At the time of this writing, the United States and the world are grappling with a deadly pandemic of respiratory infection and disease caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Only 1 year ago, our nation was concerned by another outbreak of a flu-like illness affecting mostly young people who would develop acute respiratory failure, caused by e-cigarette, or vaping, product use–associated lung injury (EVALI). A multistate outbreak was associated with 2500 cases and more than 50 deaths. The concerted efforts of treating physicians, researchers, and the US Centers for Disease Control and Prevention determined that most patients with EVALI had a history of inhaling modified vaping products that incorporated tetrahydrocannabinobid (THC) and cannabidiol in various unknown diluents, including oil-like substances such as vitamin E acetate. Rapid dissemination of these findings to the medical community and public followed. Cases have since subsided, and little is currently heard of EVALI. However, much remains to be learned.

In this issue of JAMA Network Open, Aberegg et al² revisit the clinical manifestations and management of EVALI in the third-largest cohort reported, with 31 hospitalized patients at a single academic medical center in Salt Lake City, Utah. As in previous cohorts, patients were young, had a history of vaping THC-containing products, and presented with a flu-like illness, including shortness of breath. Although 8 patients (26%) required admission to the intensive care unit, all patients survived.

The report carefully describes the radiographic manifestations of EVALI, pointing to the pattern of bilateral pulmonary opacities as most predominantly resembling organizing pneumonia (26 of 26 patients [100%] who received computed tomography imaging). These findings are concordant with those reported by Henry et al, who reviewed radiographical patterns and available lung histopathology, concluding that although distinct (eg, organizing pneumonia, hypersensitivity pneumonitis, acute eosinophilic pneumonia, or diffuse alveolar damage), these patterns represent varied manifestations of the acute immune and inflammatory host response to inhalation injury affecting the small airways and alveolar structures. To this end, Aberegg et al² report both distal lung and systemic neutrophilic inflammation, identified in bronchoalveolar lavage fluid and blood differential counts, respectively.

More than 75% of patients (24 [77%]) in this study² underwent bronchoscopy to exclude infectious and alternative etiologies, and many patients received systemic corticosteroids (24 [77%]) in addition to empirical antibiotics (26 [84%]). Because respiratory infections were ruled out in all but 1 patient, the clinical improvement was attributed to corticosteroid treatment, consistent with previous reports. The low rates of concurrent respiratory infection with EVALI, which were similar to other studies,¹ the lack of specificity of lipid-laden alveolar macrophages for a diagnosis of lipoid pneumonia, and the potential procedural complications,⁷ led the authors to conclude that "bronchoscopy rarely contributed meaningfully to the diagnosis." This informed their decision to stop using bronchoscopy for EVALI diagnosis and treatment in the final patients in the cohort.

The decreased reliance on diagnostic bronchoscopy should be interpreted with caution by the readers of the report. First, this is a retrospective single-center study that was not designed to assess the utility of bronchoscopy as a diagnostic tool for EVALI. In addition, we cannot dismiss the usefulness of bronchoscopy in boosting the diagnostic confidence and in solidifying the choice of...
treatment with systemic corticosteroids, which may have been instrumental in the good outcomes reported here. However, the decision to avoid using an invasive procedure during the EVALI outbreak highlights the importance of incorporating the knowledge of the current prevalence of the disease with the diagnostic value of the procedure into the clinical management of patients. It is important to also note that the favorable clinical outcomes and evidence-adapted clinical management of the patients with EVALI in this report were likely facilitated by a rapidly constructed clinic and group of specialists dedicated to addressing the new outbreak.

The temporal association of the EVALI outbreak with the presence of vitamin E acetate in THC-containing vaping products and in the bronchoalveolar lavage fluid of EVALI patients implicated this compound as the trigger of lung injury. Although the mechanisms of EVALI remain unknown, the outbreak provided an impetus and an opportunity to learn about the effects of vitamin E acetate on the lung. Essential for health, vitamin E is found in relatively large amounts in lung tissue. Oral supplementation of vitamin E acetate reduced lung influenza virus infection and susceptibility to lung bacterial infection in mice, but its effects when inhaled are not well described. One of the first cell types to encounter inhaled vitamin E acetate is the airspace macrophage, which may explain the high number of foamy lipid-laden macrophages in patients with EVALI, also described in the report by Abereg et al. These cells are first-line innate immune effectors that scavenge lung irritants, assist in the clearance of airway pathogens, and play an important role in acute lung inflammatory conditions, such as those described in EVALI. It remains unknown whether the lipid-laden macrophages drive EVALI pathogenesis or are simply a marker of exposure.

It is important to note that although the marked decrease in EVALI cases may be attributed to public health measures to curb the availability of vitamin E acetate–containing vaping products, not all EVALI cases have been associated with THC-containing products. This suggests that in certain individuals, nicotine-containing or flavored e-cigarettes may also cause acute lung inflammation and injury, as experimentally demonstrated. This is of particular concern at a time when schools are reopening, when young adults will face increased exposure to e-cigarettes, which may increase their risk not only of EVALI but also of more severe coronavirus disease 2019. In this context, the report by Abereg et al serves as a reminder that vaping remains a serious health threat despite the (current) decrease in EVALI prevalence.

ARTICLE INFORMATION

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