

# Anesthesia Implications of Patient Use of Electronic Cigarettes

David E. Harris, PhD, RN

Erin M. Foley, DNAP, MSNA, CRNA

*Electronic cigarettes are essentially electronic nicotine delivery systems (ENDS). Use of ENDS has increased sharply in the United States in recent years, particularly among youth. We reviewed the literature on ENDS use, based on a PubMed search, with a focus on effects that could influence anesthetic and surgical outcomes. We also included a meta-analysis of articles published between 2016 and 2018 reporting injuries from exploding ENDS. These devices deliver nicotine, which is addictive and a cardiac stimulant. The nicotine in ENDS has been linked to increased risk of heart disease and myocardial infarction. Also, ENDS deliver vapors of solvents, flavorings, and other chemicals that can cause chronic and acute respiratory diseases. Furthermore, ENDS use may pose a cancer*

*risk. However, ENDS are somewhat less dangerous than cigarettes and are used as smoking cessation devices. From the literature review, we identified 15 articles reporting injuries from ENDS fires and explosions to 93 patients. Most of these patients were young (mean age = 31.6 years) and male (91%). The most common injury sites were the thigh (62%) and hand (33%). Because the anesthetist will likely encounter increasing numbers of ENDS users in the future, it is important to identify these patients and to understand the risks of ENDS use.*

**Keywords:** Anesthesia implications, e-cigarette, electronic cigarette, electronic nicotine delivery systems, ENDS.

Electronic cigarettes have been available in the United States only since 2007.<sup>1</sup> However, in the short time since their introduction, they have exploded in popularity,<sup>2</sup> particularly among youth. The use of electronic cigarettes is referred to as “vaping” because electronic cigarettes vaporize a liquid rather than burning solid tobacco, as is the case with conventional cigarettes. The liquid in electronic cigarettes almost always contains nicotine and can also contain flavorings.<sup>3</sup> Thus, electronic cigarettes are essentially electronic nicotine delivery systems (ENDS) and will be referred to as such in this article. We will use the term cigarette to refer to conventional cigarettes containing tobacco.

Given their increasing popularity, anesthetists will likely encounter greater numbers of patients who use ENDS. This is important for at least the following reasons:

- Users of ENDS are at increased risk of a range of diseases, particularly those of the cardiovascular and respiratory systems. If present, these diseases may affect the course of a general anesthetic or the surgical outcome.
- Among ENDS users, there may be an increased risk of cancer occurrence or recurrence.
- The lithium-ion batteries in ENDS can explode, causing burns and blast injuries. Patients injured in this way often require surgical procedures that necessitate general anesthesia.
- Because ENDS can be used as smoking cessation tools, anesthetists may encounter patients who switched

from cigarettes to ENDS before elective surgery, at the advice of their surgeon.

The purpose of this article is to review the health implications of ENDS use and to address their impact on surgical and anesthetic outcomes. To this end, we searched PubMed to identify pertinent articles using the search terms *ENDS* or *electronic cigarettes* alone or combined with the terms *health effects*, *surgery*, *anesthesia*, *injury*, and *smoking cessation*. We also include a meta-analysis of articles published between 2016 and 2018 reporting injuries from exploding ENDS.

## History and Review of the Literature

• **Evolution of the Technology and Use of ENDS.** In something approaching their current form, ENDS were invented in China in 2003 and were introduced into the US market in 2007.<sup>4</sup> The most popular current form of ENDS consists of a replaceable cartridge or “pod” that holds the solution to be vaped, a heating element to vaporize the solution, a lithium-ion battery to power the heating element, a chamber in which the vaporization occurs, and a mouthpiece through which the vapor is inhaled. Modern ENDS either have an “on switch” or may be “draw activated.” They can also have a USB charging port that allows the user to recharge the battery from a computer.<sup>1,4</sup>

The liquid in ENDS generally contains nicotine derived from tobacco,<sup>4</sup> always contains a solvent (propylene glycol or vegetable glycerin),<sup>1,5</sup> and may also

contain 1 of more than 7,000 flavorings.<sup>1,4</sup> The solvents and flavorings in ENDS are usually on the US Food and Drug Administration (FDA) list of substances “generally recognized as safe” (GRAS). However, the GRAS list speaks to the safety of a substance consumed orally and gives no guarantee that the same substance is safe when aerosolized and inhaled.<sup>5</sup> Inhaling the vapor of ENDS may also expose users to heavy metals, volatile organic compounds,<sup>6-8</sup> and ultrafine particulates associated with pulmonary disease.<sup>9</sup>

US sales of ENDS nearly doubled between 2013 and 2017 to more than 121 million units, driven by an aggressive marketing campaign targeting youth.<sup>4,10</sup> The success of this marketing to attract young users is illustrated by the fact that vaping prevalence among 12th grade students rose from 12.5% in 2016 to 16.6% in 2017 and then skyrocketed to 26.7% in 2018.<sup>3</sup> One ENDS product, sold under the brand name Juul (Juul Labs Inc), dominates the ENDS market. Juul is particularly popular among youth because it has an appealing design (it looks like a computer flash drive so it is easy to hide in school), is easy to use (it is draw activated), and has pods containing liquid that has both a high nicotine content and sweet flavors that appeal to young users.<sup>2</sup> Young ENDS users may also have been convinced by advertising that ENDS are not harmful and that ENDS use is not prohibited in places where smoking cigarettes is banned.<sup>4</sup>

The most immediate reason that ENDS use among youth is a public health concern is that ENDS contain nicotine, which is addictive and carries health risks. Depending on the brand used, nicotine exposure from ENDS can equal or exceed that from cigarettes.<sup>4</sup> Once a young person becomes addicted to nicotine via ENDS use, he or she will find it very difficult to quit. Young users of ENDS will be exposed to the health dangers of ENDS and also be at 3 to 4 times greater risk to progress to cigarette smoking compared with non-ENDS users.<sup>11</sup>

• **Cardiovascular Impact of ENDS.** The cardiovascular effects of ENDS use are primarily due to the nicotine they contain. Nicotine is a cardiac stimulant by virtue of its ability to activate nicotinic acetylcholine receptors at autonomic ganglia and the adrenal medulla, causing catecholamine release.<sup>12</sup> When administered acutely, nicotine increases subjects’ heart rate, blood pressure, cardiac output, and myocardial oxygen consumption.<sup>4</sup> Nicotine has also been implicated as a possible contributor to reduced coronary artery blood flow, via arterial vasoconstriction, in those with coronary heart disease; increased heart failure risk via  $\beta$ -adrenergic stimulation of cardiac remodeling; and an increase in ventricular arrhythmias via  $\beta$ -adrenergic lowering of the myocardial fibrillation threshold.<sup>12</sup>

The long-term ability of nicotine to cause hypertension and cardiac remodeling may be further explained by its ability to upregulate angiotensin-converting enzyme (ACE), thereby enhancing the generation of angiotensin

2 from angiotensin 1. Angiotensin 2 is a vasoconstrictor and causes renal sodium retention via aldosterone release. Nicotine also downregulates ACE2, an enzyme that cleaves angiotensin 1 into a vasodilating peptide.<sup>13</sup>

Given these effects of nicotine, it is not surprising that ENDS affect the cardiovascular system. A review of National Health Interview Survey data from 2014 and 2016 found that people who used ENDS daily had a 79% higher risk of myocardial infarction compared with those who did not use ENDS, even after demographics and health characteristics were considered.<sup>14</sup> Cigarette smokers had an even greater increase in risk. Also, ENDS use has been implicated as a factor contributing to spontaneous coronary artery dissection in an otherwise healthy 2-week postpartum 41-year-old woman.<sup>15</sup>

At the level of the peripheral circulation, thermal imaging has been used to show that the acute use of ENDS reduces cutaneous blood flow in humans.<sup>16</sup> This may explain the case of a 51-year-old female user of ENDS in whom skin flap necrosis developed after bilateral mastectomy.<sup>17</sup>

• **Respiratory Impact of ENDS.** The propylene glycol or vegetable glycerin solvents in ENDS form aldehydes when heated. On inhalation, these aldehydes are known to cause cough and alterations in pulmonary function test results that mimic those of obstructive pulmonary disease: decreased ratio of forced expiratory volume in the first second (FEV<sub>1</sub>) to forced vital capacity (FVC), or FEV<sub>1</sub>/FVC ratio.<sup>5</sup> Aerosolized propylene glycol also produces ultrafine particulate matter (particles < 2.5  $\mu$ m in diameter commonly called PM 2.5) that ENDS users inhale in doses that equal or exceed those to which cigarette smokers are exposed.<sup>4,9</sup> These PM 2.5 are known to decrease lung function and to precipitate asthma attacks in susceptible individuals.

Given the described pulmonary effects of aerosolized inhalation of the solvents found in ENDS, the following clinical study results are as predictable as they are disturbing. Young, healthy men who had been using ENDS daily for at least 6 months were found to have alterations in pulmonary function test results similar to those seen in obstructive lung disease, including decreases in FEV<sub>1</sub>, FEV<sub>1</sub>/FVC ratio, and forced expiratory flow, compared with matched control participants who did not use ENDS. It is important to note that this was a chronic effect; the ENDS users had not vaped in the hour preceding the measurement.<sup>18</sup> Another example of the chronic (and lasting) pulmonary effects of ENDS use comes from an analysis of data from the Southern California Children’s Health Study showing that current and even former adolescent ENDS users were nearly twice as likely to report bronchitic symptoms (cough of  $\geq$  3 months and wheezing) in the last year compared with non-ENDS users.<sup>19</sup>

Even secondhand ENDS vapor may present a danger

to pulmonary function. Air quality measurements taken from the homes of ENDS users and nonusers demonstrate that PM 2.5 levels are higher in the homes of ENDS users.<sup>9</sup> This likely explains results from the 2016 Florida Youth Tobacco Survey showing that youth (aged 11-17 years) with asthma were 27% more likely to report an attack in the last year if they lived in a house with an ENDS user compared with youth who did not.<sup>20</sup>

Inhalation of the vapor of at least one of the flavorings popular in ENDS (diacetyl) has also been definitively linked to a serious pulmonary disease—bronchiolitis obliterans, popularly referred to as “popcorn lung”.<sup>5</sup> Bronchiolitis obliterans is a rare, untreatable form of chronic lung disease characterized by inflammation and fibrosis of the distal and terminal bronchioles resulting in small-airway obstruction. A loss of lung tissue elasticity further contributes to small-airway obstruction by causing bronchiolar collapse.<sup>21</sup> Given the known hazard of vaporized diacetyl, it is shocking that 76% of the sweet ENDS flavorings most favored by youth were found on chemical analysis to contain diacetyl and 89% were found to contain either diacetyl or a closely-related chemical compound.<sup>22</sup>

Because diacetyl is so common in flavored ENDS and the solvents propylene glycol or vegetable glycerin are found in all ENDS, it is very difficult to determine how much the pulmonary damage due to ENDS flavorings contributes to the chronic lung disease symptoms described earlier in the discussion of the impact of ENDS solvents. However, it is clear that diacetyl joins the ENDS solvents propylene glycol and vegetable glycerin as chemicals that are on the GRAS list as safe to eat but are definitely not safe when vaporized and inhaled.<sup>4</sup>

Use of ENDS has also been blamed for acute hypersensitivity pneumonitis, including a case of an 18-year-old woman in whom hypersensitivity pneumonitis developed after only 2 weeks of ENDS use. Her pulmonary status deteriorated to the point where she met the diagnostic criteria for acute respiratory distress syndrome (ARDS) and required intubation and ventilation as well as vasopressor support. She recovered after other causes of her ARDS were ruled out, the diagnosis of hypersensitivity pneumonitis was established, and she was treated with intravenous corticosteroids.<sup>23</sup>

## Discussion of State of the Art

In the United States, ENDS are so new that the science around their dangers is lagging behind the epidemic of their use. However, there are several matters that are emerging as current (and future) issues. These include injuries from explosions of ENDS batteries, the use of ENDS as smoking cessation devices, and the long-term impact of ENDS use on cancer risk.

- **Injuries From ENDS.** When the lithium-ion batteries that power ENDS short circuit, they can overheat, catch fire, or even explode.<sup>24</sup> We identified 15 articles

Characteristic	No. (%) <sup>a</sup>
<b>Demographics of injured<sup>b</sup></b>	
Age, mean (range), (n = 72)	31.6 (17-59)
Male sex (n = 78)	71 (91)
<b>Location of injury (N = 93)<sup>c</sup></b>	
Thigh	58 (62)
Hand	31 (33)
Genitalia	18 (19)
Mouth/face	19 (20)
Torso	5 (5)

**Table 1. Demographics and Site of Injury Reported From ENDS Fires/Explosions in 15 Articles Published From 2016 to 2018<sup>24-38</sup>**

Abbreviation: ENDS, electronic nicotine delivery systems.

<sup>a</sup>Except for age.

<sup>b</sup>Articles discussed a total of 93 cases. The total cases (n) used to calculate the sex and ages of patients reflect that not all articles reported this information.

<sup>c</sup>Percentages for injury location add to > 100% because some patients were burned in > 1 location.

published between 2016 and 2018 reporting a total of 93 cases of injuries caused by fires or explosions from the lithium-ion batteries in ENDS.<sup>24-38</sup> This almost certainly does not count every person injured by an ENDS explosion in that period because only cases that are part of a series or result in unusual or severe injuries are likely to be represented in the literature. Nonetheless, these cases give some idea of what an anesthetist might encounter in a patient injured by an ENDS fire. An analysis showing the demographics of the patients and characterizing the injuries they received is shown in Table 1.

The patients who sustained burns from ENDS were generally young and nearly all were male. The most common areas burned were the thigh and hand (Table 1). This distribution of injury sites reflects the fact that ENDS fires or explosions can occur when the device is being used, producing injury to the face or hand, or while it is being carried in a pocket, producing burns to the thigh or genitalia. The overwhelming representation of male patients in this sample cannot be fully explained by the higher use rates of ENDS among men.<sup>4</sup> Thus, men may be getting burned when their ENDS catch fire in their pocket while women are avoiding injury by carrying their ENDS in a purse.

Of the 93 burn cases reported here, 34 can be identified as patients who required a surgical procedure that would have necessitated some level of sedation or anesthesia. Some patients required multiple surgical procedures. These include a 17-year-old male teenager who received a blast injury to his left hand when his ENDS exploded while in use. Because of infection, this patient underwent 7 surgical procedures, the last of which

was a débridement that included removal of part of his thumb.<sup>24</sup> Another case in which the patient required multiple surgeries was that of a 19-year-old man whose ENDS exploded in his right hand. He required 4 surgical débridement procedures culminating in the amputation of his middle finger.<sup>31</sup>

Some of the more serious injuries reported from ENDS fires and explosions involve facial and oral injuries. These include the following:

- An 18-year-old man sustained facial burns and dental trauma. Three of his 4 upper incisors were avulsed or severely damaged. He required oral surgery with bone grafts.<sup>36</sup>
- A 19-year-old man sustained facial burns and dental trauma that necessitated removal of 3 of his 4 upper incisors. He recovered after bone grafts and dental implants.<sup>31</sup>
- A 59-year-old man sustained fractures of the petrous section of the temporal bone, the ethmoid bone including the cribriform plate, the nasal choanae and nasal septum, and the right medial orbital wall. He also experienced a pneumocephalus. After neurosurgery, he recovered without neurologic deficit.<sup>25</sup>
- A 27-year-old man's ENDS exploded while in use, propelling the plastic mouthpiece of the device posteriorly through the wall of his oropharynx. He sustained fractures of cervical vertebrae C1 and C2. The foreign body was removed surgically, and the cervical fractures were treated conservatively. The patient recovered without neurologic deficit.<sup>34</sup>
- There have also been 2 reports in the news media of fatalities resulting from ENDS explosions.<sup>39,40</sup>

Other major issues around ENDS fires and explosions involve the materials that make up these devices. Soot and debris from the ENDS can become embedded in a wound during an ENDS explosion. This can necessitate extensive wound irrigation as part of a surgical procedure and present an infection hazard.<sup>24,29,31,38</sup> The lithium-ion batteries that power ENDS contain a range of metals, and these too can become embedded in the patient's tissue following an ENDS explosion. One patient who received a blast injury to his hand was subsequently found to have elevated blood levels of cobalt and manganese, both of which are found in ENDS batteries. These levels fell into the normal range over 10 days without treatment.<sup>31</sup> Finally, it should be recognized that the burns from an ENDS fire can be both thermal and chemical.<sup>28,33</sup> Litmus paper testing of ENDS burns in 1 case showed pH levels as high as 10, demonstrating an alkali burn that needed to be treated with extensive irrigation.<sup>33</sup>

• **ENDS as Smoking Cessation/Reduction Devices.** Patients who smoke cigarettes are known to be at greatly increased perioperative risk of wound infections, pneumonia, myocardial infarction, stroke, graft failure in cardiac surgery, and reduced skin flap survival in plastic surgery.<sup>41</sup> Thus, it is not surprising that guidelines suggest that patients who smoke cigarettes should be

counseled to quit during the perioperative period and that nicotine replacement devices, including ENDS, are suggested as possible tools to facilitate this.<sup>42</sup>

The idea that ENDS could serve as a smoking cessation device in the perioperative period is bolstered by an observational study of patients who smoked cigarettes and were scheduled for elective surgery. These patients were given ENDS when they were seen preoperatively and for 2 weeks postoperatively. Average cigarette consumption was 51% lower at 2 weeks postoperatively than before being given the ENDS.<sup>43</sup> Although the results of this study certainly demonstrate the feasibility of using ENDS as a smoking reduction tool in the perioperative period, the study lacks a control group of preoperative smokers not given ENDS. It should also be noted that these patients received ENDS at no cost, and ENDS are not usually available free. However, the general idea that ENDS can be effective smoking cessation tools is supported by a randomized controlled trial in the United Kingdom. Cigarette smokers accessing smoking cessation services were randomly assigned to use either standard nicotine replacement devices or ENDS. One year later 19% of ENDS users but only 10% of nicotine replacement users were abstaining from cigarettes.<sup>44</sup>

• **ENDS and Cancer Risk.** There is mounting evidence of a connection between ENDS and cancer risk. Cells exposed to ENDS vapor in culture exhibit an increase in DNA damage<sup>45</sup> that could mimic a precursor to cancer, and cultured human lung cancer cells undergo changes necessary for metastasis when exposed to ENDS vapor.<sup>46</sup> Nicotine itself is not carcinogenic, but its metabolites are. One study that attempted to define the mechanism of this carcinogenesis exposed mice to ENDS vapor. The mice metabolized nicotine into chemicals that complexed with DNA in a range of mouse organs, forming DNA adducts that inhibit DNA repair mechanisms.<sup>47</sup>

The flavoring chemicals in ENDS have also been shown to stimulate tumor production in mice.<sup>48</sup> This effect is probably related to the metabolism of multiple ENDS flavoring into carbonyl compounds including formaldehyde and acetaldehyde, which are known human carcinogens.<sup>49</sup> These same carcinogens are produced when the solvents in ENDS are vaporized.<sup>6</sup> The vapor in ENDS is also known to contain carcinogenic metals including nickel, cadmium,<sup>8</sup> and copper.<sup>7</sup> Thus, the nicotine, the flavorings, the solvents, and other chemicals inhaled in ENDS vapor may all pose cancer risks.

Large-scale ENDS use is new, and ENDS users are mostly young. By contrast, cancer can take decades to develop and many cancers are predominantly diseases of older adults. Thus, it is not currently possible to quantify the cancer risk posed by ENDS use. However, analysis of the urine of ENDS users found 2 known bladder carcinogens.<sup>50</sup> There is also substantial concern that ENDS may increase oral cancer risk.

Finding	Recommendation
ENDS users draw a distinction between “smoking” and “vaping” and perceive vaping as less harmful. <sup>4</sup> Patients who vape may answer “no” when asked if they smoke in a preanesthesia interview.	Explicit questions about ENDS use should be added to preanesthesia interview checklists so that the anesthetist can identify all patients who vape.
The solvents and flavorings in ENDS have known deleterious effects on the respiratory system. <sup>5,9,18-20</sup>	Patients who use ENDS, particularly those with lung disease, should be encouraged to abstain before and after anesthesia.
The nicotine in ENDS has known deleterious effects on the heart and circulatory system. <sup>4,12-15</sup>	Patients who use ENDS, particularly those with atherosclerosis, should be encouraged to abstain before and after anesthesia.
ENDS have known deleterious effects on the microcirculation <sup>16</sup> that may contribute to skin graft failure. <sup>17</sup>	Surgical patients, particularly those having a skin graft, should be encouraged to abstain from ENDS use until well after surgery.
ENDS vapor, including secondhand vapor, can cause or exacerbate respiratory symptoms. <sup>18-20</sup> Because the nicotine in ENDS is derived from tobacco, <sup>4</sup> ENDS use would be prohibited in hospitals under rules that prohibit the use of all tobacco products.	Because people who use ENDS may not consider them tobacco products, hospital signage should be updated to explicitly forbid the use of ENDS on hospital property.
Short-term use of the nicotine in ENDS produces $\beta$ -adrenergic stimulation. <sup>12</sup> There are no guidelines concerning the administration of anesthesia to patients who have recently used ENDS, as might occur in an emergency situation.	If the procedure can be safely postponed for a short time until the effects of the nicotine have dissipated, it might be prudent to do so. The half-life of nicotine in the human body is 2 hours. <sup>12</sup>
It is not currently possible to establish a definite link between ENDS use and cancer occurrence or recurrence. However, there is evidence suggesting that ENDS may increase cancer risk. <sup>6,7,43-48</sup>	Any patient who is at increased risk of cancer and is motivated to do as much as possible to decrease his or her risk should be informed of the possible link between ENDS use and cancer.
Despite its dangers, ENDS use is almost certainly less dangerous than smoking cigarettes in the perioperative period.	Patients who previously smoked cigarettes and switched to ENDS before surgery should be encouraged to continue to abstain from cigarettes.

**Table 2.** Findings of Review and Recommendations Based on Findings

Abbreviation: ENDS, electronic nicotine delivery systems.

## Conclusion

Use of ENDS is increasing, particularly among youth, and is a risk factor for diseases of the respiratory and cardiovascular systems. It may also increase cancer risk. However, ENDS users are not always clear about their risks, and ENDS are also used as smoking cessation devices. The specific findings and recommendations of this review are summarized in Table 2. Patients who use ENDS, particularly those with lung disease or atherosclerosis, should be encouraged to abstain before and after anesthesia.

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## AUTHORS

David E. Harris, PhD, RN, is a professor in the University of Southern Maine's School of Nursing in Portland, Maine, and an adjunct professor in the University of New England School of Nurse Anesthesia in Portland, Maine, where he teaches advanced physiology and advanced pathophysiology. Email: dharris2@une.edu.

Erin M. Foley, DNAP, MSNA, CRNA, is a practicing CRNA in Maine and the director of simulation and interim assistant program director at the University of New England School of Nurse Anesthesia.

## DISCLOSURES

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