# *Electronic Nicotine Delivery Systems (E-cigarettes): Considerations for the Pediatric Otolaryngologist*

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**Introduction**

First introduced into the US market in 2007, electronic cigarettes are battery-operated devices that deliver nicotine-containing vapors to the lungs via inhalation. These battery-operated devices vaporize nicotine and the varying carrier solvents that are then inhaled for use. Inhalation of this liquid is also known as 'vaping'. Several variations of these devices exist, including e-cigarettes, electronic hookah, personal vaporizers, and cloud-chasing vaporizers. Collectively these devices are therefore referred to as electronic nicotine delivery systems (ENDS). They resemble traditional tobacco containing cigarettes in both their appearance and their method of nicotine delivery. The appeal lies in the delivery of high concentrations of nicotine without risk of the fumes associated with combustion of tobacco. At the same time, use of electronic cigarettes satisfies the oral urge associated with the act of smoking. A typical e-cigarette is composed of three parts: 1) a rechargeable battery 2) a cartridge containing a nicotine solution and 3) an "atomizing device" which aerosolizes the solution

These products are marketed as a safer alternative to traditional tobacco use and an adjunct for smoking cessation. Controversy regarding electronic cigarettes, particularly in the young population, is rising as use of this product increases [1]. Proponents advocate use of ENDS as a tool for smoking cessation, citing their lower toxicity when compared to combustible tobacco. Others share concerns regarding the lack of health care data, influence on the pediatric population, concern for use of both traditional cigarettes and electronic cigarettes together, and lack of current regulation.

**Health effects and risks**

Electronic cigarettes do not require combustion, nor do they contain many of the carcinogens found in traditional cigarettes; therefore both active use and secondhand exposure are expected to be less toxic. However, given the recent introduction of these products into the market, long-term health effects are unknown and investigations are ongoing.

E cigarette liquid is aerosolized to produce a vapor, which is then inhaled. The liquid most commonly contains nicotine, propylene glycol, glycerin, water and frequently flavorings. Multiple studies have demonstrated that content of this liquid is variable [2-4] . The nicotine content within these devices and contents of the resultant vapor varies between brands and even within the brands themselves. Product labeling has also been an issue. Some studies have demonstrated inconsistencies between the nicotine content described on labels and actual content; in fact, some products marketed as nicotine-free have even been shown to contain

nicotine, and some of these in significant concentrations [4]. Inhalation of electronic cigarettes introduces another factor to consider, as aerosolization and nicotine delivery are inconsistent during use.

Both content of the vapor and particle size within the vapor are being researched. How these affect the air within the environment is unclear. Some studies demonstrate both fine and ultrafine particulate matter within electronic cigarette vapor resulting in variable lung inhalation with active and passive exposure. Content of particulate matter emissions from e-cigs is also being studied. Pellegrino *et al* demonstrated that while particulate matter emissions from e-cigs did exceed guidelines from the World Health Organization slightly, emissions were 15 times lower than after use of conventional cigarettes [5]. Tobacco-specific nitrosamines (TSNA) are known carcinogens found in traditional tobacco. These have also been detected within vapor of most e-cigs at varying concentrations, though levels have been demonstrated to be 9-450 times lower than in traditional cigarette smoke [4]. Similarly carbonyls, other potential carcinogens, have been detected in vapors of electronic cigarettes at concentrations ranging from 'below the limit of detection' to levels comparable to standard cigarette smoke [4].

Propylene glycol and glycerol vapor are major components within the cartridges of electronic cigarettes and are known upper airway irritants. Little is known about the long-term health implications of repeated inhalation of these chemicals [2, 4, 5, 6].

Flavorings are another additive commonly found in electronic cigarettes, many of which are derived from flavorings used in food. The Flavor and Extract Manufacturers Association regulates safety of chemicals used in food flavorings, however these safety regulations are for ingestion. Hence, they cannot be applied to the inhalation of such chemicals. Aerosolized flavorings specifically contain diacetyl, a chemical that has the potential for adverse respiratory implications [7]. Early studies have specifically identified cinnamon flavoring as having cytotoxic potential [8]. This introduces yet another unknown variable in the health and safety of these products, in which more research and studies are needed.

Nicotine itself is highly addictive with known deleterious effects including adverse cognitive behavioral outcomes in children and negative stresses imposed on the cardiovascular systems [9]. Medicinal nicotine has been demonstrated to be safe when administered in non-toxic levels [10]. However, as levels of nicotine in electronic cigarettes are not yet regulated, the safety profile is unknown. Toxicity from nicotine can result from ingestion, inhalation, or absorption through skin and mucous membranes[11-13]. Acute toxicities related to nicotine are a real concern given the high nicotine content within the cartridges of electronic cigarettes.

Inadvertent exposures to the liquid nicotine contained in the cartridges of ENDS have become an increasing problem. From January 2012 to April 2015, the rate of pediatric exposure to e-cigarettes has increased from 14 monthly exposures to 223 monthly exposures. Electronic cigarettes accounted for 14.2% of all tobacco and nicotine product related exposures during this time period. What's more, children who were exposed to electronic cigarettes had a 2.6 times higher odds of having a severe outcome when compared to traditional cigarettes [34].

Accidental pediatric fatalities have been reported [35]. Charming liquid flavors and bright packaging of these products contribute to the appeal of these products to young children. Most commonly, adverse effects related to toxicity include nausea, vomiting and eye irritation. However, more serious outcomes have been documented in the literature. Tragically, two children to date have died from unintentional liquid nicotine poisoning: the first in Israel in May of 2013, and more recently a one year old died in December 2014 in the United States [13]. Burns and explosions have been documented in the literature in case reports with use of ENDS [36,37]. These injuries are attributed to the lithium ion batteries used for the devices. ENDS have also been associated with successful suicide both via intravenous delivery and ingestion [38,39].

A systematic review published by Pisinger comprehensively reviews existing literature on health consequences of "vaping" associated with electronic cigarettes, in turn demonstrating the deficiencies in present research [4]. In the absence of a standardized product without sufficient regulation, no hard conclusions can be drawn regarding the safety profile of these products. In a Cochrane review regarding the efficacy of electronic cigarettes in assisting with smoking cessation, a meta-analysis of the data confirmed the lack of data in this newly emerging field [14]. Only two randomized controlled trials were included within the analysis. They concluded smokers who used electronic cigarettes containing nicotine were more likely to stop smoking than smokers using placebo electronic cigarettes and more likely to reduce cigarette consumption than nicotine patches and placebo electronic cigarettes. But this was a low-grade conclusion due to the limited data thus far.

**ENDS in the adolescent population**

Adolescence is known to be a high-risk time for beginning of use of tobacco products [15]. In fact, eighty percent of active adult smokers began to smoke before the age of 18 [16]. According to the Center for Disease Control's (CDC) most recent data as of December 2015, 4.7 million middle and high school students are estimated to use tobacco products [17]. Of these teenagers, ENDS are the most commonly used tobacco products with the lowest perceived health risk [18]. Use of ENDS in this pediatric patient population has dramatically increased: from 2011to 2015, use of ENDS has increased from 1.5% to 16% in high school students and 0.6% to 5.3% in middle school students [17-18]. Data from a 2014 prospective, cohort study in Southern California reveals that there has been a dramatic decrease in adolescent tobacco use over the last few decades; however, the combined prevalence of use of ENDS and traditional cigarettes is comparable to adolescent smoking rates in 2001. This data suggests that use of ENDS in this population may be occurring in those who may not otherwise use tobacco products [19]. Similarly, a 2013 survey of high school students demonstrated that ENDS users had less social and behavioral risk factors than those with traditional tobacco use: raising the concern that ENDS may be attracting youths who may otherwise not use tobacco products [20]. In November of 2015, JAMA Pediatrics found that e-cigarettes use was associated with progression to traditional tobacco smoking among teenagers [21].

Dutra demonstrated that use of e-cigarettes was associated with higher odds of ever smoking or current smoking in those presently using electronic cigarettes. What's more, use of electronic cigarettes was associated with lower rates of abstinence from smoking at 30 day, 6 month and 1 year intervals. This data suggests that in the young adult population, use of electronic cigarettes may actually increase risk of traditional cigarette use, rather than discourage it [22].

With this in mind, an obvious concern arises. Will electronic cigarettes serve as a gateway to tobacco use and abuse?

**Marketing and sales**

ENDS have reached an estimated $2.5 billion dollars in sales as of 2015. Advertising expenditure has vastly increased from $6.4 million in 2011 to $115 million in 2014 [23]. Analysis of data from the 2014 National Youth Tobacco Survey demonstrates that 68.9% of middle and high school students were exposed to ENDS advertisements from at least one source, which equates to greater than 18 million students [23]

Decades ago we demonstrated that tobacco advertisements were associated with increased tobacco use in youth, and as a result we successfully campaigned to ban advertisements for cigarettes [27]. Marketing for electronic cigarettes, on the other hand, is broad and through various platforms. Advertisements are filled with themes of independence and glamour, de-stigmatizing smoking and associated tobacco related products. Marketing via television, radio and billboards utilize endorsements from celebrities and have even been featured during the Super Bowl. Television e-cigarette commercials reach an estimated population of 24 million youth, with a dramatic increase in exposure to TV ads between the years 2011 and 2013 [28]. The Internet offers an additional route for advertising and exposure, particularly in the age of social media [28,29]. "Tweets" on twitter related to ENDS have increased over the last few years, and marketing companies are using these tweets to promote ENDS use while frequently including direct links to online sales [24]. YouTube is a video sharing website which reaches billions of viewers: the majority of videos related to electronic cigarettes depict these devices as healthy and cool alternatives to smoking tobacco [24]. These tactics have long been banned in tobacco products.

Liquid contained within cartridges for electronic cigarettes are available in various "delicious" flavors. These range from more traditional flavors such as menthol or tobacco, to more youthful flavors such as "My Birthday Cake" or "Tutti Fruti Gumballs" [30]. Certain dispensing companies even provide customized blends. As of January 2014, there were 466 different brands of electronic cigarettes with 7764 unique flavors [31], and this number only continues to rise. Eighty one percent of youth have cited appealing flavors as their primary reason for using e-cigarettes [26]. On the contrary, flavoring for traditional cigarettes has been banned since 2009 due to obvious appeal to the youth.

**E-cannibis**

More recently, ENDS have been modified for marijuana inhalation [32,33]. Vaporizing cannabis can be accomplished via concentrated tetrahydrocannabinol (THC) oils, waxes, finely ground dried cannabis buds or synthetic cannabinoids. Vaping of

cannabis is less conspicuous: it creates an odor that is less detectable than smoking cannabis in the traditional sense and is therefore more discrete. Contents of this vapor are obviously not under any regulation and are widely variable. A 2014 anonymous survey of Connecticut high school students demonstrated that 18% of ENDS users and 18.4% of conventional cannabis users also had used vaporized cannabis [33].

**Regulation of ENDS**

Despite being on the US market since 2007, ENDS have only recently fallen under federal regulation. This has been the center of a national and worldwide debate.

The American Academy of Pediatrics (AAP) has issued a policy statement calling for local, state and federal regulation regarding ENDS [40]. This includes recommendations for pediatric practitioners including:

- Screening for ENDS use
- Recommendations against use of ENDS as treatment for tobacco dependence in children
- Use of counseling and other FDA approved pharmacotherapy for treatment of tobacco dependence
- Avoidance of second-hand and third-hand aerosol exposure
- Education regarding signs and symptoms of acute nicotine poisoning
- Public policy recommendations by the AAP include:
- Reduction of youth access to ENDS by banning sale of these products to youth < 21 years of age
- Banning of internet sales,
- Banning of flavoring of these devices,
- Banning advertisements and restricting media exposure of ENDS
- Protecting youth from second and third-hand exposures, inadvertent exposures and poisonings
- Taxation on these devices
- Advocating for future research efforts

The AAP also advocates for increasing the minimum age for sale of tobacco products including ENDS to 21, referred to as the "Tobacco 21" laws [41]. They argue that this is needed since 80% of smokers began smoking prior to age 18 while adolescence is a period in which people are particularly susceptible to the addictive nature of nicotine [42]. Analysis of data from Needham, Massachusetts has demonstrated a 47% reduction in the smoking rate of high school students after "Tobacco 21" laws were adopted within the community [43]. Public opinion surveys have demonstrated that the majority of Americans, smokers and non-smokers alike, are in support of this proposed rule [44,45].

Similarly, the American College of Physicians (ACP) has issued a policy position paper on ENDS in 2015 [46]. Recommendations include:

- Federal regulation under the Food and Drug Administration (FDA)
- Banning flavoring of ENDS products
- Taxation of tobacco products to include ENDS
- Support for youth tobacco prevention effects
- Regulations of clean air laws related to ENDS
- Funding for future research

In May of 2016, the European Commission released key changes regarding sales of tobacco products within the European Union (EU). Specific to ENDS, nicotine content within these devices will be regulated and must be packaged in a child-resistant and spillage proof fashion. Health warnings and labels will be mandatory and ENDS data will require monitoring and reporting of devices-related hazards [47].

In April of 2014, the FDA initially proposed rules to regulate these products on a national level. Two years later, in May of 2016, the FDA has issued a "final rule" in which all tobacco products including ENDS will fall under federal regulation [48]. These regulations include oversight of all manufacturers of ENDS and "Vape Shops" which sell liquids, regulations over product packaging and imports and exports of vaping products, and perhaps most importantly, banning sale of these products to children under 18. Regulations regarding minimum age of sale came into effect August 8, 2016. Regulations regarding product packaging and standardization will come into effect May of 2018.

While national regulation is a certainly a landmark in the recent debate, many argue the need for more. The 2016 FDA regulations do not include rules regarding flavoring of ENDS nor do they include regulations over childproof packaging. The FDA notes in their final rule that they acknowledge controversies regarding these topics, and plan for staggered legislation over the upcoming years.

**Considerations for Pediatric Otolaryngology**

In a survey by Mueller *et al*, pediatric otolaryngologists were found to have low levels of knowledge of pediatric secondhand smoke exposure and low levels of utilization of counseling guidelines [49]. The rise of electronic cigarettes only introduces more uncertainty to the pediatric otolaryngology practice. In fact, a cross sectional analysis of the 2011-2012 National Youth Tobacco Survey demonstrates an increased risk of electronic cigarette use by children who live with someone who smokes, even in those children who have never smoked traditional cigarettes [50]. Additionally, several surveys have documented public youth as viewing electronic cigarettes as a safe alternative to traditional tobacco, without proper understanding of the potential risks associated with use [51, 52]. This is an excellent opportunity for otolaryngologists to improve patient care and outcomes. Counseling adolescents and their families regarding this product represents an opportunity for our specialty to improve health and safety as well as fulfilling our requirements to document quality and safety within our practices (PQRS). Regulation of electronic cigarettes and resultant second hand vapor exposure needs to be on our advocacy agenda in caring for our patients.

**Conclusions**

Despite an abundance of literature related to adverse implications of secondhand smoke in pediatric patients, otolaryngologists have room for improvement in counseling patients and parents against secondhand smoke. Concerns regarding electronic cigarettes lie in the potential for electronic cigarettes to lead to tobacco use in adolescents, lack of quality control, and possible unknown ill health effects of vapor exposure. Federal regulation of electronic cigarettes is necessary to help standardize the product, improve research deficiencies, and oversee use in the vul-

nerable pediatric population. In doing so, we can maximize the potential for electronic cigarettes to aid in tobacco cessation, while minimizing adverse outcomes.

**Conflict of interest statement**

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