

## VIEWPOINT

## Vaping—Seeking Clarity in a Time of Uncertainty

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As of October 28, 2019, 49 states have reported more than 1600 possible cases of severe pulmonary disease related to vaping—the inhalation of a heated, aerosolized solution—to the Centers for Disease Control and Prevention (CDC).<sup>1</sup> To date, 34 deaths have been attributed to e-cigarette, or vaping, product use-associated lung injury (EVALI). This has resulted in a recommendation from the CDC that the public avoid the use of e-cigarette products, a proposed federal prohibition on certain products and flavors, and much uncertainty on the part of patients and clinicians. In the midst of this uncertainty, it is important to try to provide some clarity.

Vaping is typically associated with the use of nicotine e-cigarettes, although it is not a uniform process and involves a variety of devices, substances, and practices, each of which can cause vaping-related harms. Specifically, “closed-system” vaping devices have self-contained e-liquids (cartridges or pods) and are not meant for modifications (eg, JUUL), whereas “open-system” vaping devices can be modified, allowing users to insert a range of e-liquids, including cannabinoids. The health effects of vaping are likely to vary depending on the device, the substance being vaped, and the amount and type of exposure. For well-established nicotine e-liquids, vaping has been shown to deliver substantially lower concentrations of toxic substances per puff than conventional cigarette smoking.<sup>2</sup> However, this may not

vices and e-liquids were modified, the precise nature of each exposure (especially regarding duration of use), and the source (legal or illegal) of the products. Moreover, patients’ reports may be unreliable, particularly if illegal modifications and illicit substances are involved.

While it seems that the number of individuals presenting with EVALI increased quickly, suggesting new or emerging products, it is possible that this apparent increase represents greater surveillance for and reporting of a phenomenon that has been present all along. Responding to this uncertainty, the CDC has issued broad recommendations<sup>1</sup> for individuals that, as of October 28, 2019, include advice to (1) avoid vaping THC; (2) avoid modified or street-bought vaping products; (3) consider refraining from use of all e-cigarette or vaping products; (4) not return to smoking cigarettes among adults who are using e-cigarettes for the purpose of smoking cessation and to consider the use of FDA-approved nicotine replacement therapies; and (5) monitor for symptoms similar to those previously reported if you are an adult using e-cigarettes or vaping products. Irrespective of the ongoing investigation, children, young adults, women who are pregnant, and adults who do not currently use tobacco products should avoid vaping.<sup>1</sup>

What are the implications of these observations and health guidance? First, the risks of different vaping substances, particularly regarding THC, nicotine, and other additives, need to be more clearly distinguished. Even

though there have been sporadic reports of acute lung injury involving nicotine e-cigarettes, these products have been available since 2007 without frequent reports of severe toxicity. The Illinois and Wisconsin case series<sup>3</sup> noted a near doubling of the rate of severe acute lung injury identified by syndromic surveillance

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between June 1, 2019, and August 15, 2019, compared with the same period in 2018. This pattern suggests a new phenomenon, potentially consistent with an increase in use of illegal or user-modified nicotine e-products or non-nicotine substances. The vast majority of recently published reports of individuals with EVALI have involved THC.

apply to modified e-liquids, and little is known about the health effects of vaping cannabinoids.

Three recently published case series from separate regions of the United States describe patient presentations of EVALI. In the largest series from Illinois and Wisconsin,<sup>3</sup> 84% of the 53 cases of EVALI involved the use of tetrahydrocannabinol (THC), the psychoactive ingredient in marijuana. Multiple patterns of lung injury have been reported, and many cases of EVALI have been suggestive of acute lipoid pneumonia, a relatively rare acute inflammatory reaction resulting from inhalation of oil.<sup>4</sup> Other observed pathologic patterns of lung injury have been nonspecific, but suggestive of chemical pneumonitis.<sup>5</sup> Reports that many of the substances contained vitamin E acetate are currently being followed by the CDC and the US Food and Drug Administration (FDA). However, investigators are still gathering data surrounding this outbreak, such as which devices were used, which products were vaped, when and by whom the de-

vice and THC oils are important. Even though smoking marijuana is known to deliver a large amount of toxins to the lung,<sup>6</sup> little is known about the effects of marijuana and THC when vaporized and inhaled. An unregulated marketplace further complicates the situation because risks may depend on factors in the supply chain, delivery devices, inhalation practices, medical vulnerability, or other variables. Current cases of EVALI could stem from marijuana/THC, distinct additives in these e-liquids, or both. Rapid and robust research is needed to clarify these risks and provide guidance.

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In this context, chemicals and additives in marijuana and THC oils are important. Even though smoking marijuana is known to deliver a large amount of toxins to the lung,<sup>6</sup> little is known about the effects of marijuana and THC when vaporized and inhaled. An unregulated marketplace further complicates the situation because risks may depend on factors in the supply chain, delivery devices, inhalation practices, medical vulnerability, or other variables. Current cases of EVALI could stem from marijuana/THC, distinct additives in these e-liquids, or both. Rapid and robust research is needed to clarify these risks and provide guidance.

Second, as devastating as these instances of EVALI are for the individuals involved, it is important to keep the scale of these reports in perspective. One estimate suggests that nearly 11 million US adults use nicotine e-cigarettes,<sup>7</sup> and a smaller number vape marijuana. Considering this scale relative to the number of EVALI cases, the greater public health concern is whether individuals who participate in vaping are at increased risk of developing chronic lung disease over time,<sup>8</sup> similar to smokers who do not typically develop medical disease until after many years of persistent use. Vigilance is critical, even after a full understanding of these individuals with EVALI is reached. Long-term longitudinal studies of exposure and outcomes associated with vaping nicotine, marijuana, and other substances will be essential for understanding the true risks of these behaviors.

Third, it is critical to keep focus on the dominant public health problem: combustible cigarette smoking. Significant improvements have occurred in tobacco control, and population smoking prevalence has been reduced to its lowest level. This has occurred despite the rapid increase in e-cigarette use, and perhaps even, in part, because of it.<sup>9</sup> Yet smoking remains the leading cause of preventable death in the United States, with large disparities in smoking and smoking-related health outcomes by socioeconomic and mental health status. Some former combustible cigarette smokers may use e-cigarettes chronically as a nicotine delivery system to maintain smoking abstinence. These smokers may include individuals who had no success with conventional tobacco cessation strategies. It is important that ex-cigarette smokers who use e-cigarettes do not revert to conventional cigarettes, which likely pose much higher absolute risks of adverse health outcomes than nicotine e-cigarettes.

How should physicians approach the vaping problem in clinical practice? Clinicians could start by routinely asking patients about vaping. Important follow-up questions to a positive response include gathering information about which devices are being used and whether modifications have been made, what substances and additives are being vaped, where the products were obtained, the frequency of use, the reasons for use, the willingness to discontinue use, and the risk of relapse to conventional cigarettes if vaping is ceased. Products that are illegally purchased, modified, or of unknown quality or source to users may pose a higher risk of toxicity than those purchased from mainstream vendors, and clinicians should counsel their patients to this effect. Patient motivation to discontinue vaping may provide the opportunity for clinicians to engage patients in comprehensive care, including specialty addiction referral, behavioral counseling, and more thorough psychiatric evaluation if warranted.

Special care must be taken when communicating with adult smokers who switched to nicotine vaping or fail to respond to conventional tobacco cessation strategies. Chronic cigarette smoking is still likely to be more harmful than chronic nicotine vaping, and those who choose to vape should avoid devices or e-liquids that are modified or cannot be sold legally in the United States. These patients should be offered standard tobacco cessation strategies to try to wean off vaping, such as nicotine replacement (patches, gum, lozenges, sprays, or inhalers) or varenicline or bupropion, in addition to behavioral counseling. However, ensuring that these patients do not return to combustible cigarettes must be the priority. Nicotine vaping may reduce harm if it prevents these individuals from smoking. Longitudinal analyses and randomized trials with extended follow-up will help to more precisely understand the benefits and risks.

#### ARTICLE INFORMATION

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