

# Current Comments

## Halitosis, the Silent Affliction: A Profile of Bad-Breath Research

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There are some subjects that most people are reluctant to discuss. While theoretically nothing is taboo in the medical literature, doctors as humans are affected by social mores. So when I thought about the general subject of halitosis, or bad breath, I expected to find a dearth of literature on the subject. Actually, as is often the case, there is far more literature written on most subjects than you can absorb in a reasonable amount of time.

I got interested in the subject because an acquaintance told me he had suffered halitosis due to a chronic, "low-grade" nasal infection. An allergist recommended initial treatment with an antibiotic and then regular use of an antihistamine, and the problem was solved. But this person had not been aware of his bad breath until a close friend had the courage and the interest to tell him. It is difficult to say what percentage of the population suffers from this allergic disorder. They probably represent only a fraction of those who suffer from halitosis. The symptoms, or disease, as the case may be, could be due to a multitude of causes.

The collective prevalence of these causes is manifested in the widespread use of products designed to make us temporarily socially acceptable. Millions of people indulge in self-treatment. In fact, Americans alone spend nearly one half billion dollars per year on products designed to overcome bad breath.<sup>1</sup>

Concern about bad breath goes back to ancient times. One of the earliest discussions of offensive breath can be found in the Ebers papyrus, which dates from around 1550 BC.<sup>2</sup> This document identified various aromatic substances such as myrrh and frankincense which could be used to overcome mouth odor. Pliny the Elder (23-79 AD) wrote that bad teeth, old age, and some foods could cause bad breath.<sup>2</sup> His observations are still valid, although much more is known about the problem. In Shakespeare's *Midsummer-Night's Dream*, Bottom exhorts the other characters in the play to "eat no onions nor garlick, for we are to utter sweet breath...."<sup>3</sup>

In the literature, bad breath is usually referred to as halitosis or oral malodor. The word "halitosis" comes from the Latin *halitus*, which means "breath," and the Greek suffix *osis*, to specify a condition or a process. According to more recent medical studies, however, bad breath is anything but abnormal. Nearly everyone awakes with bad breath each morning. One experiences oral malodor after any prolonged period of decreased salivary flow,<sup>4</sup> as in fasting or sleeping.<sup>5</sup> So any drug which decreases salivation may have the same effect.

While ordinary healthy breath has been described as smelling like "blooming chestnuts,"<sup>2</sup> offensive breath manifests itself in a variety of ways depending on the cause. Mouth odors have been described as "smelling like rotten eggs"<sup>6</sup>

or "smelling fishy."<sup>7</sup> Although halitosis usually originates in the mouth, it can be the result of many causes. They vary from hormonal changes during the menstrual cycle to sinus infections.<sup>4,8</sup> I will discuss these causes later in this essay.

What causes ordinary bad breath? Scientists now concur that ordinary mouth odor is primarily caused by volatile sulfur-bearing compounds—such as hydrogen sulfide and methylmercaptan. These substances are generated through the metabolic activities of microorganisms in the mouth. Food and proteins remaining in the mouth after eating are degraded by the microorganisms into peptides and constituent amino acids. These further degrade into the highly volatile sulfur compounds.<sup>9</sup>

The species of microorganisms implicated most often in oral odor are *Fusobacterium*, *Bacteroides*, and *Klebsiella*, although other species can also be involved.<sup>10</sup> These anaerobic organisms multiply in the mouth where the lack of oxygen favors their survival.<sup>11</sup> They thrive on dental plaque, the sticky substance which accumulates on teeth. Plaque also accumulates in mouth areas such as the gingival crevice (the space between the surface of a tooth and the overlapping gum) and the tongue. They also multiply in any saliva that becomes trapped in periodontal defects, or in any area outside of the mainstream of salivary flow.

Boguslaw Krotoszynski and colleagues, IIT Research Institute, Chicago, have proposed that gas chromatography (GC) be used to diagnose the causes of mouth odors.<sup>12</sup> A gas chromatograph is an instrument which separates gases into their constituent compounds for identification. Its use in breath studies was pioneered by J. Tonzetich, University of British Columbia,<sup>13</sup> and has been followed up by other researchers.<sup>10,14,15</sup> Prior to the application of GC, volunteers or specially trained judges had to smell and evaluate samples

taken from the mouth. GC offers a number of advantages. It can distinguish small quantitative differences in compounds. GC can also identify specific components responsible for malodors, something human observers cannot do. Humans differ in their perceptions of odor intensity. What each person considers objectionable varies considerably.<sup>16</sup> Our subjective reactions to any kind of body odor are in part determined by culture. In countries where periodontal problems often go untreated, bad breath may be more common and socially acceptable. Human panels are sometimes necessary to place the results of GC studies in perspective, because only a human can tell if the substances isolated through GC are offensive.

As one might assume, diet can sometimes cause bad breath. For example, one physician reported that a patient with a vegetarian diet complained of a strong vegetable odor on his breath.<sup>17</sup> Garlic and onions have long been implicated in halitosis. When you indulge in such odor-producing foods, the volatile substances dissolve in the blood and are transferred to the expired air in the lungs.<sup>11,18</sup>

An improperly balanced or "fad" diet can cause bad breath as well. Individuals on the Atkins Diet<sup>19</sup> or on the Doctor's Quick Weight Loss Diet,<sup>20</sup> which are high in protein and low in carbohydrates, can suffer halitosis. As explained earlier, it is protein that degrades into sulfur-bearing compounds. Stomach odors can taint the breath during belching,<sup>11</sup> or by regurgitation, as with a "nervous," nauseated stomach.

It is well known that cigarette smoke and alcohol can cause unpleasant breath. Like garlic and onions, these substances yield volatile by-products which pass into the breath through the lungs. "Nicotine" breath is well known, as is the telltale sign of drinking beer, wine, or whiskey. The breath tests police perform on drivers suspected of excess

drinking use a "photometric colorimeter." This device contains a mixture of potassium dichromate and sulfuric acid. Breath passes through this mixture, which changes color in proportion to the amount of alcohol present.<sup>21</sup>

While much normal bad breath is diet-related, some studies have linked bad breath in women to the menstrual cycle. In 1970, R.E.S. Prout and Rosamund Hopps, University of Sheffield, England, pointed out that the bacteria count in saliva increases during both menstruation and ovulation.<sup>22</sup> This occurs because hormonal changes during these times cause the gums to become edemic, or bloated. This swelling traps bacteria between the gums and teeth, which in turn can cause gingivitis (inflammation of the gums).

In 1978, Tonzetich and colleagues performed follow-up research in which they studied five female subjects to observe changes during their menstrual cycles.<sup>23</sup> They found a definite tendency for volatile sulfur compounds to increase up to four times the normal level around mid-cycle at or near ovulation, and during menstruation. The researchers speculated that increases in these compounds may be related to increases in estrogen levels. The study confirms the often noticed symptom of bad breath during menstruation.<sup>23</sup> Taking this study one step further, James G. Kostelc and colleagues, Monell Chemical Senses Center, ISI®'s neighbor in the University City Science Center, have recently suggested that measurement of the volatile sulfur compounds involved in mouth odor may help to predict the time of ovulation. This could be helpful to couples who are trying to conceive.<sup>24</sup>

Bad breath is also common during pregnancy. At that time, as during ovulation, the gums become edemic, a finding reported by Harald A. Loe, University of Connecticut, School of Dental Medicine.<sup>25</sup> Again, swollen gums enhance the ability of microorganisms to

settle in the gingival crevice. After pregnancy, the gums usually return to normal. Incidentally, Loe coauthored the two most-cited papers mentioned in our recent study of the dental literature.<sup>26</sup>

Severe bad breath can be a symptom of one or more diseases of the mouth. Kostelc's group notes that the putrefying action of buccal microorganisms accelerates with periodontal disease and gingivitis.<sup>27</sup> Periodontitis is responsible for the loss of more teeth than dental cavities after age 30.<sup>28</sup> It begins as gingivitis, or inflammation of the gums, and gradually spreads to attack the tooth-supporting bone and the periodontal ligament. Pockets of soft supporting tissue are formed, which bleed readily when the gums are brushed. The teeth may loosen as the disease progresses into the supporting structures.<sup>28</sup> People with gingivitis or periodontal disease have higher bacterial counts in their saliva than do people with healthy mouths.<sup>29</sup>

In a recent study,<sup>30</sup> GC was used to isolate other volatile compounds found in the mouths of people with periodontitis—pyridine and 2-, 3-, and 4-picoline. These chemicals are absent from mouths that are healthy. This study may lead to a useful diagnostic tool for individuals suffering from periodontitis.

A small proportion of bad breath is caused by organic dysfunctions or diseases. These were recently summarized by Paul Goldhaber, Harvard University, School of Dental Medicine.<sup>28</sup> Chronic renal failure, for example, causes the patient to emit a "fishy" or "fetid" odor. A group at Thomas Jefferson University, Philadelphia, confirmed that the odor in these patients is caused by either dimethylamine or trimethylamine. Their findings suggested that intestinal bacteria rather than oral bacteria were involved in the increase in breath amines.<sup>7</sup> A 1975 study by Bennet Lorber, Temple University, Philadelphia, implicated anaerobic organisms as the cause of fetid

breath odor in some patients with lung infection. Lorber suggests that bad breath could be an early symptom of this disease.<sup>31</sup>

One of the symptoms of gonorrhea is bad breath. Lesions may spread from the primary site of infection to the mouth, causing tissues to become inflamed or ulcerated. At the same time, the saliva thickens, and the victim develops bad breath.<sup>28</sup> Syphilis of the nose can cause halitosis due to gumma formation, the soft gummy tumor characteristic of tertiary syphilis.<sup>32</sup> Cold sores caused by herpes simplex virus are also associated with a foul odor and acute gingivitis. Symptoms tend to disappear after ten to 14 days.<sup>28</sup>

Diseases of the upper respiratory tract often cause bad breath. E.L. Attia and K.G. Marshall, McGill University and Montreal General Hospital, recently reviewed these causes. They point out that chronic sinusitis and foreign bodies in the nasal passage can produce a foul-smelling discharge. Some upper gastrointestinal conditions also produce halitosis. Any condition that decreases the salivary flow can cause bad breath. Abscesses on the tonsils or the larynx are common causes, as are carcinomas of these areas.<sup>32</sup>

In some cases, patients may have no alternative to accepting bad breath, especially when needed medication is a cause. Dennis Bauman, a Cincinnati physician, reported several years ago that two of his patients taking isosorbide dinitrate to relieve angina exhibited foul breath. The problem was reversed when therapy was discontinued.<sup>33</sup> Drugs can alter the senses of taste and smell which can cause "subjective halitosis." The patient may believe he or she has bad breath but others cannot detect it.<sup>32</sup> Drugs can also be excreted through the breath. For example, dimethylsulfoxide, which is used for chronic bladder infections, is known to produce an odor of "stale oysters."<sup>32</sup>

When a patient complains of bad breath, the dentist or physician should take a thorough case history. According to Attia and Marshall, "A short duration of symptoms suggests an infectious source...or an oropharyngeal or lung abscess, recent drug use, a severe systemic disease, recent experimentation with ethnic cooking or...a foreign body in the nose."<sup>32</sup> If a patient who exercises good oral hygiene has had bad breath for a long time, then carcinoma of the mouth, pharynx, or upper respiratory tract could be the cause. Intermittent bad breath could be "food or sleep induced" or it might be a result of intermittent causes such as the draining of an abscess.<sup>32</sup> Furthermore, salivary gland dysfunction could result in decreased salivary flow, causing halitosis.

People afflicted with ordinary bad breath can use a variety of common-sense oral hygiene methods to rid themselves of it. You can easily remove mouth odors temporarily by rinsing out your mouth with water, brushing your teeth, brushing your tongue, using dental floss, and even eating a meal.<sup>34</sup> The volatile compounds causing bad breath are either dislodged from the mouth and flushed away through these efforts or are diluted by the food and drink. Eating tends to stimulate the flow of saliva.<sup>34</sup>

A variety of commercial remedies are available to individuals concerned about their breath. Atkins suggests that dieters carry chlorophyll tablets or Sen-sen to cure the bad breath caused by an unbalanced diet.<sup>19</sup> These items primarily "mask" bad breath. Breath mints and other cover-ups do work, but their effects last only around 20 minutes, or about the time it takes for the mint to dissolve in the mouth.<sup>11</sup> Some mouthwashes offer chemical neutralization as a way to deal with bad breath. The agents react with the offensive compounds to form nonodorous products.<sup>11</sup> A recent report issued by a Food and Drug Administration (FDA) panel describes the

**Table 1:** Core papers from *ISI/BIOMED*<sup>TM</sup> research front #81-2577: "Gingival effects of oral drugs."

- Löe H.** The gingival index, the plaque index and the retention index systems. *J. Periodontol.* 38:610-6, 1967.
- Löe H & Sñness J.** Periodontal disease in pregnancy. I. Prevalence and severity. *Acta Odontol. Scand.* 21:533-51, 1963.
- Ramfjord S P.** Indices for prevalence and incidence of periodontal disease. *J. Periodontol.* 30:51-9, 1959.
- Sñness J & Löe H.** Periodontal disease in pregnancy. II. Correlation between oral hygiene and periodontal conditions. *Acta Odontol. Scand.* 22:121-35, 1964.
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**Table 2:** Core papers from *ISI/BIOMED*<sup>TM</sup> research front #81-2753: "Oral bacteria associated with gingivitis and periodontal disease."

- Newman M G & Socransky S S.** Predominant cultivable microbiota in periodontosis. *J. Period. Res.* 12:120-8, 1977.
- Slots J.** The predominant cultivable microflora of advanced periodontitis. *Scand. J. Dent. Res.* 85:114-21, 1977.
- Slots J.** Subgingival microflora and periodontal disease. *J. Clin. Periodontol.* 6:351-82, 1979.
- Socransky S S.** Microbiology of periodontal disease—present status and future considerations. *J. Periodontol.* 48:497-504, 1977.
- Socransky S S.** Relationship of bacteria to the etiology of periodontal disease. *J. Dent. Res.* 49:203-22, 1970.
- Tanner A C R, Haffer C, Bratthall G T, Visconti R A & Socransky S S.** A study of the bacteria associated with advancing periodontitis in man. *J. Clin. Periodontol.* 6:278-307, 1979.

variable effectiveness of these agents.<sup>11</sup> Their success depends on how long the neutralizing agent remains in the mouth, the quantity of compounds to be neutralized, and how quickly the bad breath is being regenerated.

Probably the most controversial method of "curing" bad breath is the use of agents that inhibit bacterial growth, that is, "kill the germs that cause bad breath." This aspect of mouthwashes was also the subject of the FDA panel investigation.<sup>11</sup>

Antimicrobial agents known to work against bacteria *can* decrease bad breath as several studies have shown,<sup>35-38</sup> but there may be significant problems associated with their use. According to the FDA panel, agents that may be effective in one person may not be effective in another due to variations in the susceptibility of the microorganisms to the agent.<sup>11</sup> The panel notes that there is also ample evidence that antimicrobial effects are partial and incomplete, and that not all of the microorganisms are

killed by one application. In fact, the agent would have to be *reapplied every three to four hours*. Therefore, the FDA panel emphasizes that mouth odors without the presence of symptoms are "not indicative of the existence of a pathologic state and the use of antimicrobial and other therapeutic agents for their elimination is unwarranted."<sup>11</sup>

It's not surprising that the major impetus for bad-breath research comes from the pharmaceutical companies which produce mouthwashes. Each of the companies has a major stake in showing that its product can indeed control bad breath. Much of the independent research on bad breath has been carried out at Monell Chemical Senses Center. Although Tonzetich is a professor at the University of British Columbia, he did much of his work on halitosis, in collaboration with the Kostelc group, while a visiting scientist at Monell.

In 1957, Maynard K. Hine, Indiana University, School of Dentistry, offered a few thoughts on the social implications of

bad breath. He noted that humans are forced to live in close contact with each other, so that anything about them which is unpleasant can interfere with their acceptance by others. He added that this problem is especially acute among dentists, who work in close proximity to their patients. Also, the recognition that halitosis is both common and unpleasant causes fear that "can reduce a person's confidence in approaching others and can interfere with his effectiveness."<sup>8</sup>

Incidentally, in one of the few studies on this subject, men and women rated the intensity and pleasantness of breath odors from 14 men and 19 women who performed no oral hygiene procedures. The breath odors of the men were rated as more intense and less pleasant than those of the women, and women were more likely to make this judgment.<sup>39</sup>

While bad breath is a social concern, it is also a legitimate biomedical research area. The close relationship between halitosis research and other areas of basic research is demonstrated by ISI's biomedical data base *ISI/BIOMED*<sup>™</sup>. I looked up the research fronts listed under "oral bacteria" in the 1982 *Index to Research Fronts in ISI/BIOMED*.<sup>40</sup> As a result, I found two recent papers by Kostelc<sup>30</sup> and Tonzetich<sup>41</sup> by using the codes for "Gingival effects of oral drugs"

(#81-2577), and "Oral bacteria associated with gingivitis and periodontal disease" (#81-2753). Besides the current relevant papers, I also found the core papers for these research fronts. They are listed in Tables 1 and 2.

Research on bad breath is now branching into new areas not envisioned by those who first undertook its study. For the original researchers, halitosis study represented a way to understand a serious social concern. That they successfully showed the causes of bad breath is an important accomplishment. That they went beyond this restricted area proves the value of basic research on a subject that some people, such as Senator William Proxmire, consider unworthy of taxpayer support. Many will benefit from the fruits of halitosis research in stronger, healthier teeth and gums and greater understanding of the degenerative processes that cause periodontal disease. But as we have seen, this research may also provide significant benefits in other areas of medicine as well.

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