stringent diet can be enough (Malaguarnera, 1997).

In the endocrinological range of problems, the underlying diseases should be treated before to eliminating other possibilities of halitosis causes.

iv. Food and drugs

Garlic and onion are the foods that most commonly cause bad breath. Immediately after garlic intake, the thiol allyl mercaptan, containing a reactive -SH group, is only measured in the mouth air and not in alveolar air, indicating that the mouth is the site of origin of allyl mercaptan. Three hours after garlic intake, the neutral sulphide allyl methyl sulphide (AMS) is the predominant sulphur gas in alveolar air. AMS is a neutral and stable compound and it can be transported by blood from the gut into alveolar air and breath. The most of AMS originated from the gut is responsible for the well-known persistence of malodorous breath long after garlic ingestion (Tangerman, 2002). While the garlic intake is responsible for elevated concentration AMS, the onion consumption is tied with the elevation of onion sulphides: methyl 1-propenyl sulphide and methyl propyl sulphide (Suarez, 1999).

Various drugs like alcohol, tobacco, betel, solvent misuse, chloral hydrate, nitrites and nitrates, dimethyl sulphoxide, disulphiram, some cytotoxic agents, phenothiazines and amphetamines have also been known to cause halitosis (Saleh, 2015).

2.6. Detection

Nowadays, the gold standard for the detection of bad breath is the organoleptic scoring, i.e., smelling the odour of the patient mouth. Anamnesis has an important role and should contain the main complaints, medical, dental and halitosis history, and information about diet and habits. Halitosis history should be discretely and intermittently recorded. Questions such as frequency, duration, time of appearance within a day, whether others have identified the problem (excludes pseudo-halitosis from genuine halitosis), list of medications taken, habits (smoking, alcohol consumption) and other symptoms (nasal discharge, anosmia, cough, pyrexia, and weight loss) should be carefully recorded. An investigative protocol was designed for the diagnosis of oral malodour that can be used in clinical practice and is of significance to family health care practitioners (Table A.1, in annex) (Donaldson, 2007).

i. Odour characteristics

Odour threshold values are important in odour research. Three odour thresholds have been determined: 1- perception threshold, 2- recognition threshold and 3- objectionability threshold. At the perception threshold, one is barely certain that an odour is present, but it is too faint to identify it further. The recognition threshold is the concentration at which 100% of the odour panel defined the odour as being representative of the odorant being studied. The objectionability threshold represents the lowest concentration of an odorant producing an objectionable smell (Verschuren, 1983). To be considered halitosis, the concentration of the odorant in the breath must exceed the threshold of objectionability

of that odorant (Tangerman, 2007). Usually, volatiles with the lowest recognition threshold are the most odorous ones. Unsaturated mercaptans (allyl mercaptans in garlic) and the unsaturated sulphides (allyl methyl sulphide in garlic) are the most odorous ones, followed by saturated mercaptans (propyl mercaptan in onion, methyl mercaptan, hydrogen sulphide), disulphides (dimethyl disulphide) and sulphides (methyl propyl sulphide in onion and dimethyl sulphide) (Verschuren, 1983).

To make sure that a volatile might contribute to halitosis, the concentration of the suggested odorant is measured in the breath and artificial gas mixtures with the measured concentration of the odorant are made in order to simulate the breath. These artificial gas mixtures must produce a certain smell, similar to the halitotic breath, in order to conclude that the odorant is an important contributor to halitosis (Tangerman, 2007).

ii. Organoleptic score

In expired air, more than 150 different components have been detected. The perception of these molecules is dependent of the olfactory response, the threshold concentration, the strength of the odour and the volatility of the molecules. When organoleptic scoring is performed, a well-trained clinician determines if the odour samples smell bad or not, giving a score to the intensity. These scores go from 0 up to 5 (Suarez, 1999).

From every patient, different samples are analysed from mouth, saliva, tongue, interdental (a floss is used), nasal and prosthesis. The patient should refrain from spicy foods, garlic or onion the day before the examination. At least 12 h before the consultation, teeth should not be cleaned or rinsed, perfumes should be avoided and, at least 6 h before the examination, the intake of food or liquids should be avoided. Smoking should be stopped at least 24 h before any examination (Seemann, 2006).

The advantages of organoleptic scoring are: inexpensive, no equipment needed and a wide range of odours is detectable. As disadvantages, the extreme subjectivity of the test, the

lack of quantification, the saturation of the nose and the lack of reproducibility can be mentioned (Seemann, 2006).

iii. Portable gas analysis

The Halimeter (Interscan corporation, Chatsworth, California, USA) (Figure 1) and the OralChroma (Abimedical corporation, Miyamae-ku Kawasaki-shi, Kanagawa, Japan) (Figure 2) are electronic devices available to detect some of the VSCs in expired air. The Halimeter can only give an idea of the total amount of VSCs present in a sample. The OralChroma is a portable gas chromatograph offering higher performance and more user-friendly operations than conventional gas chromatographs by limiting the target gases to three types: 1- H_2S, 2- MM, 3- DMS. Also, an interpretation of the results can be shown to the patients.

These portable machines have a lot of advantages: easy to handle, fast results, portable and reproducible. Furthermore, they are rather inexpensive and can be controlled by untrained staff. As disadvantage, the limited diversity in the explored gases should be stated. More recently, it was shown that the OralChroma may produce a more comprehensive assessment of VSC production by oral microflora than the Halimeter. It would be desirable to select one machine as a gold standard to make different studies comparable in the future (Salako, 2011).

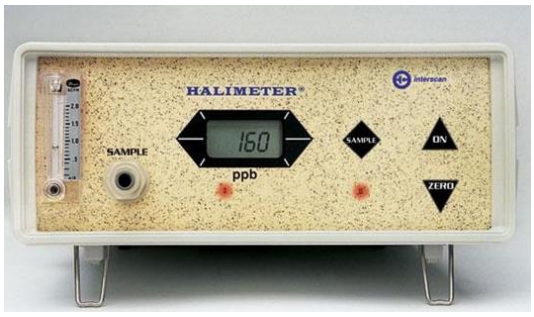

Figure 1 – Halimeter (reprinted from https://www.halimeter.com/wp-content/uploads/2012/01/hallie11.jpg).

Figure 2 – The OralChroma (reprinted from www.fisinc.co.jp/en/products/oralchroma.html).

iv. Gas chromatography

Gas chromatography (GC) analysis can be performed on breath, saliva and tongue debris. GC has several advantages: an analysis of almost all components with high sensitivity and specificity. The method is non-invasive, but expensive, and a well-trained staff is needed. The progression of the method takes much more time and the machine cannot be used in daily practice. The other objective measurements of the breath components are rarely used in routine clinical practice, as they are expensive and time-consuming (Tonzetich, 1991).

2.7. Therapy

i. Treatments approach

Specific investigations should be carried out to isolate the source that should be either pharmaceutically (e.g. broad spectrum antibiotic coverage for pharyngitis, drugs such as proton pump inhibitors for GERD) or surgically (tonsillectomy/adenotonsillectomy,

liver/kidney transplantation) managed. Also, in the endocrinological and metabolic disorders, the underlying diseases should be treated (Feller, 2005).

ii. Masking effect

The usage of masking agents like rinsing products, sprays, toothpaste containing fluorides, peppermint oil, mint tablets or chewing gum only have a short-term masking effect. Mostly, they increase the saliva production, which is useful since dry mouth may result in halitosis and also because it allows retaining more soluble sulphur components for a short period of time (Kleinberg, 2002; Haghgoo, 2013).

The patient's diet is another factor that should be discussed when recommending a plan to combat oral malodour. The patient should be instructed to quit smoking, avoid tobacco products and to use baking soda dentifrices (Thosar, 2013).

iii. Probiotics

Several studies were performed to replace bacteria responsible for halitosis with probiotics as *Streptococcus salivarius* (K12), *Lactobacillus salivarius* or *Weissella cibaria*. The objective is to prevent re-establishment of non-desirable bacteria and thereby limit the re-occurrence of oral malodour over a prolonged period (Burton, 2006).

2.8. Halitophobia

Halitofobia is the fear of having bad breath that other people find offensive. Moreover, 0.5% to 1% of the adult population is affected with this problem in their social live. These patients consider having bad breath, do not have it, but get not convinced during diagnosis and therapy. Non-real halitosis or halitophobia is understood by the compulsive idea to suffer from bad breath and to irritate others by this. Consultation hours for halitosis should be prepared for patients with non-real halitosis and build up corresponding interdisciplinary contacts. The ‘treatment' of these patients is impossible, since they do not believe in the arguments stated by a physician. Mostly, these patients hop from clinic/specialist to clinic/specialist to find an argument for their self-esteem problem. Imagined halitosis is poorly documented in the psychiatric literature (Nagel, 2006).

III. DISCUSSION

There is a huge variety of shortcomings in the methodology of the overall research projects (Vandekerckhove, 2009) and there is not uniformity in evaluation methods, both for organoleptical and for mechanical measurements (Rayman, 2008). Halitosis is subdivided into three diverse types of odour: fruity, urine-like and faecal odour (Tanaka, 2004). Overall, diamines, polyamines, DMS, MM and H_2S play a role in halitosis, but the majority is caused by DMS (Krespi, 2006). Investigations to identify the specific compounds associated with a particular odour and to utilise odour index and odour thresholds are highly important to differentiate between intra-oral and extra-oral halitosis (Quirynen, 2009; Saito, 2012), in order to make a complete diagnosis and find the adequate treatment (Faveri, 2006), however this is scarcely done in the field.

Two thirds of the extra-oral malodour cases originate from ENT region (Aylikci, 2013). Moreover, tonsillitis is the most important ENT origin of halitosis (Lanza, 2004).

In regard to blood-borne halitosis, Kinberg believe that gastrointestinal pathology is one of the most common extra-oral causes (Kinberg, 2010). Moreover, trimethylaminuria and hypermethioninemia are the major causes of undiagnosed body malodour (Mudd, 1995; Mackay, 2011).

Currently, organoleptic score is the gold standard for the bad breath detection (Donaldson, 2007), but odour threshold values should be the priority option in odour research. Tangerman reported that the concentration of the odorant in the halitotic breath must exceed the threshold of objectionability of that odorant when measured in machines as OralChroma (Tangerman, 2007).

Dentists, regardless of their specialty, become more accurate when they use objective methodologies. Consequently, equipment that shows threshold values of halitosis tests and their maximum acceptable limits, as well as identification of the responsible gas, deserve special attention of the scientific community that is focused on halitosis subject.

Then, machines have a lot of advantages, namely allow objectivity and reproducibility of the results and may be controlled by untrained staff, however the limited diversity in the explored gases is a disadvantage. OralChroma and Halimeter are the portable devices available to detect VSCs present in a sample, though the first one provides a more comprehensive evaluation than the second (Salako, 2011). Gas chromatography analysis is a very sensitive and specific method, however it is expensive, and a well-trained staff is needed, therefore, it cannot be used in daily practice (Tonzetich, 1991). OralChroma seems the best option of the moment to diagnosis efficiently halitosis because it can differentiate the three most important gases involved and can be used in a daily basis.

IV. CONCLUSION

Halitosis is a common condition, affecting around 25% of the general population. The origin of the problem largely arises from intra-oral causes, whereas only a limited number of cases are the result of extra-oral or systemic problems. The majority of extra-oral

blood-borne halitosis is caused by the presence of DMS. Nevertheless, proper investigation and management of these extra-oral causes is important for the total understanding of this phenomenon. Halitosis from an extra-oral origin can be the sign of an underlying systemic disease. Therefore, it is important to organize halitosis consultations in a multidisciplinary setting to better understand and treat the problem.

Threshold values must be determined for each gas present in a particular case of halitosis, in order to differentiate which one is the responsible for the bad breath and what is the origin of the problem.

A limited number of successful treatment regimens have been described, but more research on the long-term outcomes of these therapies will be required, as well as on more efficient treatments.

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VI. ANNEX

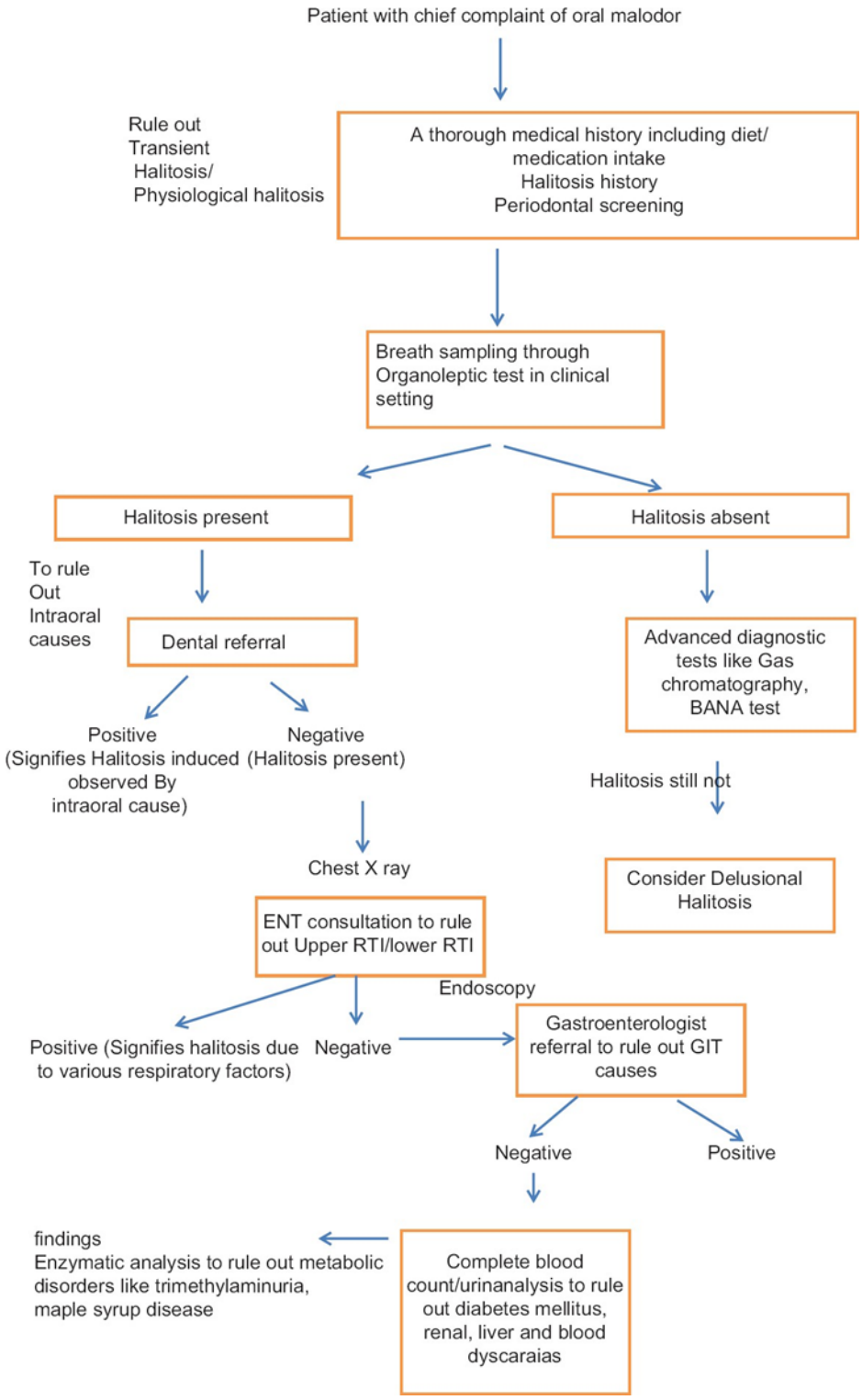
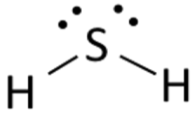
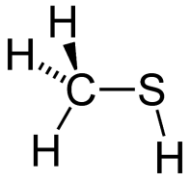


Table A.1 – Diagnosis protocol (reprinted from Donaldson, 2007).

a) 

b) 

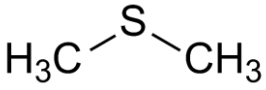
c) 

Figure A.1 – Chemical structures of a) hydrogen sulphyde, b) methyl mercaptan and c) dimethyl sulphyde (reprinted from: a) http://study.com/cimages/multimages/16/hydrogen_sulfide.png, b) https://upload.wikimedia.org/wikipedia/commons/7/7f/Methanethiol2D.png and c) https://upload.wikimedia.org/wikipedia/commons/thumb/8/83/Dimethyl_sulfide_structure.svg/2000px-Dimethyl_sulfide_structure.svg.png).