Electronic Cigarettes: Exposure and Use Among Pediatric Populations

Joseph M. Collaco, MD, PhD, and Sharon A. McGrath-Morrow, MD, MBA

Abstract

As an emerging inhalational exposure, electronic cigarettes (e-cigarettes) have rapidly gained public awareness with increasing use among adolescents and adults, leading to increased primary use by adolescents and increased secondhand exposure to emissions in infants, children, and adolescents. Although the long-term health risks for primary use and secondhand emission exposure are unknown, limited data from animal studies suggest that there is the potential for long-term lung injury and altered neurocognitive development in children with exposure to nicotine-containing aerosols. In this pediatric-focused review, we discuss the history of e-cigarettes, the demographics of adolescent users, effects on health, and current legislative efforts to protect infants, children, and adolescents from exposure.

Keywords: adolescent, children, e-cigarette, electronic cigarette, exposure, infants, pediatric, secondhand

Electronic Cigarettes: Background and History

ELECTRONIC CIGARETTES (E-CIGARETTES) are designed to deliver vaporized nicotine (or non-nicotine)-containing solutions for absorption via the respiratory tract, when activated by the user manually or through inspiration. First-generation e-cigarettes were introduced in China in 2004, Europe in 2006, and the United States in 2007.⁽¹⁾ Although the main components of e-cigarettes include a cartridge (or tank) containing a solution that may contain nicotine, a heating element that vaporizes the solution, and an electric power source for the heating element, variations in these e-cigarette components can lead to differing experiences and exposures for the user.^(2,3)

The original first-generation e-cigarettes are disposable and were designed to mimic the appearance of conventional cigarettes unlike later e-cigarettes.⁽⁴⁾ Later, first-generation and second-generation devices incorporate refillable cartridges or tanks and rechargeable lithium batteries. Third-generation e-cigarettes (mechanical mods) include more features such as customizable electronics and variable voltage.⁽³⁾ The next-generation e-cigarettes may include variable heating elements, temperature control, and reduced resistance (sub-ohm) atomizers.

In addition to the variability in performance properties seen between commercial e-cigarettes of the same brand,⁽⁵⁾ customization of e-cigarettes using these features may lead

to alterations in particle size, aerosolization, chemical degradation with heat, and aerosol volume delivered.⁽⁶⁾ Differences in puff topography, which can vary significantly between naive and experienced users, can also influence systemic absorption of vapor constituents.^(7,8)

E-cigarette solutions (E-liquid) generally contain a carrier agent(s), typically propylene glycol, vegetable glycerin, or a combination of the two. A higher percentage of propylene glycol may provide more intense flavor and a stronger “throat hit” or sensation, whereas a higher percentage of vegetable glycerin may enhance vapor production.⁽⁹⁾ Solutions containing different concentrations of nicotine (0%–5.4%) are commercially available, but there may be significant variation in nicotine content (as much as 12%) within the same batch of the same brand of e-cigarettes,⁽¹⁰⁾ and some e-cigarettes marketed as 0% nicotine may actually contain nicotine.⁽¹¹⁾ Finally, e-cigarette solutions may also contain added flavorings based on traditional tobacco blends, fruits, candy, cocktails, and menthol, some of which may be very appealing to adolescents.⁽¹²⁾

Thus, owing to the variability in the characteristics of the devices themselves, variation in solutions within and between brands, and the user topography, it has been difficult to study the effects of e-cigarettes on primary adolescent users, children of users, and infants who may have had *in utero* exposure.^(6,13) In this review, we aim to describe the potential health effects within pediatric populations from

this emerging exposure. We would also emphasize that both the technologies used to deliver nicotine and research into health effects of these delivery systems are rapidly progressing, and we expect additional data to confirm the harmful effects on exposed children and young adults.

Primary User Demographics Among U.S. Youth

E-cigarette use exceeded conventional cigarette use among youth in the United States for the first time in 2014, reflecting a shift toward nonconventional cigarette tobacco products.⁽¹⁴⁾ Although current e-cigarette use (within the past 30 days) increased from 1.5% of high school students to 11.3% between 2011 and 2016, the percentage of high school students reporting current use in 2016 was actually a decrease in reported use for the first time (11.3% in 2016 vs. 16.0% in 2015).⁽¹⁴⁾ E-cigarette use among adolescents and young adults has been associated with increased intentions to smoke and a future risk of smoking.^(15–17)

Even though adolescents who have ever used e-cigarettes are less likely to be smokers than adults who have ever used e-cigarettes,⁽¹⁸⁾ almost half (47.2%) of the 20.2% of high school students who reported current use of any tobacco product also reported use of two or more tobacco products, suggesting that dual use may not be uncommon.⁽¹⁴⁾ In addition to conventional cigarettes, adolescent users of e-cigarettes may be more likely to use other substances, including marijuana, blunts, hookahs, and/or alcohol, but these associations may not always be consistent in different populations.^(19,20)

Focus groups have described reasons for experimentation with e-cigarettes, including curiosity, appealing flavors, and peer influences.⁽²¹⁾ Another study reported that reasons for using e-cigarettes among middle and high school students may include their low cost, the ability to use them anywhere with limited risk of detection, and smoking cessation.⁽²²⁾ The ease of use may translate into common locations for adolescent use of e-cigarettes, including everywhere (38%), school bathrooms (26%), home (21%), school staircases (11%), and school cafeterias (4%), based on focus group data from male high school students from the U.S. Southwest.⁽²³⁾

Youth may also engage in e-cigarette use behaviors that may put them at higher risk for potential health consequences from e-cigarette use. “Dripping” is a technique through which e-liquid is dripped onto an atomizer directly resulting in a high-temperature vapor that is inhaled immediately, which may lead to higher concentrations of toxic chemicals (e.g., aldehydes).^(24,25) One survey of high school ever e-cigarette users found that 26.1% had engaged in dripping.⁽²⁵⁾ E-cigarettes can also be modified or used to vaporize cannabis (hash oil, wax infused with tetrahydrocannabinol (THC), or dried cannabis leaves),⁽²⁶⁾ and in another survey, 27.9% of high school e-cigarette users reported vaporizing cannabis.⁽²⁷⁾ Youth who use e-cigarettes may also be at risk of “unintentional” nicotine exposure. In one study of middle and high school students who reported e-cigarette use within the past 30 days, 28.5% reported using e-liquid that did not contain nicotine and 37.4% reported using e-liquid with nicotine, but 34.1% were unaware of the nicotine concentration of their e-liquid.⁽²⁸⁾

It is less clear whether youth engage in other known e-cigarette use behaviors that lead to greater exposure. For

example, naive and experienced users may have different systemic exposures due to different patterns of inhalation and exhalation.⁽⁷⁾ One study found that naive users of e-cigarettes, even those who smoke conventional cigarettes, had lower plasma nicotine levels than experienced users owing to shorter puff duration.⁽⁸⁾ The topography of adolescent e-cigarette users, and thus risk profile based on use, is unknown. Also, while there are larger commercially available devices known as “tanks,” which operate with higher voltages resulting in vapors containing carcinogens (e.g., formaldehyde) in similar levels to conventional tobacco smoke,⁽²⁹⁾ which e-cigarette device youth tend to preferentially use are also not known. However, a majority of current adolescent e-cigarettes users (68.4%) report using flavored e-cigarettes.⁽³⁰⁾

Health Risks of Primary Exposure to E-Cigarette

There are a few published studies regarding the short-term health effects of e-cigarette use for adolescents and young adults. Chronic bronchitic symptoms (chronic cough, phlegm, or bronchitis) are reported to be twice as common among adolescent e-cigarette users compared with never users.⁽³¹⁾ In addition, e-cigarette use among adolescents may be associated with an increased prevalence of physician-diagnosed asthma and school absences secondary to asthma symptoms, even after adjusting for conventional cigarette use.⁽³²⁾ Daily e-cigarette use among middle and high school students has also been associated with self-reported oral symptoms, including cracked/broken teeth and tongue/cheek pain.⁽³³⁾

Data on the long-term health effects of e-cigarettes for adolescent and young adult users are very limited owing to the limited time frame these devices have been on the market. Potential long-term effects may include cancers, nicotine dependence, and chronic lung conditions. Neoplastic risk may be associated with any of the components of e-cigarettes (i.e., nicotine, carrier agents, or flavorings). Nicotine exposure is not necessarily associated with tumor development, but it has been shown to promote tumor growth and metastasis.⁽³⁴⁾ Thus, it is possible that long-term use of e-cigarettes could increase the risk of malignancy in users with an underlying predisposition for tumor development or those who also smoke conventional cigarettes.

Known and potential carcinogens such as formaldehyde, acetaldehyde, and acrolein can be produced when carrier agents such as propylene glycol or vegetable glycerin are heated,⁽³⁵⁾ and production of these compounds may be increased with the higher temperatures associated with “dripping” or variable heating devices. Other toxins and/or carcinogens have been identified through chromatographic and spectroscopic analysis; an analysis of 12 brands of e-cigarettes detected carbonyls, volatile organic compounds, nitrosamines, and heavy metals, although in levels 9–450 times lower than those found in conventional cigarette smoke.⁽³⁵⁾ A recent study detected high but variable levels of nickel in e-cigarette solutions collected from the cartridges of several different commercial brands.⁽³⁶⁾

Nicotine dependence is also a long-term risk with the use of e-cigarettes containing nicotine. While a recent study found that certain subgroups of adolescent smokers were more likely to become nicotine dependent,⁽³⁷⁾ it is unknown

whether there exist subgroups of adolescents who are at higher risk of becoming nicotine dependent with e-cigarette use. With certain devices and experienced e-cigarette users, nicotine delivery via e-cigarettes can exceed that of combustible cigarettes.⁽³⁸⁾

With respect to the development of permanent respiratory conditions, data from human airway cells and mice suggest that the development of features of chronic obstructive pulmonary disease (COPD) (cytokine profiles, airway hyper-reactivity, and lung architecture destruction) with exposure to e-cigarettes is possible.⁽³⁹⁾ Chronic exposure to nicotine-containing e-cigarettes in mice has been associated with decreased mucociliary clearance,⁽⁴⁰⁾ compared to carrier agent alone, which could predispose to recurrent infections or chronic bronchitis.

Although some e-liquid manufacturers advertise their products as made from USP (U.S. Pharmacopeial Convention) or food grade ingredients, this is based on oral consumption and the inhalational properties of the chemical compounds have not necessarily been assessed. A recent study of flavored e-cigarettes detected diacetyl in 39 of the 51 e-cigarettes tested; of note the flavoring chemical diacetyl has been associated with bronchiolitis obliterans (“popcorn lung”) in employees of microwave popcorn manufacturers.⁽⁴¹⁾ A number of candy and fruit e-cigarette flavors that are appealing to youth have been shown to have cytotoxic and/or mutagenic effects in cell culture.⁽⁶⁾

With regard to youth perception of the risks of e-cigarette use, data from the 2014 National Youth Tobacco Survey of U.S. middle and high school students indicate that many youth view e-cigarettes as less harmful (73.0%) and less addictive (47.1%) than conventional cigarettes.⁽⁴²⁾ In this same survey, use of tobacco products by youth was associated with decreased harm perception and addictiveness.

Health Risks of Secondhand and Thirdhand Exposure to E-Cigarettes

Secondhand exposure to e-cigarette emissions may be common. One survey of parents in the U.S. Midwest reported that e-cigarette use was reported in 12.3% of households, frequently in use with conventional cigarettes as well.⁽⁴³⁾ There are limited data on the health effects for children exposed to secondhand e-cigarette emissions. In contrast to exposure to secondhand smoke from conventional cigarettes, e-cigarettes do not generate combustion by-products, and side-stream emissions are minimal.⁽⁴⁴⁾ In general, several studies have shown that indoor air nicotine levels and particle concentrations during e-cigarette use are higher than background levels, but lower than levels generated by conventional cigarette smoking.^(44–46)

However, serum levels of the nicotine metabolite have been reported to be similar after secondhand exposures to e-cigarettes and conventional cigarettes in nonusing adults.⁽⁴⁷⁾ In addition, saliva and urine cotinine levels are similar among nonusing adults living with smokers versus those living with e-cigarette users.⁽⁴⁸⁾ Secondhand exposure to non-nicotine-containing e-cigarettes may still have risks as at least one study has measured increased particulate levels with use of e-cigarettes without nicotine versus those with nicotine.⁽⁴⁵⁾ Overall, the evidence indicates a measurable exposure in the environment and biomarker data confirming

nicotine absorption in nonusers, but the long-term effects of exposure for children are unknown. Nevertheless, data from neonatal mice suggest that both alveolar lung and overall growth are impaired with exposure to e-cigarette emissions,⁽⁴⁹⁾ and exposure during early life may lead to persistent behavioral changes in adult mice.⁽⁵⁰⁾

Thirdhand exposure from conventional cigarettes and/or e-cigarettes is defined as the residual emission products that deposit on surfaces, and may be involuntarily inhaled, ingested, or dermally absorbed.⁽⁵¹⁾ For example, the effects of thirdhand smoke have been detected in neonatal intensive care unit (NICU) settings when mothers who smoke visit their infants who have never been home (and thus never exposed to secondhand smoke) through infant urine cotinine and surface nicotine levels.⁽⁵²⁾ Children who live with smokers also have detectable levels of nicotine on their hands.⁽⁵³⁾ With regard to e-cigarettes, nicotine can be detected on surfaces after e-cigarette use, thus constituting a potential thirdhand exposure.⁽⁵⁴⁾

Health Risks of Maternal E-Cigarette Use on the Fetus

Limited data suggest that e-cigarette use among pregnant women is associated with attempts with smoking cessation and their use among pregnant smokers may be more common than FDA-approved smoking cessation therapies.⁽⁵⁵⁾ Although there are no data regarding the health effects of maternal e-cigarette use on human fetuses, data from animal studies may provide some correlates for nicotine exposure *in utero*. *In utero* nicotine exposure in animal studies can lead to permanent lung architectural abnormalities of not only airways and alveoli^(56–58) but also of lung vasculature.⁽⁵⁹⁾ A number of animal studies have demonstrated that *in utero* nicotine exposure may lead to small effects on cognitive performance of offspring.⁽⁶⁰⁾ While the health effects of *in utero* exposure to e-cigarettes are unknown, the rapid brain, lung, and other organ development that occurs during gestation leaves these organs vulnerable to environmental pressures.

Health Risks of Exposure to E-Cigarette Solutions and Batteries

Exposure to e-cigarettes, usually unintentionally, can pose health risks, particularly as childproof caps or locks are not in universal use in the United States to prevent children accessing e-liquid.⁽⁴³⁾ A recent analysis of calls to poison centers in the United States and its territories documented 5807 phone calls between September 2010 and December 2014 with 88% involving the e-cigarette device and 12% involving e-liquid.^(61,62) Adverse health effects were commonly reported (57.8% of calls where severity information was recorded).

Commonly reported effects included vomiting, nausea, and eye irritation, but at least two fatalities were associated with e-cigarette calls, including one ingestion in a child aged 0–5 years. Most pediatric exposures to e-cigarettes reported to poison centers affect children 0–5 years old (88.1% of exposures in individuals ≤20 years old). Common routes of reported exposures included ingestion (68.9%), inhalation (16.8%), ocular (8.5%), and dermal (5.9%). Suicides via oral and intravenous self-administration of e-liquid in adults have also been reported.^(62–64) Finally, the lithium batteries used in many e-cigarette devices can ignite or explode, either while

recharging or spontaneously, resulting in burns.^(65,66) One review of the literature indicates that nearly half of these reported burns require surgical intervention.⁽⁶⁵⁾ One recent case report documented a cervical fracture associated with an explosion with the device in use.⁽⁶⁷⁾

Healthcare Providers and E-Cigarettes

Knowledge concerning e-cigarettes among healthcare providers who provide care to pregnant women, children, and adolescents may be limited. With respect to prenatal counseling, a 2012 survey of the American College of Obstetricians and Gynecologists reported that only 5% of members felt fully informed about e-cigarettes, and of the surveyed members, 13.5% believed that they had no health effects at all.⁽⁶⁸⁾ With regard to parental use, only 15.3% of households where e-cigarettes were used in the home reported that their pediatrician was aware of use in one U.S. survey.⁽⁴³⁾

A 2013 survey in Minnesota reported that 92% of healthcare providers treating adolescents were aware of e-cigarettes, but most providers (83.1%) reported knowing little to nothing about e-cigarettes.⁽⁶⁹⁾ In addition, many providers (65.5%) believed that e-cigarettes were safer than conventional cigarettes. A 2014 online survey of primary care providers of adolescents in the United States reported that many physicians (41%) would inform their patients that e-cigarettes are less harmful than conventional cigarettes, and some (24%) would recommend them for smoking cessation.⁽⁷⁰⁾ However, in a series of focus groups in another study, none of the participating pediatricians would recommend them for smoking cessation.⁽⁷¹⁾ In general, few physicians (14%) have been reported to routinely screen for e-cigarette use among adolescents, but almost all (91%) support governmental regulation that prevents minors from purchasing e-cigarettes.⁽⁷⁰⁾

E-Cigarette Use for Smoking Cessation

Systematic reviews and meta-analyses have not provided strong evidence that the use of e-cigarettes aids in smoking cessation over more typical cessation therapies,^(72,73) or that e-cigarettes are associated with lower quit rates among smokers.⁽⁷⁴⁾ A 2014 survey of U.S. middle and high school students reported that e-cigarette use was not associated with a desire to quit using conventional cigarettes nor with recent quit attempts.⁽⁷⁵⁾ An online study of Korean students aged 13–18 years reported that e-cigarette use was associated with an attempt to quit conventional cigarettes, but that the use of e-cigarettes may have actually inhibited smoking cessation.⁽⁷⁶⁾ At the current time, there are no published studies on the effectiveness of e-cigarettes as a means for cessation of conventional cigarette use in adolescents.

E-Cigarette Policy Statements

A July 2014 position statement from the Forum of International Respiratory Societies, which includes the American College of Chest Physicians, the American Thoracic Society, and the European Respiratory Society among others, called for restrictions or bans on electronic nicotine delivery devices as a precaution pending the availability of additional safety data.⁽⁷⁷⁾ The 2015 American Academy of Pediatrics public policy statement recommended regulation of e-cigarettes,

including prohibition of promotion and sales to youth, and comprehensive bans in public spaces of tobacco-related products that produce emissions.⁽⁷⁸⁾ A 2014 policy statement from the American Heart Association supported regulation of e-cigarettes also including prohibiting sales and marketing to minors with taxes high enough to discourage youth use.⁽⁷⁹⁾

E-Cigarette Legislation

The World Health Organization's Framework Convention on Tobacco Control, a treaty signed and ratified by most nations (although notably not the United States), released a report on e-cigarettes during its seventh session in 2016.⁽⁸⁰⁾ Recommendations from the Framework Convention on Tobacco Control are considered to be legally binding for signatories. This report recommended that signatory parties ban the sale of e-cigarettes to minors and also recommended prohibiting the use of e-cigarettes in indoor spaces to protect bystanders from secondhand emissions.

With regard to access for minors, regulation of e-cigarettes varies widely by country as in some countries sales are completely banned (e.g., Brazil), in other countries sales of only nicotine-containing e-cigarettes are banned (e.g., Canada), in others sales to minors are prohibited (e.g., European Union and the United States), and in still others sales are unregulated, thus minors can purchase them (e.g., the Philippines). Currently, indoor bans are largely enacted by local and state jurisdictions, but there are some nationwide bans (e.g., Belgium and Spain).⁽⁸¹⁾

Conclusions

As an emerging inhalational exposure, e-cigarettes have rapidly gained public awareness with increasing use among adolescents and adults. Although the long-term health risks for primary use and secondhand emission exposure are unknown, limited data from animal studies suggest that there is the potential for long-term lung injury and altered neurocognitive development in children with exposure to nicotine-containing aerosols. Further research is needed to determine the scope of health effects associated with primary and secondhand e-cigarette exposure. Finally, public policy organizations and legislators have taken steps to restrict access of sales to youth younger than 18, and smaller steps to limit children's exposure to secondhand emissions in public areas. Likewise, pediatricians and other child healthcare providers should screen for use and exposure to e-cigarettes and be prepared to counsel on reducing or eliminating this exposure.

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Reviewed by:
Jonathan Klein

Address correspondence to:
Joseph M. Collaco, MD, PhD
Eudowood Division of Pediatric Respiratory Sciences
Johns Hopkins Medical Institutions
David M. Rubenstein Building
200 North Wolfe Street
Baltimore, MD 21287
E-mail: mcollac1@jhmi.edu