E-cigarettes and Vaping: A Global Risk for Adolescents

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While the marketing and sale of electronic cigarettes (e-cigarettes) in India is forbidden since September, 2019, vaping represents a significant risk to the health and safety of Indian adolescents. Though the prevalence of youth e-cigarette use in India remains unknown, pediatricians are often brought to provide care to youth who vape. In this commentary, background information on e-cigarettes including a review of the different types of vaping devices and of the substances contained in e-cigarette liquids is provided. The short- and long-term health risks associated with vaping, including risks for the developing brain, acute lung injuries and long-term mental health effects, and a practical approach for clinical management of e-cigarette use for Indian pediatricians is presented. Public health measures to prevent and reduce youth vaping and a review of current Indian laws and policies around e-cigarette use are also mentioned.

Keywords: *ENDS, Nicotine, Smoking, Substance use.*

In the span of less than a decade, electronic cigarettes, also called electronic nicotine delivery systems (ENDS), or e-cigarettes, have completely changed the landscape of nicotine product use among adolescents and young adults [1]. Initially introduced as a harm reduction and smoking cessation strategy for adult cigarette smokers, e-cigarettes and other vaping devices have rapidly become popular among youth around the world. Aggressive youth-directed marketing from e-cigarette companies, easy and widespread access to vaping products, low cost, low perceptions of risk, youth-friendly flavors and designs, as well as highly effective nicotine delivery leading to intense psychoactive effects are a few reasons for their popularity [2].

While there is a wide variety of e-cigarettes and vaping products, most of them share a common mechanism. A reservoir or cartridge filled with an e-cigarette liquid (or e-liquid) connected to a battery-powered heating metal coil, produces a mix of vapor and fine particles (aerosol), which is then inhaled through a mouthpiece [3]. Most e-liquids contain nicotine, often in high concentrations and flavoring agents. The solvents used for nicotine or flavored products are water based like propylene glycol. E-liquids may also be oil-based and contain substances like tetrahydrocannabinol (THC), the main psychoactive component found in cannabis [4]. They also contain small amounts of chemicals and heavy metals such as acrolein, acetaldehyde, nickel and lead, which can be toxic or carcinogenic **Table I** [2,5].

The use of e-cigarettes among youth is increasing in most parts of the world [6]. In the US, the prevalence of past-month e-cigarette use increased from 0.6% in 2011 to 10.5% in 2019 among middle school students (ages 11-14) and from 1.5% to 27.5% among high school students (ages 14-18) [7]. In Great Britain, lifetime e-cigarette use increased from 7% in 2016 to 11% in 2017 among 11-16 year-olds [8]. Estimates of lifetime e-cigarette use across Asia include 4.4% among 15-17 year-old adolescents in Taiwan [9], and 9.3% among secondary school students in Hong Kong [10].

E-CIGARETTE AND VAPING PRODUCTS

E-cigarettes come in many different shapes and sizes. Earlier models often resembled traditional cigarettes and had a limited appeal for youth [11]. The first surge in popularity among teens occurred between 2013-2015 with the proliferation of pen-like and larger, complex devices made available in a wide range of youth-friendly flavours [12]. A second rapid increase in popularity was between 2017-2019 with the arrival of small, pod-based devices using pre-filled cartridges [13]. **Fig. 1** presents a schematic representation of various e-cigarette devices [14].

The amount of nicotine contained in most e-liquids varies between 15 and 50 mg/mL. E-cigarettes exposes adolescents to nicotine toxicity and potential nicotine overdose [15] as they can absorb high amounts of nicotine in a short time period [16,17]. For example, a typical 2mL e-cigarette pod at 5% concentration would contain 100 mg of nicotine which could be consumed in as

Table I Substances Found in E-cigarette Liquids and Aerosols

Substances identified	*Carcinogens*
Nicotine	*Class 1 Potent carcinogens*
Humectants/solvents (e.g. propylene glycol and glycerol)	Formaldehyde
Flavorings	Benzene4-(methylnitroso-amino)-1-(3-pyridyl)-1-
Carbonyl compounds (including aldehydes)	Butanone
Tobacco alkaloids	Cadmium
Tobacco-specific nitrosamines (TSNAs)	*Class 2a Probable carcinogens*
Free radicals and reactive oxygen species (ROS)	Acetaldehyde
Volatile organic compounds (VOCs) and phenolic compounds	1,2-Propanediol
Residual solvents	Isoprene
Polycyclic aromatic hydrocarbons (PAHs)	Benzo(a)pyrene
Phthalates	Benzo(b)fluoranthene
Metals	Benzo(k)fluoranthene
Caffeine	Indenol(1,2,3-cd) pyrene
Pharmaceutical compounds	Chromium
+Microorganisms	Lead
Substances present in combustible cigarettes but typically not identified in e-cigarette aerosols	*Class 2b Possible carcinogens* Acrolein
Carbon monoxide	Toluene M,p-xylene
Tar	Phenol
	Benzo(e)pyrene
	Benzo(g,h,i) perylene
	Chrysene
	Nickel (more in e cig.)

Adapted from reference 11.

little as one hour with uninterrupted use [17,18]. The lethal dose of nicotine has been said to be between 30 and 60 mg for adults, but may be much higher [19].

HEALTH RISKS

E-cigarettes are associated with several acute and long-term health risks. **Supp. Table I** summarizes the properties and physiological effects of the different constituents found in e-cigarette liquids [11].

Use of nicotine during adolescence is associated with altered brain development and long-term impairments in memory, attention capacity and executive functioning [20-23]. Consuming large amounts of nicotine through vaping can lead to nicotine toxicity, which presents with headaches, abdominal pain, nausea, vomiting, heart palpitations, hand tremors, difficulty concentrating, and in some cases, seizures and cardiac arrhythmia. Nicotine is also a long-term risk factor for poor cardiovascular health [24-26].

Regular nicotine use through vaping can also lead to withdrawal symptoms if adolescents try to quit or are temporarily unable to access vaping products. Withdrawal symptoms can appear after as little as a few weeks of use and can interfere with normal daily functioning [27-29].

Acute injuries like facial and limb burns due to malfunction of vaping devices have also been described [30]. Additionally, vaping aerosols include carcinogenic and irritating substances that may lead to chronic respiratory symptoms such as cough, bronchitis, asthma exacerbation and decreased exercise tolerance [31,32].

More than 2,800 cases of severe e-cigarette or vaping-associated lung injury (EVALI) were reported in Canada and the US in 2019 and early 2020, of which approximately 15% cases were reported in youth under the age of 18 years [33]. EVALI consists of a sterile inflammatory pneumonitis that presents with cough, chest pain, and shortness of breath, which can be severe and lead to hospitalization and even death [33]. While no cases have been reported in India, and much remains unknown about this condition, it is suspected that vitamin E acetate (found in several cannabis-containing e-liquids) may lead to such presentations [33].

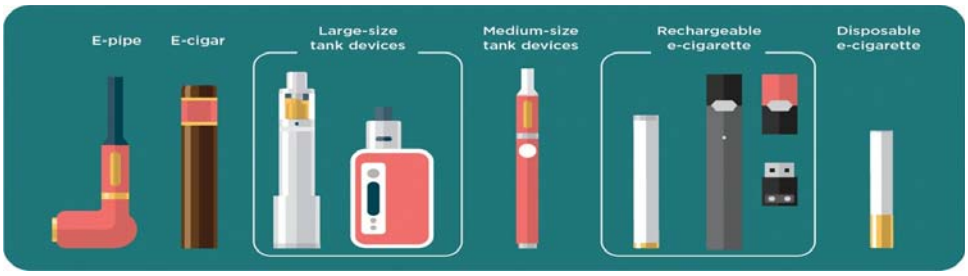

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Fig. 1 E-cigarettes and other vaping devices.

CLINICAL MANAGEMENT OF E-CIGARETTE USE

Screening and Brief Intervention

Pediatricians should ask adolescent patients if they have tried vaping, if they currently vape, and discuss vaping-associated health risks with all adolescents. The discussion should include commercial brand names for more clarity and details should be asked about products and substances used, motives, context, frequency, intensity and motivations to quit if applicable [34,35]. Using standardized scales for nicotine dependence (such as the Hooked on Nicotine Checklist) or diagnostic criteria for cannabis use disorder according to the Diagnostic and Statistical Manual of Mental Disorders (DSM–5) can also be useful to understand the severity of the vaping habit and addiction to nicotine and/or cannabis.

A 5-step Algorithm–The 5 A's

Ask, Advise, Assess, Assist, and Arrange–initially developed for smoking cessation, can also be a helpful framework for an effective vaping counseling intervention [35,36]. After asking about vaping, pediatricians should advise all adolescents not to initiate or to quit vaping and discuss one or two of the health risks associated with vaping (e.g. EVALI). Pediatricians can then assess the young person's motivation to quit or cut down, for instance, by using a 10-point scale (i.e. "on a scale from 1 to 10, how motivated are you to quit/cut down on vaping?"). Based on the response, the pediatrician can then offer to assist the adolescent with vaping cessation. Finally, pediatricians should arrange a follow-up plan, involving families and/or other health care providers when applicable.

Vaping Cessation

As there are no evidence-based pharmaceutical treatments tested specifically for adolescents with vaping addiction, the first line of treatment for vaping cessation relies on behavioral strategies. Strategies that have proven effective for tobacco dependence should be considered including individual or group counseling, motivational inter-viewing, cognitive-behavioral therapy, contingency management, mindfulness-based inter-ventions, as well as smartphone and web-based strategies [34,35].

Considering that most vaping liquids contain nicotine, often in high amounts, nicotine replacement therapy such as patches, gums and lozenge can be used safely with adolescents in addition to behavioral strategies [34]. The use of anti-craving medications such as bupropion and varenicline can also be considered alone or in addition to nicotine replacement [34].

E-cigarettes for Smoking Cessation: Adults vs Adolescents

A recent Cochrane review suggests that among adults, e-cigarettes used alone or in combination with other pharmaceuticals or behavioral methods may be of similar effectiveness for smoking cessation as approved nicotine replacement products [36]. People who oppose the recent ban on e-cigarettes in India, support that e-cigarettes are a valuable tool for Tobacco Harm Reduction (THR) as an aid for adult smokers hoping to quit smoking. A meta-analysis of 299 articles established that newer generations of e-cigarettes may serve as an efficient means of meeting the nicotine demand of a person addicted to smoking, with significantly reduced health consequences compared to conventional cigarettes [37].

However, whether this adult data can be extrapolated to youth remains unknown [36]. The evidence for pharmacotherapy for youth e-cigarette cessation remains extremely limited. Adolescents, with a still-developing pre-frontal cortex, are more vulnerable to the addictive properties of nicotine, which may impact the level to which adult data can be extrapolated.

Although, e-cigarette use may cause youth to transit to combustible tobacco products, it could also increase adult cessation of combustible tobacco cigarettes. The net public health effect, harm or benefit, of e-cigarettes depends on three factors: *i*) Effect on youth initiation of

combustible tobacco products, *ii*) Effect on adult cessation of combustible tobacco products, and *iii*) Intrinsic toxicity. E-cigarette use by adult smokers needs to lead to long-term abstinence from combustible tobacco cigarettes to lead to considerable benefit to public health. Without that, e-cigarette use could cause considerable harm due to the inherent harms of exposure to e-cigarette toxicants and to the harms related to potential subsequent combustible tobacco use by those who begin using e-cigarettes in their youth [11].

Prevention and Public Health Measures

In January 2020, the Society for Adolescent and Medicine issued a new policy statement by a collaborative group of Adolescent Medicine Providers from India, Canada, the US and the UK with recommendations to prevent e-cigarette use and protect youth from the harms of e-cigarettes (**Box I**) [38].

Box I Suggestions from the Society of Adolescent Health and Medicine to Prevent e-Cigarette Use

- Advocate for policies and regulations to prevent marketing and sales of e-cigarettes products to youth.
- Support public health–led education campaigns and educational curricula for schools, community programs, and health providers warning about the health risks of e-cigarette use by adolescents and young adults (AYAs).
- Increase research to develop evidence-based guidelines for e-cigarette prevention and cessation for AYAs.
- Support training for health providers to integrate screening for e-cigarette use into routine health visits for AYAs and increase the availability of evidence-based counseling and treatment resources for e-cigarette use cessation.

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E-CIGARETTE USE IN INDIA

India has well-established tobacco cessation strategies, under the umbrella of the National Tobacco Control Programme (NTCP). The support for tobacco cessation is multipronged, ranging from brief advice to comprehensive counselling and support for nicotine-replacement therapy [39]. Tobacco consumption, mainly cigarette smoking, has declined by 1% between 2010 and 2017 in India, in response to several tobacco control measures [40]. There are recent surveys regarding tobacco consumption and e-cigarette sales and consumption in India [41]. A study on Indian Internet e-cigarette search query patterns concluded that searches for vaping products by Indians have been increasing over time [42].

Some of the most serious concerns have been expressed by school principals in Delhi regarding the increasing trend of youth vaping among young students [43]. The sale of vaping devices has spiraled upward since their introduction in the Indian market in 2007 to the point that many schools have become surrounded by vape shops [43]. In September 2019, India became one of the first countries to enact a complete ban on all e-cigarette products. This ban followed an intense period of discussion and debate weighing the advantages and potential disadvantages of such a ban [44], and the publication of a white paper from the Indian Council of Medical Research a few months prior [45].

CONCLUSION

Though the ban on e-cigarettes in India was mainly implemented to prevent e-cigarette use among youth, one must consider its potential negative effects among adults. There is still very limited data in India regarding use of e-cigarettes among adolescents, and even less so, regarding its effects on rates of youth use. Pediatricians can play a vital role in protecting youth against the known and potential risks of e-cigarette use. By staying informed on recent developments related to the health effects of e-cigarettes and offering effective screening and treatment interventions to youth who use them, Indian pediatricians can help mitigate the impacts of what has become a global risk for adolescents.

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Supplementary Table I Constituents Found in e-Cigarette Liquids and Aerosols and Their Physiological Effect on the Human Body

Constituent Properties	*Effects on Body*
Nicotine: A colorless, odorless liquid water-soluble alkaloid with an oily consistency, acquires a brown color and gives off a strong odor of tobacco when exposed to air.	• Short-acting stimulant with rewarding and addictive properties. • Triggers the release of epinephrine from the adrenal glands and sympathetic response (increase in heart rate, blood pressure, etc.) • Lethal dose in children and adolescents remains unknown.
HUMECTANTS/SOLVENTS *Propylene Glycol*: Clear, colorless, slightly syrupy liquid at room temperature. Practically odorless and tasteless, listed (GRAS) by the Food and Drug Administration (FDA).	• Allergic reactions, upper respiratory irritation, asthma. • Increased risk of toxicity in liver and kidney impairment and high-dose oral or intravenous administration. • No data for vapor inhalation & absorption.
Glycerol (Glycerine): Oily, hygroscopic liquid with a warm, sweet taste. Less irritant than PG Listed GRAS by FDA	Mild headache, dizziness, nausea, vomiting, thirst and diarrhea at unspecified dosages
Ethylene Glycol: An odorless, clear, slightly viscous liquid. Where present, it is at levels that are not likely to contribute significantly to adverse health effects.	• It is a respiratory irritant and is associated with markedly enhanced toxicological hazards when compared with conventionally used glycerol and PG
Flavorings: More than 7,000 unique e-liquid flavors available. Concentrations vary widely. Fruity e-cigarette are often preferred among both smokers and non-smokers. Diacetyl, acetylpropionyl (2,3-pentanedione), acetoin, Cinnamaldehyde are chemicals used. Often named as a primary reason for e-cigarette use.	• Flavors may have cooling and local anesthetic effects • Reasons for uses include increased satisfaction and enjoyment, variety and customization, better feel and taste than cigarettes, food craving suppression, social impacts. • Menthol reinforces effects of nicotine on tobacco smoking behaviors - results in increased nicotine dependence and a greater chance of tobacco-attributable disease. • Formation of aldehydes—vanillin and ethyl vanillin, thujone, menthol (pulegone, eucalyptol) which is associated with adverse respiratory health outcomes. Increased incidences of chronic cough, bronchitis, asthma, and bronchiolitis obliterans. • Even at low concentrations, cinnamaldehyde in e-cigarette products is cytotoxic, genotoxic, adversely affects cell

Constituent Properties	*Effects on Body*
	processes and survival. It may also impair homeostasis in the respiratory system.
Carbonyl compounds: Formaldehyde, Acetaldehyde, Acrolein, Glyoxal, Propanal, Crotonaldehyde, Butanal and Methylglyoxal which have been found in e-cigarette aerosols. Aerosols generated from PG-based e-liquids were found to have the highest levels of carbonyls. Compared to combustible cigarettes, very high levels of formaldehyde are found in aerosols from E-cig	• Lower liquid levels within the cartridges or tanks may increase air flow and promote overheating of the wire if no safety features are incorporated to maintain a constant and lower temperature. This leads to the formation of carbonyls, which are potentially hazardous and/or carcinogenic
Minor Tobacco Alkaloids: Impurities including minor alkaloids: Nornicotine, Anatabine, Anabasine, Cotinine, Nicotine *N*-Oxides, Myosmine, Nicotyrine and Nornicotyrine. These minor alkaloids may arise from biosynthetic processes in the living tobacco plant or by bacterial action or oxidation during tobacco processing and can thus be found in e-cigarette liquids derived from tobacco products	Nicotine-related impurities are thought to be less toxic than nicotine
Tobacco-specific nitrosamines: *N*'-nitrosoanatabine (NNN), NNK, *N*'-nitrosoanabasine (NAB). TSNAs are potent carcinogenic chemicals.	Carcinogenic potential
Free Radicals and Reactive Oxygen Species (Ros): Activating the e-cigarette's heating element and aerosolizing the e-liquid produces ROS; these species are drawn into the lungs directly from the device. Oxidants are also derived from a device's lithiumion battery, similar to that used in combustible tobacco cigarette filters and e-cigarette cartomizers	They cause oxidative stress, which damages cellular proliferation, metabolism, and health, and can be involved in the development of several cardiovascular, respiratory neurodegenerative disorders, rheumatoid arthritis, and some types of cancers.
Volatile Organic Compounds (Vocs) And Phenols: Benzene, Toluene, Ethylbenzene, *M*-Xylene, *P*-Xylene, *O*-Xylene, Styrene, Ethyl Acetate, Ethanol, Methanol, Pyridine, Acetylpyrazine, 2,3,5-Trimethylpyrazine and Octa- Methylcyclotetrasiloxane	• Irritant to upper and lower respiratory tract • Central nervous system and end-organ damage at high concentrations • Carcinogenic potential
Residual Solvents: The thermal degradation of sugars can produce toxic furans, such as 5-hydroxymethylfurfural and furfural	• Irritant to Upper Respiratory Tract
Polycyclic aromatic hydrocarbons (PAHs): Products of combustion which can form small particles or bind to other small particles	• Irritant to Upper Respiratory Tract • Carcinogenic potential

Constituent Properties	*Effects on Body*
Phthalates: Diethyl phthalate (DEP) and diethylhexyl phthalate (DEHP) IARC classifies DEHP as "possibly carcinogenic to humans".	• These antiandrogenic, estrogen-like compounds have been shown to lead to gynecomastia
Metals: Chromium, Nickel, Lead, Manganese, Aluminum, Tin, and Iron in e-liquid emissions originate from several parts of the device, including the metallic coil, a complex alloy that heats the e-liquid to produce the aerosol that is inhaled by the user. Lead, Nickel, Tin quantified at significantly higher concentrations in e-cigarette aerosols than combustible tobacco smoke	• Specific Metal related toxicities
Caffeine: E-liquid flavors like coffee, tea, chocolate, and energy drinks.	• Very little is known about the effects of caffeine inhalation, and health risks cannot be estimated.
Pharmaceutical drugs: Weight loss medication (Rimonabant) not approved by FDA (2007) has been found in e-liquids. E-liquids can contain an analogue (amino tadalafil) active ingredient found in Cialis, an erectile dysfunction drug	• Adverse neurological events such as seizures and suicide • Undetermined or harmful health effects
Microorganisms: Bacteria, fungi, parasites	• Presence of micro-organisms could lead to bacterial/fungal/parasitic infections

Adapted from: Eaton DL, Kwan LY, Stratton K, editors. Public Health Consequences of E-Cigarettes-Toxicology of E-Cigarette Constituents. National Academies Press (US). 2018; 5