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# E-cigarettes: How “safe” are they?

Without tobacco, tar, ash, or carbon monoxide, e-cigarettes are marketed as “healthier” alternatives to cigarettes. But they are not without risk.

## PRACTICE RECOMMENDATIONS

› *Inform patients that e-cigarette vapors contain toxic substances, including the heavy metals lead, cadmium, and nickel.* **A**

› *Educate all patients—particularly young people and those who are pregnant or lactating—about the potential health risks of e-cigarettes.* **B**

### Strength of recommendation (SOR)

- A** Good-quality patient-oriented evidence
- B** Inconsistent or limited-quality patient-oriented evidence
- C** Consensus, usual practice, opinion, disease-oriented evidence, case series

**E**lectronic cigarettes (e-cigarettes) have become increasingly popular over the last decade. Although they are perceived by many to be safer than traditional cigarettes, many of the devices still contain nicotine, and inhaling their vapors exposes users to toxic substances, including lead, cadmium, and nickel—heavy metals that are associated with significant health problems.<sup>1</sup> (For more on how e-cigarettes work, see “Cigarettes vs e-cigarettes: How does the experience (and cost) compare?” on page 383.)

In addition, many people use e-cigarettes as a means to stop smoking, but few who do so achieve abstinence.<sup>2,3</sup> They frequently end up utilizing both, increasing their health risks by exposing themselves to the dangers of 2 products instead of one.<sup>1</sup>

Further complicating the issue is that the manufacture and distribution of e-cigarettes has not been well regulated. Without regulation, there is no way to know with certainty how much nicotine the devices contain and what else is in them.

Things, however, are changing. The Food and Drug Administration (FDA) recently announced that e-cigarettes and other tobacco products like cigars and hookahs will now be regulated in the same way the government regulates tobacco cigarettes and smokeless tobacco.<sup>4</sup> The rule will not take effect immediately because companies requested time to comply, but once it is enacted, packaging will be required to list what the products contain, among other changes.

Keeping up on the latest information on e-cigarettes is now—and will continue to be—important as family physicians are increasingly asked about them. What follows is a review of what we know about their potential risks.

## A nicotine system developed by a pharmacist

E-cigarettes, or electronic nicotine delivery systems, were patented in 2003 by a Chinese pharmacist.<sup>5</sup> Since their introduc-



## INSTANT POLL

Have you ever recommended e-cigarettes to a patient as a means to quit smoking?

- Yes
- No

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Since many individuals continue to use traditional and electronic cigarettes, they end up in double jeopardy of toxicity through exposure to the dangers of both.

tion to North America and Europe in 2007, the devices have become known by over 400 different brand names.<sup>6</sup> Consumption among adults doubled by 2012, and by 2014, about 4% of US adults used e-cigarettes every day or some days.<sup>7</sup> Many of them are dual users of tobacco and electronic cigarettes. In fact, Jenkins and colleagues reports in this issue of *JFP* (see "E-cigarettes: Who's using them and why?" on page 390) that over half of cigarette smokers (52%) in their study use e-cigarettes, usually to either lower their cigarette consumption or aid in smoking cessation. (Throughout this article, we will use "cigarettes" and "smoking" to refer to the use of traditional tobacco cigarettes.)

In addition to concern over an increase in use among the general population, there is significant concern about the increase in e-cigarette use among US middle and high school students.<sup>1,8,9</sup> In 2015, e-cigarettes were the most commonly used smoking product among middle and high school students, with 620,000 middle school students and nearly 2.4 million high school students using the battery-powered devices in the past 30 days.<sup>10</sup>

Many factors have contributed to the growing popularity of e-cigarettes.

- **Perceived safety.** With tobacco's dangers so thoroughly documented, many advertising campaigns tout e-cigarettes as less dangerous than conventional cigarettes in terms of their ability to cause cardiac and lung

diseases and low birth weights. This is largely because e-cigarettes do not produce the combustion products of tar, ash, or carbon monoxide. In addition, many consumers are mistakenly less fearful about the nicotine added to many e-cigarettes.

- **Expectation that it helps smokers quit.** Many smokers view e-cigarettes as an aid to smoking cessation.<sup>6</sup> In fact, testimonials of efficacy in tobacco cessation abound in promotional materials and on the Web, and e-cigarettes are recommended by some physicians as a means to quit or lessen smoking of tobacco cigarettes.<sup>11</sup>
- **Wide availability and opportunities for use.** The use of electronic nicotine delivery devices is sometimes permitted in places where smoking of conventional cigarettes is banned, although rules vary widely in different parts of the country. In addition, e-cigarettes are readily available for purchase on the Internet without age verification.
- **Extensive advertising.** There are increasing concerns that advertising campaigns unduly target adolescents, young adults, and women.<sup>12-155</sup> In addition to advertising, the media and social influences play significant roles in young people's experimentation with "vaping," the term for inhaling electronic cigarette aerosols.<sup>14,15</sup>

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**>**  
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■ **Regulation, legislation remain controversial.** Currently, e-cigarettes are not required to be tested before marketing,<sup>16</sup> but that may change with the FDA's new regulations. The British National Public Health body, Public Health England, has documented public health benefits of e-cigarettes when used as a way to quit smoking, and provides evidence that the devices are less dangerous than traditional cigarettes.<sup>17</sup> But this issue and public policy are the subject of ongoing debate. In 2015, the United Kingdom made it illegal to sell e-cigarettes or e-liquids to people younger than 18 years of age and urged child-proof packaging.

**What's "in" an e-cigarette—and are the ingredients toxic?**

Because e-cigarettes are relatively new to the global marketplace, little research exists regarding the long-term effects and safety of their use, especially among habitual users.

■ **Vapor/refills.** E-liquids may contain a variety of substances because they have been largely unregulated, but they generally include some combination of nicotine, propylene glycol, glycerin, and flavorings. In fact, up to 7000 flavors are available,<sup>6</sup> including such kid-friendly flavors as chocolate, cherry crush, and bubble gum.

When the refills do contain nicotine, users generally derive less of the substance from the electronic devices than they do from a conventional cigarette. Researchers found that individual puffs from an e-cigarette contained 0 to 35 µg nicotine per puff.<sup>1,18</sup> Assuming an amount at the high end of the spectrum (30 µg nicotine), it would take about 30 puffs of an e-cigarette to derive the same amount of nicotine (1 mg) typically delivered by a conventional cigarette.

The chemical make-up of the vapor and the biologic effects on animal models have been investigated using 42 different liquid refills.<sup>19,20</sup> All contained potentially harmful compounds, but the levels were within exposure limits authorized by the FDA. These potentially dangerous chemicals include the known toxins formaldehyde, acrolein, and hydrocarbons.<sup>20</sup>

An inflammatory response to the inhalation of the vapors was demonstrated in

mouse lungs; exposure to e-cigarette aerosols reduced lung glutathione—an important enzyme in maintaining oxidation-reduction balance—to a degree similar to that of cigarette smoke exposure.<sup>20</sup> Less of the enzyme facilitates increased pulmonary inflammation.

In addition, human lung cells release pro-inflammatory cytokines when exposed to e-cigarette aerosols.<sup>20</sup> Other health risks include:

■ **Harm to indoor air quality/secondhand exposure.** Even though e-cigarettes do not emit smoke, bystanders are exposed to the aerosol or vapor exhaled by the user, and researchers have found varying levels of such substances as formaldehyde, acetaldehyde, isoprene, acetic acid, acetone, propanol, propylene glycol, and nicotine in the air. However, it is unclear at this time whether the ultra-fine particles in the e-cigarette vapor have health effects commensurate with the emissions of conventional cigarettes.<sup>1,21,22</sup>

■ **Cartridge refill ingestion by children.** Accidental nicotine poisonings, particularly among children drawn to the colors, flavors, and scents of the e-liquids, have been problematic. In 2014, for example, over 3500 exposures occurred and more than half of those were in children younger than 6 years of age. (Exposure is defined as contact with the substance in some way including ingestion, inhalation, absorption by the skin/eyes, etc; not all exposures are poisonings or overdoses).<sup>23</sup> Although incidence has tapered off somewhat, the American Association of Poison Control Centers reports that there were 623 exposures across all age groups between January 1, 2016 and April 30, 2016.<sup>23</sup>

■ **Environmental impact of discarded e-cigarettes.** Discarded e-cigarettes filling our landfills is a new and emerging public health concern. Their batteries, as do all batteries, pollute the land and water and have the potential to leach lead into the environment.<sup>24</sup> Similarly, incompletely used liquid cartridges and refills may contain nicotine and heavy metals, which add to these risks.<sup>24</sup>

■ **Explosions.** Fires and explosions have been documented with e-cigarette use, mostly due to malfunctioning lithium-ion batteries.<sup>25</sup> Thermal injuries to the face and hands can be significant.

■ **Heavy metals.** The presence of lead,

## Cigarettes vs e-cigarettes: How does the experience (and cost) compare?

If you were to ask a smoker to describe how cigarette smoking compares to using e-cigarettes, he or she would probably tell you that while the *process* of drawing on an e-cigarette is similar to that of a conventional cigarette, the *experience* in terms of reaching that state of relaxation or getting that "smoker's high" is not.

In fact, a recent national survey of current and former smokers found that more than three-quarters of current smokers (77%) rated e-cigarettes less satisfying than conventional cigarettes and stopped using them.<sup>1</sup> "Being less harmful" was the most highly rated reason for continuing to use the devices among people who switched from conventional to e-cigarettes.

**How do they work?** E-cigarettes do not burn anything and users do not light them. E-cigarettes work in much the same way as a smoke or fog machine. They use battery power (usually a rechargeable lithium battery) to heat a solution—usually containing nicotine, flavorings, and other chemicals—to the point that it turns into vapor. Much of whatever substances are in the vapor enter the bloodstream through the buccal mucosa, rather than the lungs.

Devices typically have an on/off button or switch, an atomizer containing a heating coil, a battery, and an LED light, which is designed to simulate a burning cigarette. A sensor detects when a user takes a drag and activates the atomizer and light. Some of the devices can be charged with a USB cord.

Because e-cigarettes don't burn anything, they don't have any smoke. They also don't have any tar, ash, carbon monoxide, or odor (except perhaps a faint, short-lived scent matching the flavor liquid chosen). But the issues of second-hand exposure and effects on air quality are still being investigated.

With over 500 brands available, devices generally fall into one of 3 categories:<sup>2</sup>

• **Cigalikes:** About the same size and shape of a conventional cigarette, these cigarette look-alikes may come pre-

filled with about a day's worth of liquid and then may be discarded, or they may be non-disposable and have a replaceable cartridge.

• **eGo's:** Also known as "vape pens," these devices tend to be longer and wider than cigalikes, have a more powerful battery, and usually are refillable or have a replaceable cartridge.

• **Mods:** Short for "modules," these "vaporizers" tend to be the largest and most expensive type of e-cigarette. They may be refilled with e-liquid or accept replaceable cartridges and have even more powerful batteries.

**What do they cost?** A pack of cigarettes (containing 20 cigarettes) costs anywhere from \$5 to \$14, depending on where one lives.<sup>3</sup> The price of e-cigarette devices starts at about \$8 and can climb higher than \$100. A 5-pack of flavor cartridges or a refill tank of e-liquid (which may last as long as about 150 cigarettes) costs about \$10 to \$15.<sup>4</sup>

To put this in perspective, a pack-a-day smoker in New York might spend about \$5000 a year on cigarettes (\$14 per pack x 365 days in a year), whereas someone who uses an e-cigarette device (\$10) plus a refill tank per week (\$14 x 52 weeks per year) will spend about \$740 a year. (The actual cost will be higher because atomizers or devices as a whole must be replaced periodically, with some lasting only days and others lasting weeks or months, depending largely on how often one uses them. Although the cost of atomizers ranges widely, many can be found for \$3-\$5.)

Of course, the difference between cigarettes and e-cigarettes will be less dramatic in states where cigarettes are cheaper.

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cadmium, and nickel in inhaled e-cigarette vapor is another area of significant concern, particularly for younger people who might have long-term exposure.<sup>1</sup> All 3 heavy metals are known to be toxic to humans, and safe levels of inhalation have not been established.

Inhalation and/or ingestion of lead, in particular, can cause severe neurologic damage, especially to the developing brains of children.<sup>26</sup> Lead also results in hematologic dysfunction. Because of the risks associated with inhalation of this heavy metal, the sub-

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stance was removed from gasoline years ago.

Inhaled cadmium induces kidney, liver, bone, and respiratory tract pathology<sup>27</sup> and can cause organ failure, hypertension, anemias, fractures, osteoporosis, and/or osteomalacia.<sup>28</sup> And inhaling nickel produces an inflammatory pulmonary reaction.<sup>29</sup>

**■ Pregnancy/lactation.** Since no clear evidence exists on the safety of e-cigarette use during pregnancy, women should avoid exposure to these vapors during the entire perinatal period. Similarly, the effects of e-cigarettes on infants who are breastfeeding are not established. Pregnant and breastfeeding women should not replace cigarettes with e-cigarettes.<sup>30,31</sup> For pregnant women who smoke, the US Preventive Services Task Force (USPSTF) advises using only behavioral methods to stop cigarette use.<sup>32</sup> And until more information becomes available, exposing infants and young children to e-cigarette vapor during breastfeeding is not recommended.

On the flip side, without tobacco, tar, ash, or carbon monoxide, e-cigarettes may have some advantages when compared with the use of traditional cigarettes, but that has not been substantiated.

### **Don't substitute one form of nicotine for another**

The USPSTF has not determined the benefit-to-harm ratio of using e-cigarettes as a smoking cessation aid, but recommends prescribing behavioral techniques and/or pharmacologic alternatives instead.<sup>32</sup> Because the devices have been promoted as an aid to smoking cessation, intention to quit using tobacco products is a reason often stated for utilizing e-cigarettes.<sup>2,33,34</sup> Indeed, use of e-cigarettes is much more likely among those who already utilize tobacco products.<sup>35-37</sup>

At least one study reports that e-cigarettes have efficacy similar to nicotine patches in achieving smoking abstinence among smokers who want to quit.<sup>38</sup> Former smokers who used e-cigarettes to quit smoking reported fewer withdrawal symptoms than those who used nicotine skin patches.<sup>39</sup> In addition, former smokers were more likely to endorse e-cigarettes than nicotine patches as a tobacco cigarette cessation aid. Significant reduction

in tobacco smoke exposure has been demonstrated in dual users of tobacco and electronic cigarettes;<sup>40,41</sup> however, both of these nicotine delivery systems sustain nicotine addiction.

Despite many ongoing studies to determine if e-cigarettes are useful as a smoking cessation aid, the results vary widely and are inconclusive at this time.<sup>42</sup>

### **E-cigarettes do not increase long-term tobacco abstinence**

Contrary to popular belief, research shows that e-cigarette use among smokers is not associated with long-term tobacco abstinence.<sup>1</sup> E-cigarette users, however, may make more attempts to quit smoking compared with smokers not using them.<sup>43</sup> In addition, even though there is some evidence that e-cigarettes help smokers reduce the number of cigarettes smoked per day, simply reducing the daily number of cigarettes does not equate with safety.<sup>44</sup> Smoking just one to 4 cigarettes per day poses 3 times the risk of myocardial infarction and lung cancer compared with not smoking.<sup>44</sup> And since many individuals continue to use traditional *and* electronic cigarettes, they end up in double jeopardy of toxicity through exposure to the dangers of both.

### **A gateway to other substances of abuse?**

There is also fear that nicotine exposure via e-cigarettes, especially in young people, serves as a “gateway” to tobacco consumption and other substance abuses, and increases the risk for nicotine addiction.<sup>34</sup> Such nicotine-induced effects are a result of changes in brain chemistry, and have been documented in humans and animals.<sup>34</sup>

These concerns about negative health consequences, combined with the fact that e-cigarettes are undocumented as a smoking cessation aid, add urgency to the need for legislative and regulatory actions that hopefully can curb *all* nicotine exposures, particularly for our nation's youth. In the meantime, it is important for physicians to advise patients—and the public—about the risks of e-cigarettes and the importance of quitting all forms of nicotine inhalation because nicotine—regardless of how it is delivered—is still an addictive drug.

**JFP**

## CORRESPONDENCE

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