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Can Vaping Affect Oral Health? CME / ABIM MOC / CE

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Clinical Context

Within the oral cavity is an open microbial ecosystem including **more than 700 bacterial species**. Sustained oral health requires maintaining a stable, health-compatible microbial ecosystem, whereas adverse changes within these bacterial communities trigger a florid inflammatory host response resulting in disease.

E-cigarettes containing **potentially toxic substances, volatile organic compounds**, and metals are used by 6% of Americans, including 3 million who are still in high school. They are legal, reported on by the media as being safer than cigarettes, promoted as smoking cessation aids, and often used in places where smoking is not permitted. The goal of this study, which is the first human study of the effects of e-cigarette exposure on the oral cavity, was to investigate changes in the subgingival microbiome linked to e-cigarette use and corresponding effects on the immunoinflammatory response.

Study Synopsis and Perspective

Clinicians have been worried that vaping can cause pulmonary damage. Now researchers report that vaping, even for a few months, can push healthy mouths toward **serious periodontal disease**.

In the first human study of vaping's effect on the oral cavity, the researchers found this electronic drug delivery system **negatively alters the microbial** ecosystem of the mouth, creating an ideal breeding ground for pathogenic bacteria whose damaging reach extends beyond the mouth to the cardiovascular system.

"E-cigarettes increase risk for oral diseases by shifting health-compatible ecosystems to virulence-rich communities," the authors write.

Sukirth M. Ganesan, BDS, PhD, and colleagues from The Ohio State University in Columbus, report their findings in an article published online May 27 in *Science Advances*. Dr Ganesan is currently an assistant professor in the Division of Periodontology at the University of Iowa in Iowa City.

The researchers studied immunoinflammatory responses and microbial dynamics in the oral ecosystems of 123 systemically and periodontally healthy individuals ranging in age from 21 to 35 years. They examined subgingival plaque samples from 5 groups within the 123 participants: 25 current smokers, 25 nonsmokers, 20 e-cigarette users, 25 former smokers turned vapers, and 28 simultaneous cigarette smokers and vapers.

Those vaping for at least 3 months had pathogen overgrowth, higher microbial virulence signatures, and a robust proinflammatory signal, all of which are changes resembling those in patients with severe periodontitis. Even longtime current and former smokers of conventional cigarettes had worsened oral profiles after 3 to 12 months of vaping, suggesting the pathogenetic mechanisms triggered by vaping may differ from those triggered by smoking.

Although e-cigarettes have been presented as a strategy to reduce combustible tobacco harms, these findings counter claims that vaping is a safe alternative to smoking. "If you stop smoking and start vaping instead, you don't move back toward a healthy bacterial profile but shift up to the vaping profile," senior author Purnima S. Kumar, BDH, PhD, a professor of periodontology at The Ohio State University, said in a university news release. "Knowing the vaping profile is pathogen-rich, you're not doing yourself any favors by using vaping to quit smoking."

The authors say the oral cavity harbors more than 700 microbial species, with oral health depending on stable health-compatible bacterial communities. Destabilization of this environment triggers a fulminant disease-promoting inflammatory response.

The most notable effect of vaping chemicals was their **alteration of oral biofilm architecture**. "[T]he nicotine-free aerosol consisting of **glycerol and glycol, viscous sugar alcohol fluids** that generate the cloud when vapers exhale, functioned as a nutrition source to fuel the altered oral

environment," the authors explained in the news release.

Moreover, as the **damaging effects were seen with or without nicotine**, these heated and pressurized liquids in e-cigarette cartridges are the main culprits in microbial shifts leading to **oral dysbiosis**, the researchers believe. Previous research has found that **vaping harms vasculature even in the absence of nicotine**.

E-cigarettes cause stress in the subgingival environment, the authors explain, which was clear from the significantly greater abundance **of genes regulating the stress response** in the human metagenome that emerged with vaping exposure.

"Further, longitudinal studies, preferably in humans or animal models using an oral mode of exposure to e-cigarette vapor, are urgently needed to understand the manifold effects of these drug delivery devices on human health," the authors write.

Other clinical evidence suggests e-cigarette users have worse periodontal health than nonsmokers, Chun-Teh Lee, DDS, DMSc, director of periodontics research at the University of Texas Health School of Dentistry in Houston, told *Medscape Medical News*. "However, since many vapers are young or just started vaping a few years ago, we may not see immediate and significant harm to their oral and periodontal health," said Dr Lee, who was not involved in the current study.

"But these results show that since e-cigarette smokers have more harmful bacteria and stronger inflammatory responses than nonsmokers, they may well have periodontal disease in the future," Dr Lee said. In the meantime, their periodontal health might not currently be as bad as that of long-time smokers.

According to the authors, among the 6% of Americans who use e-cigarettes, some 3 million are teenagers, but Dr Lee believes age alone is not a problem. "It's about how long, how often, and how much you use," he said.

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Study Highlights

- E-cigarettes have been available in the United States since 2009, but little is known regarding their effects on the oral ecosystem.
- To examine immunoinflammatory responses and microbial functional dynamics in subgingival plaque samples of e-cigarette users with good clinical systemic and periodontal health, the investigators combined comparative metagenomics with a rigorous case-control human study.
- Of the 123 subjects aged 21 to 35 years, 25 were current smokers, 25 nonsmokers, 20 e-cigarette users, 25 former smokers who began vaping, and 28 simultaneous users of cigarettes and e-cigarettes.
- E-cigarette users vs nonusers had significantly greater abundances of genes regulating stress response in the human metagenome, a brisk proinflammatory response, and robust, positive correlations between these cytokines and virulence factors.
- The bacterial overrepresentation of pathogens, higher virulence signatures, and brisk proinflammatory signal in subjects vaping for at least 3 months were equivalent to those seen in patients with severe periodontitis.
- After 3 to 12 months of vaping, even longtime current and former smokers of conventional cigarettes had worsened oral microbiome profiles.
- To validate their findings, the investigators used metatranscriptomics and confocal microscopy on an in vitro longitudinal model of biofilm colonization.
- RNA sequencing and confocal and electron microscopy showed that the carbon-rich glycol/glycerol vehicle used in vaping is an important catalyst in transforming biofilm architecture within 24 hours of e-cigarette smoking.
- **The primary biofilm** had the greatest up-regulation of stress response, whereas the **secondary and tertiary biofilms** showed down-regulation of stress.
- With vaping exposure, there was a significantly greater abundance of genes regulating the stress response in the human metagenome.
- The single most influential characteristic of e-cigarette users was an increase in genes participating in cell wall and capsule.
- Exposure of *Streptococcus oralis*, *Streptococcus mitis*, *Veillonella parvula*, *Neisseria mucosa*, *Actinomyces naeslundii*, and *Streptococcus sanguis* to e-cigarette aerosol resulted in increased transcription of legionaminic acid, neuraminic acid, and several other sialic acids.
- The investigators developed a machine-learning classifier using the metagenomic signatures of e-cigarettes, which identified as e-cigarette users persons using e-cigarettes to quit smoking, as well as those using both e-cigarettes and cigarettes.
- On the basis of their findings, the investigators concluded that the harmful changes in the oral cavity microbiome and stress to the subgingival environment with e-cigarettes raise concerns about their safety and about the advertising campaigns that suggest harm reduction with e-cigarette vs cigarette smoking.
- However, the findings suggest that the risk for harm from e-cigarettes is different from, but not less than, that of conventional cigarettes.

- As the smokers in this study smoked for at least 5 years and e-cigarette users had an average of 7 months of vaping history, the effects of e-cigarettes on the oral microbiome may become apparent much earlier than with smoking.
- The in vitro model showed significant differences in the effects of e-cigarettes on biofilm vs the effect of cigarette smoke, as commensal transcriptional activity was significantly lower after cigarette smoke exposure.
- When vapers exhale, they generate a cloud of nicotine-free aerosol consisting of glycerol and glycol, which are viscous sugar alcohol fluids that act as a nutrition source to fuel the altered oral microbiome.
- As these heated and pressurized liquids in e-cigarette cartridges are primarily responsible for microbial shifts leading to oral dysbiosis, the harmful effects of vaping occur even in the absence of nicotine.
- Glycerol is an essential precursor for synthesis of lipids and of lipoteichoic acids in many Gram-positive bacteria, and it plays an important role in intracellular growth of pathogenic bacteria.
- Although the oral microbiomes of both smokers and e-cigarette users are rich in pathogens, findings of this study suggest potentially different underlying pathogenetic mechanisms of action, given the worsening of oral microbiome after 3 to 12 months of vaping in long-term current and former smokers of conventional cigarettes.
- The significantly greater abundance of genes regulating the stress response in the human metagenome seen with vaping suggests that e-cigarettes cause stress in the subgingival environment.
- To clarify the far-reaching effects of e-cigarettes on human health, additional longitudinal studies, preferably in humans or animal models, using an oral mode of exposure to e-cigarette vapor are urgently needed.
- Study limitations include cross-sectional design precluding time-to-event inferences.
- An expert consulted by *Medscape Medical News* indicated that there may be a dose-response effect of vaping on periodontal health, with worse harm with higher dosage and longer duration and frequency of use.
- Although other clinical evidence indicates worse periodontal health in e-cigarette users than in nonsmokers, many vapers are young and have not been vaping for more than a few years, and may therefore have delayed effects and future periodontal disease.

Clinical Implications

- Healthy e-cigarette users have oral cavities similar to those seen in severe periodontitis, including harmful microbiome changes, according to the first human study of the effects of vaping on human health.
- The findings raise concerns about the safety of e-cigarettes and about the advertising campaigns that suggest harm reduction with e-cigarette vs cigarette smoking, as the risk for harm from e-cigarettes is different from, but not less than, that of conventional cigarettes.
- Implications for the Healthcare Team: As the smokers in this study smoked for at least 5 years and e-cigarette users had an average of 7 months of vaping history, the effects of e-cigarettes on the oral microbiome may become apparent much earlier than with smoking. Members of the healthcare team should be aware of this study and able to educate individuals currently vaping or considering vaping on the impact on oral health.

Earn Credit

References

1. Ganesan SM, Dabdoub SM, Nagaraja HN, et al. Adverse effects of electronic cigarettes on the disease-naive oral microbiome. *Sci Adv.* 2020;6(22):eaaz0108. Published online 2020 May 27. <https://advances.sciencemag.org/content/6/22/eaaz0108.full>. Accessed May 28, 2020.

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