Editorial

Electronic cigarettes: the new face of nicotine delivery and addiction

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Electronic or "e" cigarettes are increasing in popularity worldwide as nicotine delivery devices. Chinese pharmacist Hon Lik initially developed this drug delivery device in 2003 with the goal of creating a more effective smoking cessation tool. Electronic cigarettes use batteries to heat liquid containing nicotine, which is atomized to create an inhalable aerosol. The aerosol is a mixture of propylene glycol, vegetable glycerin, nicotine, flavorings, and other toxic and non-toxic chemicals in droplet and gaseous forms.

E-cigarette use (vaping) has rapidly increased globally in the past decade. Sales have exceeded $2 billion (US) per year and are more than doubling annually; they are predicted to exceed $10 billion in sales by 2017 (1). Currently, combustible cigarettes garner about $80 billion in sales but are projected to be overtaken by e-cigarettes by 2021. The largest tobacco companies, who vigorously lobby in the interests of their products, already own 48% of the e-cigarette market in the U.S. and are projected to own more than 80% within 10 years. E-cigarettes are being aggressively marketed to smoking and non-smoking men, women, and children as a healthier, safer alternative to conventional cigarettes. In fact, they are being marketed as safe for recreational use by the general population.

We would like to emphasize a number of points about e-cigarettes, recognizing that scientific data remain incomplete:

(I) The use of e-cigarettes as a means of facilitating smoking cessation via treatment of nicotine addiction and oral fixation is not established. The more promising initial studies were sponsored by the e-cigarette industry and had serious design flaws (2-6). More recent trials with appropriate study design and unbiased participants have shown no higher efficacy of e-cigarettes in smoking cessation compared to other nicotine replacement approaches. In a recent Lancet study, only 7.3% of e-cigarette users ceased smoking combustible cigarettes at 6 months compared to 5.8% using conventional nicotine patches, a difference that was not significant (7). Instead of using them for smoking cessation, a considerable number of people are using both e-cigarettes indoors as well as combustible cigarettes outdoors. Thus total nicotine intake may increase because of this dual use.

(II) The vast majority (99%) of e-cigarette liquids contain nicotine, and therefore, vaping exposes the user to the toxic effects of nicotine. Apart from its well-known cardiovascular risks, nicotine activates carcinogenic pathways, including proliferation, angiogenesis, suppression of apoptosis, and promotion of cell motility (8). Nicotine impacts brain development, as early as in utero through adolescence, putting young populations at particular risk (8). Secondhand e-cigarette exposure leads to the same blood levels of nicotine as secondhand cigarette smoke inhalation, which confirms that switching from combustible cigarettes to e-cigarettes does not remove the adverse effects on bystanders, unlike other nicotine-replacement products (9,10).

(III) Addiction can be considered a form of learning,

and relapse as a persistent memory of the drug experience (11), which has both hereditary and experiential components (12). Converting short-term to long-term memory involves growth of new synaptic connections, which requires synthesis of messenger RNAs and protein in neurons (13). Two of the key actions of nicotine in regions of the brain associated with memory and addiction are histone acetylation and microRNA expression (14). Histones control gene expression by wrapping around DNA and preventing transcription. MicroRNAs bind gene targets and block translation. Both of these epigenetic mechanisms alter gene expression and can have life-long consequences. These mechanisms can explain why addicts can experience relapse years after abstinence. It has been demonstrated that smokers who have quit suffer the same degree of increased urge to smoke a conventional cigarette when they witness someone vaping an e-cigarette as they do when they witness conventional cigarette smoking (15).

(IV) The Centers for Disease Control and Prevention has recently reported that about 1 in 10 children and 1 in 5 teenagers in the United States have tried e-cigarettes (16). In a 2014 study of school-going children, as many as 1 in 4 high school students and 1 in 13 middle school students used a tobacco or nicotine-containing product within the 30 days prior to the questionnaire. This finding represents a 3-fold increase in use compared to only 1 year earlier, and numbers are likely higher in other countries (16). In many cases, these consumers are new users of nicotine products rather individuals trying to stop smoking. The increasing social acceptance of using e-cigarettes due to the positive portrayal in the social media and the ease of obtaining these devices by people of all ages are, in large part, responsible for the surging use of these products (17). For example, Williams and colleagues demonstrated that minors were able to order e-cigarettes successfully online and have the devices, e-liquids and flavors delivered 93.7% of the time (18).

(V) In recent years, there has been an increase in the number of calls to poison control centers and emergency room visits due to nicotine toxicity. Ingestion or skin contact of the flavored liquid nicotine refills by children and occasionally adults has resulted in tachycardia, hypertension, seizures, respiratory failure, and death (19). The lack of uniformity of the nicotine delivered in different products and differences in nicotine delivery between combustible cigarettes and e-cigarettes can lead to poisoning even in willing users taking in what they consider an appropriate amount. Moreover, electronic cigarettes are now being used as a delivery device for other drugs such as heroin, cocaine, and hashish. Dissolving psychotropic drugs in e-cigarette liquids has led to toxic effects and an increase in emergency department visits. Recipes for using illegal drugs in the e-liquids are widely available online (20).

(VI) The e-cigarette aerosol has been shown to contain high levels of formaldehyde and other carcinogens in some experimental settings (21). First and second generation e-cigarette devices used lower voltages (about 3.7 volts, leading to 3-9 watts, depending on the resistance), but the more recent devices can apply up to 8 volts (leading to 10-53 watts), which heats the e-liquid substantially more and may improve the efficiency of nicotine delivery, while also leading to the formation of more formaldehyde. Nitrosamines and other carcinogens like acetaldehyde, polycyclic aromatic hydrocarbons, and arsenic have been confirmed in e-cigarette liquids and aerosols in multiple studies (22,23). Many of these toxins are also found in combustible cigarette smoke, but e-cigarettes may have unique toxicities. Work from cell culture and animal models has demonstrated that e-cigarette vapor may increase bacterial virulence and impair host defenses (24). The possibility exists that e-cigarettes may contribute to pneumonia and other respiratory infections via mechanisms that are different from conventional tobacco.

(VII) China has the largest population of cigarette smokers in the world, making the issue of tobacco abuse particularly important in this country where e-cigarettes were invented. China produces 43% of the world's cigarettes and consumes 1/3 of them. Currently about 45% of men and 2% of women in China are smokers. Chinese women and children have some of the highest secondhand smoke exposures in the world. We applaud the people of China for banning indoor smoking and banning smoking of tobacco around schools

and hospitals in Beijing. E-cigarettes will likely become significantly more popular in Beijing, as a substitute for smoking indoors. A major concern is the lack of information about the health effects of electronic cigarettes, which highlights the need for further research. Unfortunately, epidemiological studies may take decades to define long-term safety and population effects. If electronic cigarette use is allowed to continue to grow, the world may find that the tobacco epidemic of the last century is being repeated. Therefore, we believe that cell culture and animal models, in addition to large scale human clinical and epidemiologic studies, will be required to guide clinical decision making and public policy for the present.

In summary, this editorial is written to caution against the use of e-cigarettes as an alternative to conventional tobacco. Nicotine is highly addictive and may predispose to inflammatory, infectious, and neoplastic diseases. Worse yet, youth are the most vulnerable population and these devices are falling into the hands of children who are more susceptible to its toxicity and addiction.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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