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COVID-19

LITERATURE REVIEW

Aftermath of COVID-19 in Adults

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On Jan. 30, 2020, the World Health Organization (WHO) recognized coronavirus disease 2019 (COVID-19) as a public health emergency. By March 2020, WHO declared a pandemic.[1] Reports of lingering post-COVID symptoms emerged in the spring of 2020, and, by January 2021, a syndrome technically known as postacute sequelae of SARS-CoV-2 infection (PASC) obtained the dubious honor of official recognition by WHO.[1-3] The pathogen responsible for COVID-19 is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[4] Persistent and long-lasting symptoms from other coronavirus infections, such as SARS in 2003 and Middle East respiratory syndrome (MERS) in 2012, have been documented among survivors of these infections. This raises concern that the effect of the current global COVID-19 pandemic has potential for following these precedents and causing long-lasting health problems.[4,5]

The risk factors, prevalence, and course of the syndrome following COVID-19 remains ill-defined. In fact, there is no widely accepted standard terminology: long-COVID-19, postacute COVID-19, chronic COVID-19, long-haulers, and PASC are among the names describing persistent symptoms of postacute disease.[6] Given that a SARS-CoV-2 with the ability to replicate has not been isolated three weeks beyond initial disease, most authors use the three- or four-week mark as the onset for the post-COVID syndrome period.[6,7]

This review of studies, conducted in a variety of settings, covers diverse perspectives and illustrates conceptualization of the post-COVID syndrome in adults at the time of publication. The studies presented range from small studies focused on one geographic region to a Veterans Health Administration (VHA) study of six-month outcomes of 73,000 nonhospitalized COVID-19 patients to a large meta-analysis drawn from 10 countries and 15 studies. The specific investigations discussed in this paper are selected to illustrate the widespread interest and range of techniques and approaches employed to investigate the post-COVID period.

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Summary Points

- This review of investigations centered on long-term effects following acute coronavirus disease 2019 (COVID-19) illness in adults illustrates an evolving understanding of the aftermath of this viral infection.
- In general, long-term effects of COVID-19 are defined as symptoms or abnormal clinical findings persisting more than three weeks after onset of disease without remission or return to baseline.
- Small studies from around the world consistently have identified disabling fatigue as a major post-COVID-19 symptom. A meta-analysis including 47,910 patients found 80% of the participants reported one or more long-term symptoms, with fatigue noted in 58%. A large Veterans Health Administration study also found a higher risk of death six months postacute COVID-19 infection.
- Controlled and methodologically robust studies are needed to fully understand risk. Mitigating factors potentially include sex/gender, age, disease severity, viral load, ethnicity, comorbid health conditions, and vaccination status.
- Most investigators conclude there is an urgent need for a multidisciplinary, individualized approach to patients during the post-COVID-19 period. By definition, the integrative provider may be uniquely qualified to create and coordinate such an approach for patients to prevent, address, and/or halt the progression of long-term COVID-19 effects.

A discussion of the post-COVID period is incomplete without a nod to the mobilization of social networks in drawing groups of COVID survivors together to discuss symptoms and exchange information. Perhaps the best known of these groups is the Long COVID support group founded in May 2020 by Claire Hastie, a business consultant from the United Kingdom whose experience with lingering symptoms after COVID-19 led her to reach out to others with similar experiences. This support group has been involved in recruitment and outreach efforts for scientists and clinicians studying the post-COVID period.[8] It is useful to keep in mind that, with worldwide incidence of COVID-19 rising during the first half of 2021, our early understanding of this syndrome inevitably will be modified as more patients enter the postacute illness stage.[9]

TOWNSEND ET AL[10]

From Ireland, Townsend et al administered the Chalder Fatigue Score (CFQ-11) to characterize the degree of fatigue after recovery from the acute phase of COVID-19 in 128 individuals recruited from an outpatient setting.[11] The mean age of this study group was 49.5 ± 15 years. More than half (55.5%) had been admitted to the hospital during the acute course of COVID-19, and 51.6% were healthcare workers. The median interval between study participation and either hospital discharge or 14 days following outpatient diagnosis was 10 weeks, with no patient recruited earlier than six weeks from these landmarks. At the time of the assessment, fewer than half the patients (42.2%) reported feeling back to baseline health, and 31% of the 105 employed patients were not yet back to work. The CFQ-11 measures physical and psychological/emotional fatigue. In this study, subscores were combined; 52.3% of the participants exceeded the cutoff for clinically relevant fatigue.

Townsend et al noted that chronic fatigue syndrome (CFS) is characterized by persistent fatigue lasting six months or longer without an alternate etiology and cited several studies of CFS postviral illness, including other coronaviruses. For example, a study of 233 survivors of SARS noted that more than 40% of patients reported chronic fatigue at 40 months postacute infection.[12] If the profound fatigue post-COVID-19 follows this same course, Townsend et al noted that prospective studies beginning early in the postacute course may be able to unearth temporal relationships between inflammation, depression, anxiety, and CFS.

For now, Townsend et al advised that post-COVID-19 fatigue may need to be treated similarly to CFS, with a gradual increase in activity level, exercise, and cognitive behavioral therapy. Additionally, the team highlighted that 31% of the employed participants in this study had not yet returned to work at the time of the study. If this number is generalizable, the effect on workforce, including healthcare workers, would be considerable. Educating employers and enlisting occupational health in ongoing rehabilitation and recovery efforts may be key.

LOGUE ET AL[13]

From the University of Washington, Logue et al designed a study to look at long-term sequalae of COVID-19 infection. A follow-up questionnaire was administered to 177 volunteers one month to nine months (median of 169 days) after illness onset and to 21 healthy patient "controls." Of the 177 study participants, 150 (84.7% of the total) remained outpatient during the acute illness and characterized the course as "mild."

Symptom persistence was reported by 32.7% of the patients in this study (but only by patients who were symptomatic during COVID-19 infection). Fatigue and loss of taste and smell were the most reported symptoms, with 13.6% of the patients endorsing one or both. Other symptoms included "brain fog," cough, gastrointestinal disturbance, and headache. Health-related quality of life (HRQoL) was assessed via a sliding scale (from 0 to 100) and compared with pre-illness perception of the same. Almost 30% (53 individuals) reported at least a 10-point drop in HRQoL, with most of these patients drawn from the symptomatic group. These two studies represent early efforts to investigate and predict the course of post-COVID-19. These clearly are preliminary studies with barriers to generalization — including limited numbers of participants, single-sites, and self-reported symptoms. The authors are open about these and other limitations; all recommend large-scale, robust investigations going forward to better characterize and address a post-COVID picture.

NALBANDIAN ET AL[14]

Larger published studies include the work of Nalbandian et al with a review of studies regarding the "postacute COVID-19 syndrome" in *Nature Medicine*. This work, drawing on nine studies from around the world and written from an organ-specific perspective, defines the post-COVID- 19 period as beginning four weeks from the onset of symptoms. This team highlights the multiorgan effect of post-COVID-19. Table 1 summarizes relevant findings according to organ system.

Nalbandian et al noted, "care for patients with COVID-19 does not conclude at the time of hospital discharge" and emphasized the need for early rehabilitation programs to address the functional deterioration reported by many COVID-19 survivors. Additionally, the team recommended large-scale clinical trials to better characterize, understand, and treat patients during the post-COVID-19 period.

AL-ALY ET AL[15]

From the VHA comes a retrospective chart review of six-month follow-up of 73,435 nonhospitalized patients testing positive for COVID-19 and surviving at least 30 days compared with 4,990,835 non-COVID-positive and nonhospitalized patients in the same health system. Al-Aly et al found an increased risk of death in the COVID-19-positive arm, with a hazard ratio of 1.59 when comparing death rates between the groups. This translates to an estimated eight more deaths in the former group for every 1,000 persons over the six-month period.

Table 1. Findings According to Selected Organ Systems in a Review of Nine Studies

Organ System	Symptoms	Findings	Notes
Pulmonary	Dyspnea, decreased exercise capacity	Ground glass opacity and fibrotic changes on imaging studies	Home monitoring may be indicated; pulmonary rehabilitation
Dermatologic	Hair loss	Often self-diagnosed	Noted in 20% of patients — usually self-limited
Cardiovascular	Palpitations, chest pain	May have abnormal electrocardiogram and/or arrhythmias	Serial monitoring may be indicated
Neuropsychiatric	Fatigue, myalgias, headache, "brain fog"	Anxiety, depression, sleep disturbances	Noted in 30% to 40% of COVID-19 survivors in several of these studies
Renal	May be asymptomatic	Reduced estimated glomerular filtration rate in 35% of patients at month 6 post-COVID-19 in one large Chinese study	Watch for persistent impaired renal function (check urine for protein and renal panel)
Endocrine	Diabetic ketoacidosis, subacute thyroiditis	Includes new onset diabetes and worsening of control of existing diabetes	Appropriate lab tests and consider referral to endocrinologist

As in the Nalbandian et al study, Al-Aly et al noted multiple system and organ groups affected during the post-COVID-19 period, with the most common problems involving the respiratory system, followed by the nervous system, mental health disorders, and then disorders of the cardiovascular, gastrointestinal, and metabolic systems. Malaise and fatigue were prominent complaints. This group also noted a higher use of multiple pharmaceutical agents, including pain medications, antidepressants, antihypertensives, and hyperglycemic medications.

Al-Aly et al also compared six-month outcomes of 13,654 hospitalized COVID-19 patients with 13,997 patients hospitalized with influenza. All patients in the cohort survived 30 days after discharge from the hospital. Again, a higher risk of death in the post-COVID-19 era was detected, with a hazard ratio of death for the COVID-19 group of 1.51 compared to the influenza group. The COVID-19 arm had significantly higher rates of disease in multiple systems and organs, as well as a higher rate of fatigue and malaise. Extensive analysis revealed that the risk of long-term effects from COVID-19 increased with severity of initial COVID-19 disease, with the highest risk in patients hospitalized in intensive care and the overall risk higher than patients with influenza. Overall, Al-Aly et al estimated the risk of long-term effects after an acute COVID-19 illness is 8% to 10%.

LOPEZ-LEON ET AL[16]

Perhaps the most comprehensive study yet was this systematic review and meta-analysis covering 15 English-language studies published before January 2021 with a minimum of 100 participants in each. Nine studies were drawn from the United Kingdom/Europe, three were from the United States, and one each came from Australia, China, Egypt, and Mexico. The studies included 47,910 adult patients. While most of these studies collected only self-reported symptoms, three of the studies included a clinical evaluation, and two reviewed data from medical records. Follow-up time ranged from 14-110 days postacute viral infection. Notably, six of the studies focused only on patients hospitalized for COVID-19, and the remainder included a population with mixed disease severity (mild to severe) without stratifying results. Analysis of results revealed that an estimated 80% of these patients with acute COVID-19 infections developed at least one long-term symptom (defined as occurring beyond two weeks from initial infection). A total of 55 signs and symptoms (including abnormal laboratory values) were identified. However, as the authors noted, all studies predefined the type of symptoms to survey and which lab values to check, meaning it is likely that additional long-term effects have not yet been identified.

The five most common long-term effects cited in this meta-analysis were fatigue in 58% of the respondents, headache in 44%, attention disorder in 27%, hair loss in 25%, and dyspnea in 24%. Anosmia persisted at a slightly lower prevalence, with 21% of patients reporting this symptom. Anxiety, insomnia, and memory loss occurred in 11% to 16% of the study population. Lopez-Leon et al noted the resemblance of fatigue in these studies to the disabling and severe fatigue seen in CFS and echoed the message of other researchers that "recovery from COVID-19 should be more developed than checking for hospital discharge or testing negative." Integrative providers, often well-versed in caring for patients with complex, multisystem diagnoses (e.g., joint hypermobility, fibromyalgia, and chronic fatigue) are well-situated in caring for patients with long COVID.

Only two studies looked at radiographic changes during the post-COVID-19 period. These cited a 34% prevalence of abnormal chest X-ray or computed tomography (out of 529 patients). Other studies noted elevated or abnormal markers, including D-dimer (20%), C-reactive protein (8%), serum ferritin (8%), and interleukin-6 (3%), possibly indicating hypercoagulative and inflammatory states.

WHAT DO WE KNOW ABOUT MECHANISM AND TREATMENT?

Understanding the specific etiology of persistent symptoms following acute COVID-19 infection may help point to effective prevention and treatment interventions. For now, most researchers speculate that the symptoms arise from a combination of elements, including direct viral infection/tissue damage, hyperactivation of the immune system, autoimmunity, and indirect effects, including psychosocial and economic effect of this illness.[15-17]

Most investigators agree with the need to perform studies to ferret out the risk factors and any mitigating factors potentially influenced by variables, such as sex/gender, age, disease severity/viral load, ethnicity, comorbid health conditions, and vaccination status. Studies looking at effective intervention during the post-COVID-19 period are limited; most researchers point to the need for ongoing monitoring and early rehabilitation. In December 2020, 1,031 U.K. providers responded to a survey regarding anticipated needs of patients during post-COVID recovery. More than 90% of the respondents endorsed a need to educate patients about management of fatigue, breathlessness, mood disturbances, and provide support for social isolation (especially during COVID-19 restrictions) immediately following the acute viral period.[18]

The second portion of the survey addressed six to eight weeks post-illness. The most frequently recommended intervention at this time included a rehabilitation program focused on a return to physical movement and exercise. With recognition of potential limitations due to the pandemic, this included advice on home-based aerobic and resistance training. Advice on management of fatigue, support for anxiety and depression, support for social isolation, and psychoeducation regarding post-traumatic stress symptoms and management also were highly rated.[18]

There is preliminary evidence suggesting rehabilitation with an individualized program, including progressive light aerobic activity, breathing exercises, and psychological support may be effective for some patients recovering from COVID-19.[17] For example, a six-week rehabilitation program with these elements was associated with improvement in multiple areas (including lung function and quality of life) in 72 older COVID-19 survivors.[18] However, there also are risks to rehabilitation, especially if there has been pulmonary or cardiac damage during the COVID-19 course. A physical evaluation and a review of exclusion criteria before recommending a course of rehabilitation is recommended.[17]

SUMMARY

Studies focused on the post-COVID-19 period represent early efforts to characterize the long-term effects of this new illness. While each study has limitations, a common theme is the persistence of specific symptoms past the stage of acute viral illness. Severe, incapacitating fatigue is cited in most studies, although prevalence and risk factors are inconsistent among the investigations. Townsend et al noted disability linked with this symptom in about one-third of respondents, and Longue et al noted a significant decrease in HRQoL in about the same percentage of patients.[10,13] These results are worth highlighting and considering in terms of individual patients and public health. Another consistent finding is involvement of multiple organs and systems and consistent recommendations for a multidisciplinary approach during the post-COVID-19 period. Al-Aly et al (the VHA study) echoed the call of most of the researchers in the field and noted "the need for holistic and integrated multidisciplinary long-term care of patients with COVID-19."[15]

At the time of this publication, the COVID-19 pandemic remains active worldwide, unfortunately ensuring a fresh supply of data and information about the post-COVID period. It truly is a tribute to researchers and the medical community that research efforts continue during this very difficult and chaotic time. Establishing standard definitions and consistent terminology is a priority to ensure generalizable, clinically relevant information from studies. Controlling for variables and performing large-scale, controlled studies will come. However, the studies we have highlight the potential health consequences of COVID-19 beyond the acute stage. Our patients cannot wait for evidence-based treatments.

The integrative provider, with a holistic approach to each patient, is well situated to develop an early intervention plan for patients following a COVID-19 infection based on the limited information at hand. Being transparent about the state of medical knowledge may help mobilize a sense of engagement in recovery effort (i.e., "We are learning about this together"). Experience with CFS can help guide the provider toward an individualized, whole-person treatment strategy to address the profound fatigue experienced so often after COVID-19. Educate patients about health risks to multiple organ systems after COVID-19, pay attention to mental health status as well as indications of overall wellbeing, and draw on evolving available information while partnering with patients to achieve pre-COVID-19 functional status. ■

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ABSTRACT & COMMENTARY

Adverse Effects of Electronic Cigarettes on the Disease-Naive Oral Microbiome

By Lindsey N. Clark, MD, and Taimur K. Mian, MD

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SYNOPSIS: A robust metagenomic comparison study of the effects of electronic cigarettes on oral microbiomes suggested that the unique aerosol component of electronic cigarettes poses increased risk to development of oral cavity disease.

SOURCE: Ganesan SM, Dabdoub SM, Nagaraja HN, et al. Adverse effects of electronic cigarettes on the disease-naive oral microbiome. *Sci Adv* 2020;6:eaaz0108.

The human oral cavity is host to a diverse group of bacterial communities, with more than 1,000 species across seven phyla having been identified. Imbalances in the oral microbiome communities and increased inflammatory responses to oral bacteria have been associated with diseases, such as periodontitis, dental caries tooth loss, and oropharyngeal cancer.

The effects of cigarette use, chewing tobacco, and alcohol consumption on the oral cavity have been studied widely, with results showing that these habits offset the healthy balance of oral bacterial communities and create the potential for harmful bacterial species to be introduced into the oral cavity, increasing the risk for disease development.[1,2] However, the effects of electronic cigarettes (e-cigarettes) on the oral microbiome, and their potential for harm, remain understudied. Considering that e-cigarettes are relatively novel by delivering nicotine in a unique heated aerosol component, more insight into their effects on the oral microbiome is needed to determine their risk for oral cavity illness.

Ganesan et al provided new evidence regarding the effects of e-cigarettes on the oral cavity in a comparison study analyzing the subgingival microbiomes across e-cigarette users, smokers, and nonsmokers. The study recruited 123 individuals considered systemically and periodontally healthy. Periodontal health, or gingival inflammation assessment, was defined as attachment loss of < 1, fewer than three sites with 4 mm of probe depths, and a bleeding index of < 20%. Systemic health was established using the American Society of Anesthesiologists Physical Status Classification. Participants were placed in one of five groups based on their current tobacco use status: smoker, nonsmoker, e-cigarette user, former smoker currently using e-cigarettes, and concomitant cigarette and e-cigarette user. Current smoking was defined as at least a five-pack-year history. Nonsmokers were defined as people having consumed fewer than 100 cigarettes in their lifetimes. E-cigarette users were defined as having used e-cigarettes daily for at least three months, with at least one cartridge per day, or 1 mL of liquid per day. Sample size was determined to have at least an 80% chance of detecting clades of bacterial genes that differed in abundance by 1%. Exclusion criteria consisted of presence of controlled or uncontrolled diabetes, human immunodeficiency virus infection, use of immunosuppressant medication, bisphosphonates, steroids, antibiotic therapy or oral prophylactic procedures within the past three months, and fewer than 20 teeth in dentition.

Subgingival plaque samples using sterile endodontic paper points and gingival crevicular fluid collections were taken from each participant at 15 sites within the oral cavity. Bacterial deoxyribonucleic acid (DNA) was isolated from the paper point samples and quantified using Qiagen DNA MiniAmp kits and Qubit fluorometers. Phylogenetic profiles for each participant's oral microbiome were created using Kraken v1.1 software and complete genome data lists from the Human Oral Microbiome Database. Each phylogenetic profile then was tested for alpha (within-group) and beta (between-group) genetic diversity using PhyloToAST v1.4 and QIIME v1.9.

For quality control, all DNA samples were sequenced in two runs, and samples were randomly assigned to each run. Each participant's gingival crevicular fluid samples also were used to determine cytokine assays, measuring levels of interferon-gamma (INF-gamma), interleukin 2 (IL-2), IL-4, IL-6, IL-8, IL-10, granulocyte-macrophage colony stimulating factor (GM-CSF), and tumor necrosis factor-alpha (TNF-alpha).

To assess and compare the genetic variability and gene clustering in the oral microbiome community between each participant cohort, Ganeson et al generated principal coordinate analysis (PCoA) plots using the software

Summary Points

- A comparison study attempted to identify the effects of electronic cigarette use on oral bacterial communities by comparing the oral microbiome genetic profiles of 123 participants divided into five cohorts: electronic cigarette users, smokers, nonsmokers, former smokers, and dual users.
- Robust methodologies of deoxyribonucleic acid isolation, metagenomic sequencing, principal coordinate analysis, and linear determinate analysis identified the oral microbiome of electronic cigarette users as significantly different from that of smokers and nonsmokers.
- Results showed electronic cigarette users to have significantly more bacterial genetic clusters related to pathogenic species, bacterial virulence factors, and proinflammatory signals.

PhyloToAST (PcoA.py). The significance of identified genetic clustering in participant cohorts was determined using permutational multivariate analysis of variance (MANOVA) (adonis function, vegan package for R). Additionally, the relative abundance of functional genes across participant cohorts was assessed using linear discriminant analysis (LDA) (scikit-learn v0.18.0). Wilk's lambda was used to test for significance of LDA identified functional gene clustering.

Overall, Ganeson et al compared oral microbiomes of 20 e-cigarette users, 25 nonsmokers, 25 current cigarette smokers, 25 former smokers, and 25 dual users. E-cigarette users were 21 to 35 years of age, predominantly Caucasian, and reported using e-cigarettes with 6 mg to 18 mg of nicotine. Interpretation of PCoA and LDA plots revealed three significantly different oral microbial profiles of e-cigarette users, smokers, and nonsmokers ($P = 0.008$, MANOVA/Wilks). There was no significant microbial profile difference between e-cigarette users, dual users, and former smokers who had switched to e-cigarettes ($P = 0.27$ and 0.35).

Further nonmetric multidimensional scaling analysis of variance in the user groups showed that the duration of e-cigarette use (< 6 months vs. > 10 months) was the strongest source of variation, with nicotine concentration and type of flavoring not contributing to variations seen in the oral microbial profiles. Furthermore, 70% of the metagenome in e-cigarette users was shared by more than 80% of subjects, whereas the smoker and nonsmoker cohorts only shared 40% and 50% of their metagenomes, respectively. This presence of a large, core microbiome present in a majority of the e-cigarette users that differed significantly from the microbiome of smokers and nonsmokers suggests that the aerosol effects of e-cigarettes alters the oral cavity bacterial community via different mechanisms than traditional cigarettes. (*See Table 1.*)

Furthermore, the metagenome profile of e-cigarette users showed a greater abundance of genes related to virulence factors when compared to smokers and nonsmokers ($P < 0.05$), including cell wall and capsular polysaccharides, peptidoglycan, and lipopolysaccharide biosynthesis, stress response, quorum sensing and biofilm formation, and resistance to antibiotics and toxic compounds. These findings suggest that the unique oral bacterial community found in e-cigarette users could increase exposure to bacterial factors that cause disease in human hosts.

Additional analysis of the cytokines assays taken from the participant's gingival crevicular fluid showed e-cigarette users to have significantly higher levels of proinflammatory cytokines IL-2, IL-6, GM-CSF, TNF-alpha, and INF-gamma, and lower levels of anti-inflammatory cytokine IL-10 ($P < 0.05$, Dunn's test). These findings suggest that the e-cigarette user microbial profile creates a higher inflammatory burden and response when compared to cigarette users and nonsmokers.

It is important to note that cigarette users showed a similar increase in proinflammatory cytokines when compared to never smokers as well with increases in cytokines IL-2, IL-6, and IL-8, TNF-alpha, and INF-gamma, and lower levels of IL-10. The authors noted that this difference may suggest that, while both e-cigarette and cigarette use increase inflammatory response cytokines in the oral microbiome, different biological pathways are involved.

■ COMMENTARY

Ganeson et al presented the results of a robust, rigorous comparison study combined with comparative metagenomics, adding to our knowledge of the effects of e-cigarette use on the oral cavity. Ultimately, the study shows that e-cigarette use creates the potential to shift the oral microbiome community to a state with increased

Table 1. Comparison of Significant Variance in Oral Microbiome Profiles

	Smokers	Nonsmokers	Dual Users	Former Smokers (Current E-Cigarette Users)
E-cigarette users	$P = 0.008$*	$P = 0.008$*	$P = 0.27$	$P = 0.35$

*Statistically significant values

exposure to bacterial virulence factors and increased host inflammatory response, both states that can predispose an individual to oral cavity diseases. The authors point out that, while none of their e-cigarette users currently had been diagnosed with periodontitis, the functional genetic profile of their oral microbiome "bore remarkable resemblance to individuals with periodontitis."[3,4] Ganeson et al hypothesized that the glycerol and glycol component of e-cigarette aerosol may serve as a nutrient source for bacteria, altering the microbial profile and biofilm structures in the oral cavity of e-cigarette users.

While e-cigarettes have been on the market for 17 years, and studies have begun to show the potential for harmful effects on the respiratory system, little remains known about their effect on the oral cavity and the oral microbiome.[5,6] Because the heated aerosol contains fewer harmful chemicals than an ignited tobacco device, it has been suggested that their use is safer than cigarettes, and they often have been advertised as a smoking cessation device.[7]

However, studies show that the biggest user group of e-cigarettes is a young population that is taking up e-cigarette use as a new habit vs. a tool for smoking cessation. One study has even found that 20% of high schoolers in the United States admitted to trying e-cigarettes at least once a month.[8] Given these numbers, physicians are incredibly likely to encounter a young patient who is using e-cigarettes recreationally.

Physicians should consider the results of the Ganesan et al study, along with the growing body of literature, which demonstrates that e-cigarettes expose users to a unique aerosol-nicotine compound that may increase the risk for oral cavity disease. Talking to adolescent and adult patients about e-cigarette use and the effects on their oral health may be beneficial for reducing the risks of developing oral cavity diseases associated with e-cigarette use. ■

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CME QUESTIONS

1. **The long-term effects of COVID-19:**
   a. are a product of social media mobilization and hysteria; although there may be scattered patients with such symptoms, there is no medical proof.
   b. are well-documented and characterized; these are very similar to long-term effects from similar viruses and some strains of influenza.
   c. may involve multiple organ systems and commonly includes fatigue; an individualized multidisciplinary integrative approach is recommended.
   d. may involve multiple organ systems, but usually are self-limited and resolve with reassurance and time.

2. **The analysis presented in the 2020 study by Ganesan et al suggests that electronic cigarette use alters the oral microbiome of users by increasing the presence of what bacterial features?**
   a. Species diversity
   b. Virulence factors
   c. Anaerobic metabolism
   d. Anti-inflammatory responses

[IN FUTURE ISSUES]

Yoga Breathing for COVID

Cannabis Use and Associated Health Conditions

High-Dose Electronic Media Use in 5-Year-Olds