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Good Bacteria for Bad Breath

Curing halitosis requires the right balance of oral microbes

Most adults have bad breath occasionally, particularly when their mouth dries out after, say, a full night's sleep or a long, dehydrating plane flight. About 25 percent of people worldwide, however, have chronic foul breath. Researchers around the world figured out years ago that gas-emitting bacteria on the tongue and below the gum line are largely responsible for rotten breath. But determining how best to eradicate these microbes' tenacious odors has been difficult.

Solutions to date offer only temporary relief. Even scrupulously skipping onions and garlic, swishing mouthwash after every meal, and brushing and flossing one's teeth until they gleam like pearls will probably not sweeten a case of stubbornly stinky breath. Lightly scraping away any coating on the tongue can greatly improve the fragrance of one's breath for at least a few hours. Certain bacteria-slaying mouthwashes provide short-term freshness, too, although many produce unpleasant side effects, such as a tingling sensation in the mouth.

Lately some scientists have developed innovative mouth rinses that neutralize the rancid compounds produced by bacteria.

Recent evidence from international research suggests, however, that the most effective strategy for beating back bad breath may be more about nurturing helpful bacteria in the mouth than about destroying the offending germs and their by-products. Instead of singling out ostensible culprits, microbiologists are now shifting their focus to entire communities of microbes on the tongue, gum and teeth to figure out why some people have a sweeter-smelling oral village than others.

BREATH'S CHEMICAL CODE

BAD BREATH has, of course, plagued humans for ages. Young girls, Hippocrates advised, should regularly rinse their mouths with wine, anise and dill seed. By the early 1970s Joseph Tonzetich of the University of British Columbia had begun to tackle the problem with technology. He used his lab's gas chromatograph, a machine that separates a complex gaseous bouquet into its constituent compounds, to tease out reeking breath's signature chemicals.

Sulfur compounds that easily vaporize were among the stinkiest chemicals Tonzetich identified in bad breath, especially hydrogen sulfide, which smells like rotten eggs, and methyl mercaptan, which smells like rotten cabbage. Since then, scientists have detected around 150 molecular components of human exhalations, many of them putrid. Dimethyl sulfide (think rotten

GREG CEO *Getty Images (mouth)*; LEFT, TOP TO BOTTOM: SCIENCE SOURCE; HAZEL APPLETON *Health Protection Agency Center for Infections/Science Source*; LINDA M. STANNARD *University of Cape Town/Science Source*; RIGHT, TOP TO BOTTOM: KARI LOUNATMAA *Science Source*; A. BARRY DOWSETT *CAMR/Science Source*

seaweed) and the tellingly named cadaverine, putrescine and skatole are just a few such pungent molecules. Still, hydrogen sulfide and methyl mercaptan stand out: in study after study, the higher the levels of these two molecules in breath, the more that breath offends the human nose.

These smelly compounds are waste products released by the millions of bacteria feasting on particles of food and tissue in our mouth. Above the gum line, gram-positive species, which have relatively simple cell walls, dominate dental plaque—the living film of bacteria coating teeth. *Streptococcus mutans* and other sugar-loving gram-positives spew acid and dissolve enamel but are not heavy producers of foul-smelling compounds. In contrast, gram-negative bacteria—which have an extra cell wall layer—live mostly below the gum line and are much gassier. Some of these resilient bacteria, including *Porphyromonas gingivalis, Treponema denticola* and *Prevotella intermedia,* thrive in gaps between the gum and tooth and in the mosh pit crevices of the tongue.

Common Scents

Researchers have identified around 150 different molecules in human breath, many of which offend the human nose. Here are what some of the more malodorous compounds smell like.

Rotten eggs
Hydrogen sulfide (H_2S)

Rotten cabbage
Methyl mercaptan (CH_3SH)

Garlic
Allyl mercaptan (C_3H_6S)
Allyl methyl sulfide (C_4H_8S)

Fish
Dimethylamine (C_2H_7N)
Trimethylamine (C_3H_9N)

BACTERIAL COLLEAGUES

GRAM-NEGATIVE BACTERIA on the tongue may produce most of the foul odors in breath, but recent research emphasizes that no single type of oral bacterium creates bad breath on its own. Mel Rosenberg, an emeritus professor of microbiology at Tel Aviv University, and his colleague Nir Sterer recently found, for example, that some strains of gram-positive bacteria secrete an enzyme that clips sugar molecules off the proteins found in food, which in turn makes those proteins more digestible for nearby gram-negative organisms. The more proteins the gram-negatives digest, the more odors they emit.

Such interactions illustrate why researchers are increasingly interested in oral ecology, viewing the mouth as a kind of densely populated tide pool. Fresh breath reflects a healthy mouth, which is not necessarily one that lacks "bad" bacteria, scientists are realizing, but rather one in which overlapping bacterial colonies hold one another in check.

Bacterial geneticists contributing to the Human Microbiome Project, funded by the National Institutes of Health, have so far identified about 1,000 species of bacteria that commonly inhabit human mouths. Yet one person's particular mix of "bacterial colleagues," as Rosenberg calls them, is probably quite different from another's. "Each person has maybe 100 to 200 of those bacterial species colonizing their mouth at any given time," says Wenyuan Shi, a microbiologist at the University of California, Los Angeles.

During birth our previously sterile mouth picks up some of our mother's bacteria, and in childhood we quickly acquire new microbial colonizers. Studies suggest that a preschooler's population of mouth microbes most closely mimics his or her primary caregiver's. As the years go on, diet, stress, illness, antibiotics and other forces can shift the demographics of an individual's microbial community—and change its collective aroma. When bacteria that release smelly compounds dominate, chronic bad breath may be one of the consequences.

Many current treatments do not improve oral ecology—in fact, they might make matters worse. Although some mouthwashes merely mask unpleasant odors, alcohol-based rinses sold in drugstores and prescription rinses containing chlorhexidine or other antiseptics target all oral bacteria, stinky and otherwise. Shi says that approach has several drawbacks. A chlorhexidine rinse, for example, may improve breath for as long as 24 hours but can temporarily change the taste of food. In one study, 25 percent of subjects experienced a tingling or burning sensation on the tongue after a week of use. Heavy use of rinses with alcohol can dry out the mouth, sometimes exacerbating bad breath. Further, wiping out too many of the mouth's native bacteria could disrupt the usual checks and balances, making way for opportunistic species responsible for gum disease and other infections to move in and take over.

A number of researchers are now working on promising alternatives to basically carpet bombing all oral bacteria. Some new mouthwashes go after the stink rather than the stinkers with ions of zinc or other metals that bind and neutralize sulfur compounds. Rosenberg, who started his career as a petroleum microbiologist, has developed a two-phase oil-and-water rinse that temporarily reduces bad breath by sopping up some of the oral debris and microbes that toothbrushing, flossing and tongue scraping miss.

Other teams are investigating whether probiotics rife with a gram-positive bacterial strain known as *Streptococcus salivarius* K12 can fight halitosis. A common resident of the mouth and respiratory tract, *S. salivarius* K12 is benign and known to produce substances that deter harmful bacteria. In a recent study by researchers in New Zealand and Australia, volunteers gargled with a chlorhexidine mouthwash to clear their palate of many native bacteria and subsequently sucked on lozenges laced with K12. Seven and 14 days later they had much sweeter breath. Presumably K12 outcompeted its foul-smelling kin, opening up niches for less offensive species.

At U.C.L.A., Shi and his team are working on a mouthwash that contains a peptide—a chain of amino acids smaller than a protein—tailored to selectively kill *S. mutans,* the ringleader behind tooth decay. Researchers could develop an analogous peptide to weed out the bacteria behind bad breath, Shi says. A rinse containing such peptides might free up real estate on the tongue for less malodorous microbes, if used in moderation. Rinsing every day risks a sudden and drastic shift in oral ecology that could have unexpected repercussions.

Shi himself brushes and flosses daily but does not use a mouthwash or even a tongue scraper because his family assures him that his breath smells fresh. "I'm one of the lucky ones," he says. "My goal is to help other people be lucky, too." SA

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