E-Cigarette/Vaping Danger

Physician Focus Series
In a recent Physician Focus series article, “E-cigarettes, Vaping, and the FDA’s Dilemma” (http://bit.ly/2wdmOSM), Lindsey Marcellin, MD, MPH explained what e-cigarettes are and what they contain, including what the term vaping means. Dr. Marcellin also explained the adverse effects of e-cigarettes and the FDA’s difficulty in regulating these products.

The National Cancer Institute defines an electronic cigarette, or e-cigarette, as:

…a device that has the shape of a cigarette, cigar, or pen and does not contain tobacco. It uses a battery and contains a solution of nicotine, flavorings, and other chemicals, some of which may be harmful. When electronic cigarettes are used, the nicotine solution turns into a mist that can be inhaled into the lungs. The amount of nicotine in individual e-cigarettes can vary. (https://www.cancer.gov/publications/dictionaries/cancer-terms/def/electronic-cigarette).

Substances that are often inhaled in e-cigarettes, in addition to nicotine, are heavy metals, fine particles, volatile compounds, tetrahydrocannabinol (THC), and other harmful substances. The devices can be tampered with to affect the concentration and potentially the toxicity of the substances inhaled. Since 2014, e-cigarettes have been the most commonly used tobacco product by youth in the United States.1 From 2017 to 2018, use of e-cigarettes among US high school students rose to 20.8%.2 Sporadic case reports have been published describing pulmonary illnesses from e-cigarettes in the past, but no major clusters were reported until recently.

As a medical toxicologist and member of the American College of Medical Toxicology, I receive email notifications when members post on the forum. The ACMT forum is an online moderated discussion for members that facilitates the debate, discourse, and dissemination of information that is of interest to the medical toxicology community. On August 5, there was a post from someone who was treating a 16-year-old with severe pulmonary issues that the physician thought could be related to vaping. At that time, 11 cases of lung disease in Wisconsin had been identified that were linked to vaping (https://www.dhs.wisconsin.gov/news/releases/080219.htm).

As the month of August progressed, several more toxicologists in different parts of the US posted cases on the ACMT forum concerning patients who had severe lung injury related to vaping. On August 30, the CDC Health Alert Network issued a Health Advisory entitled “Severe Pulmonary Disease Associated with Using E-Cigarette Products” (https://emergency.cdc.gov/han/han00421.asp). In the Advisory, the CDC describes 215 possible cases, as of August 27, from 25 states, with others under investigation, and one death. On September 5, a second death linked to vaping and marijuana in Oregon was announced; the death toll is up to six as of this writing. At this point the exact cause of the problem is not certain. The only connection is that all patients used e-cigarettes; however, many have reported also using cannabinoid products such as THC or cannabidiol (CBD).

Symptoms start anywhere from a few days to weeks after e-cigarette use and include cough, shortness of breath, and chest pain. Some patients also report gastrointestinal symptoms and general symptoms like fatigue and fever. Many develop severe difficulty breathing that requires admission to the intensive care unit and placement on a ventilator. Antibiotics do not seem to be effective and no infectious etiologies have been identified, but steroid treatment is of benefit in some. Several causes have been suggested, including use of illicit substances and modifications in the method of use of the apparatus. Some users drip the liquid directly on the hot coils (“dabbing”), which can produce higher concentrations of substances like THC.
The New England Journal of Medicine published an online article on September 6, entitled “Pulmonary Illness Related to E-Cigarette Use in Illinois and Wisconsin—Preliminary Report,” by Layden, et al. The authors reported 53 cases of pulmonary infiltrates and illnesses in patients who had used e-cigarettes within 90 days before becoming ill. All patients had similar symptoms and presentations. While the cases could not be attributed to any other causes, the exact agent was not identified. One death occurred in this group; 84% reported using THC products.

A letter published online in NEJM on September 6 from Maddock et al. at the University of Utah Health reported six similar cases. The letter details the most severe case of a patient who vaped nicotine and THC daily, who developed severe respiratory failure but recovered with respiratory support (extracorporeal membrane oxygenation [ECMO]) and steroid treatment. Fluid recovered from brochoalveolar lavage (BAL) in this patient demonstrated lipid-laden macrophages but no evidence of infection. Lipid-laden macrophages were also found on analysis of BAL fluid in the five other Utah cases, suggesting some common pathophysiology.

Finally, an NEJM online editorial by Christani published on September 6 also addresses the phenomenon of injury related to vaping. The editorial points out that multiple toxic compounds contained in e-cigarettes have serious known pulmonary effects by themselves. But the effects that can occur by mixing them may produce further toxicity that is responsible for the pulmonary consequences of vaping.

Also on September 6, the CDC and Morbidity and Mortality Weekly Report (MMWR) released an alert regarding acute lipoid pneumonia (https://www.cdc.gov/mmwr/volumes/68/wr/mm6836e1.htm). Over a two-month period, five patients in North Carolina developed respiratory failure. All used street-purchased THC vaping concentrates or oils in electronic vaping pens/e-cigarettes that had refillable chambers or interchangeable cartridges.

All patients received antibiotics, although no organisms were isolated. BAL analysis demonstrated lipid-laden macrophages, and all survived after treatment with steroids. Inhalation of the aerosolized oils may produce an inflammatory response that causes the lung injury related to e-cigarettes, but other factors may still be implicated with further study.

The CDC and the FDA are working together to determine the cause of the illness and the cause of death. They are looking for any link to specific devices, ingredients, contaminants, or substances. For any cases that are reported, the devices and substances involved can be tested by the local or state health departments. The FDA provides laboratory assistance to examine the contents of the liquids used. They are recommending that no one buy any products off the street, that the products not be modified, and not to add any substances not recommended by the manufacturers of the products.

Many adverse effects were already known to be associated with e-cigarettes, including injury from a malfunctioning device, nicotine dependence and addiction, cardiovascular and neurologic effects of nicotine, other respiratory diseases, adverse effects in pregnancy, and the many adverse effects associated with the exposure to other additives in solutions. Now there is another serious illness related to e-cigarettes and no known cause. Legislation may quickly affect the sale and use of these devices. On September 4, 2019, Michigan became the first state to ban flavored e-cigarettes; San Francisco was the first US city to ban the sale of e-cigarettes. While it would be great if this added risk decreased the use of nicotine, it may only alter the way it is used.
The following are the CDC Recommendations for Clinicians

1. Report cases of severe pulmonary disease of unclear etiology and a history of e-cigarette product use within the past 90 days to your state or local health department. Reporting of cases may help CDC and state health departments determine the cause or causes of these pulmonary illnesses.

2. Ask all patients who report e-cigarette product use within the last 90 days about signs and symptoms of pulmonary illness.

3. If e-cigarette product use is suspected as a possible etiology of a patient’s severe pulmonary disease, obtain detailed history regarding:
   • Substance(s) used: nicotine, cannabinoids (eg, marijuana, THC, THC concentrates, CBD, CBD oil, synthetic cannabinoids [eg, K2 or spice], hash oil, Dank vapes), flavors, or other substances
   • Substance source(s): commercially available liquids (ie, bottles, cartridges, or pods), homemade liquids, and re-use of old cartridges or pods with homemade or commercially bought liquids
   • Device(s) used: manufacturer; brand name; product name; model; serial number of the product, device, or e-liquid; if the device can be customized by the user; and any product modifications by the user (eg, exposure of the atomizer or heating coil)
   • Where the product(s) were purchased
   • Method of substance use: aerosolization, dabbing, or dripping
   • Other potential cases: sharing e-cigarette products (devices, liquids, refill pods, or cartridges) with others

4. Determine if any remaining product, including devices and liquids, are available for testing. Testing can be coordinated with the local or state health departments.

5. Consider all possible causes of illness in patients reporting respiratory and gastrointestinal symptoms and of e-cigarette product use. Evaluate and treat for other possible causes of illness (eg, infectious, rheumatologic, neoplastic) as clinically indicated. Consider consultation with specialists (pulmonary, infectious disease, critical care, medical toxicology) as appropriate.

6. Clinical improvement of patients with severe pulmonary disease associated with e-cigarette use has been reported with the use of corticosteroids. The decision to use corticosteroids should be made on a case-by-case basis based on risks and benefits and the likelihood of other etiologies.

7. Lipoid pneumonia associated with inhalation of lipids in aerosols generated by e-cigarettes has been reported based on the detection of lipid-laden alveolar macrophages obtained by bronchoalveolar lavage BAL and lipid staining (eg, oil red O). The decision about whether to perform a BAL should be based on individual clinical circumstances.

8. Lung biopsies have been performed on some patients. If a lung biopsy is obtained, lipid staining may be considered during pathologic examination, and is best performed on fresh tissue. Routine pathology tissue processing (including formalin-fixation and paraffin-embedding) can remove lipids. Conducting routine tissue processing and histopathologic evaluation is still important. Consider consultation with specialists in pulmonary medicine and pathology to help inform any evaluation plan.

9. Patients who have received treatment for severe pulmonary disease related to e-cigarette product use should undergo follow-up evaluation as clinically indicated to monitor pulmonary function.
References

1. CDC: 2016 Surgeon General's Report: E-Cigarette Use Among Youth and Young Adults. 
   https://www.cdc.gov/tobacco/data_statistics/sgr/e-cigarettes/index.htm

2. Cullen KA et al: Notes from the field: use of electronic cigarettes and any tobacco product 
   among middle and high school students — United States, 2011–2018. 

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