EDITORIAL

Vaping-Induced Lung Injury

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A number of environmental agents are known to cause acute or subacute inhalation injury to the lung parenchyma. Indeed, emergency response guidelines for medical personnel describe toxic inhalation pneumonitis as a heterogeneous group of chemically induced injuries to the lung parenchyma as well as to the upper respiratory tract. The manifestations of such injury depend on the characteristics (e.g., solubility, composition) and the amount of the toxic compound or compounds inhaled.[1] Much of what we know about toxic inhalation syndromes derives from high levels of exposure in either occupational settings (e.g., exposure to metals, solvents, acids, bases, ozone, phosgene, or chlorine dioxide) or community settings where fires or accidents may occur (e.g., factory explosions, derailments of chemical-bearing train cars, and overexposure to household cleaning agents). Depending on the type of chemical agent and the amount of material inhaled, patients may experience symptoms ranging from minor respiratory tract discomfort to acute airway injury and damage to the parenchyma with pneumonitis, alveolar edema, respiratory failure, and death. A common pathophysiological pathway includes inflammation, edema of airways with epithelial sloughing, alveolar inflammation, and edema with hypoxemia.[2]

Layden et al.[3] now report in the *Journal* a cluster of cases from Illinois and Wisconsin in which patients presented with acute, severe respiratory distress after using e-cigarette (vaping) products. Two letters also published in the *Journal* add further support to vaping-induced respiratory distress: a 6-case cluster from Utah[4] and a report of imaging changes seen in a range of cases.[5] The Centers for Disease Control and Prevention reported in late August 2019 that at least 215 acute, severe respiratory distress cases have been identified, spanning 25 states, and as of this writing at least 2 deaths have occurred.[6] Although more investigation is needed to determine the vaping agent or agents responsible, there is clearly an epidemic that begs for an urgent response.

The cases demonstrate a heterogeneous collection of pneumonitis patterns that include acute eosinophilic pneumonia, organizing pneumonia, lipoid pneumonia, diffuse alveolar damage and acute respiratory distress syndrome (ARDS), diffuse alveolar hemorrhage, hypersensitivity pneumonitis, and the rare giant-cell interstitial pneumonitis. Though the precise manifestations of the respiratory injury may be diverse, there are clues to the precipitants that warrant attention. About 80% of the persons who vaped and became ill reported having used both nicotine products and tetrahydrocannabinol (THC) or cannabidiol (CBD) products. Active infection (which would include live bacterial contamination of e-cigarette fluids) does not appear to explain the clinical presentation, but acute toxic lung injury does seem to fit. Mixing of multiple ingredients with primary compounds and potential contaminants may result in in vitro (or even in vivo) production of new agents that may be toxic. E-cigarette fluids have been shown to contain at least six groups of potentially toxic compounds: nicotine, carbonyls, volatile organic compounds (such as benzene and toluene), particles, trace metal elements according to flavor,[7] and bacterial endotoxins and fungal glucans.[8] Two flavorants alone, diacetyl and 2,3-pentanediol, have been shown to perturb gene expression pathways related to cilia and cytoskeletal processes in normal human bronchial epithe-

lial cells.[9] The effect of adding ingredients such as THC or CBD to this mix needs to be investigated.

Until the investigation into the cause of this epidemic of vaping-induced respiratory injury is complete, no conclusions can be drawn as to which compound or compounds are the causes of injury. In light of these cases, however, efforts should be made to increase public awareness of the harmful effect of vaping, and physicians should discourage their patients from vaping.

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1. Kales SN, Christiani DC. Acute chemical emergencies. N Engl J Med 2004;350:800-8.
2. Matthay MA, Zemans RL, Zimmerman GA, et al. Acute respiratory distress syndrome. Nat Rev Dis Primers 2019;5:18.
3. Layden JE, Ghinai I, Pray I, et al. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin — preliminary report. N Engl J Med. DOI: 10.1056/NEJMoa1911614.
4. Maddock SD, Cirulis MM, Callahan SJ, et al. Pulmonary lipid-laden macrophages and vaping. N Engl J Med. DOI: 10.1056/NEJMc1912038.
5. Henry TS, Kanne JP, Kligerman SJ. Imaging of vaping-associated lung disease. N Engl J Med. DOI: 10.1056/NEJMc1911995.
6. Centers for Disease Control and Prevention. Outbreak of severe pulmonary disease associated with using e-cigarette products: investigation notice. August 30, 2019 (https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html).
7. Lee MS, LeBouf RF, Son YS, Koutrakis P, Christiani DC. Nicotine, aerosol particles, carbonyls and volatile organic compounds in tobacco- and menthol-flavored e-cigarettes. Environ Health 2017;16:42.
8. Lee MS, Allen JG, Christiani DC. Endotoxin and (1→3)-β-D-glucan contamination in electronic cigarette products sold in the United States. Environ Health Perspect 2019;127:47008.
9. Park HR, O'Sullivan M, Vallarino J, et al. Transcriptomic response of primary human airway epithelial cells to flavoring chemicals in electronic cigarettes. Sci Rep 2019;9:1400.

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