More Questions Than Answers Surrounding E-Cigarette Debate

By Nancy Nelson

We need to find out if we’re playing with fire,” said Peter G. Shields, MD, professor of medicine at Ohio State University, at the American Association of Cancer Research’s annual prevention meeting in October. He was referring to the increasing use of e-cigarettes among middle and high school students, encouraged by a market with none of the restrictions currently in place for the access of minors to regular cigarettes. (See http://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM336940.pdf.)

One danger, as public health officials see it, is that e-cigarette use could lead to more nicotine addiction and thus become a gateway to using cigarettes, cigars, and smokeless tobacco. Since about 90% of smokers pick up the habit as teenagers, the rising use among teens is particularly worrisome. According to the Centers for Disease Control and Prevention, e-cigarette use among high school students rose from 4.7% to 10.0% from 2011 to 2012.

An e-cigarette is a nicotine inhaler designed to imitate smoking regular cigarettes. Inside the “cigarette,” a thin plastic or metal tube, is a small battery and a solution of nicotine suspended in a mixture of glycerin or propylene glycol with water. Inhaling from the tube, known as vaping, heats up the solution, creating the nicotine vapor. Although flavor additives may be present, such as vanilla, cherry, or peach, most of the toxic combustion products in tobacco smoke are absent in e-cigarette vapor.

But does that mean they’re safe? It depends on whom you ask. According to several studies, e-cigarettes appear safer than regular cigarettes. In 2009, the US Food and Drug Administration tested two brands of e-cigarettes, including 18 cartridges of various flavors, with and without nicotine. Nicotine was found in some samples labeled nicotine-free, and a range of nicotine was detected in cartridges labeled as having the same amount, suggesting imperfect quality control in their manufacture. Also, tobacco-specific nitrosamines, known human carcinogens, were found in half the samples, and tobacco-specific impurities suspected of being harmful to humans—anabasine, myosmine, and β-nicotyrine—were found in most samples. One sample had diethylene glycol.

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In a similar study, Maciej Goniewicz, PhD, of the Roswell Park Cancer Institute in Buffalo, NY, and colleagues analyzed vapors from 12 brands of e-cigarettes for the presence of carcinogens found in tobacco smoke, focusing on four groups: carbonyl compounds, volatile organic compounds, tobacco-specific nitrosamines, and metals. These groups included toxins such as formaldehyde, benzene, nitrosamines, benzopyrene, carbon monoxide, and cadmium (Tob. Control 2013;0:1–7). Although some toxins were present in e-cigarette vapor, the levels were 9–450 times lower than in regular cigarette smoke. So formaldehyde and acrolein were 9 and 15 times, respectively, more concentrated in regular cigarette smoke than in e-cigarette vapor, whereas the concentration of acetaldehyde was 450 times greater.

Weighing these data along with about 50 additional studies on the chemistry of aerosols and liquids of electronic cigarettes, Igor Burstyn, PhD, from the school of public health at Drexel University in Philadelphia, published a comprehensive technical report in July 2013: Peering through the Mist: What Does the Chemistry of Contaminants in Electronic Cigarettes Tell Us about Health Risks? Using the standards for workplace safety, he found no evidence that vaping produces exposures to contaminants from the aerosol that would warrant health concerns.

Polycyclic aromatic hydrocarbons were not detected in most of the aerosols analyzed, and although the levels of tobacco-specific nitrosamines varied in liquid cartridges, the amounts were 1/1000 the concentration of tobacco-specific nitrosamines in smokeless tobacco products. Also, the volatile organic compounds detected in vapor were judged to be less than 1% of the threshold limit value (TLV) commonly used as workplace standards. The two exceptions were acrolein, measured to be about 1% of TLV, and formaldehyde, between 0 and 3% of TLV.

Most of the inorganic compounds were not detected, including arsenic, beryllium, chromium, cadmium, lead, and nickel. Mercury was detected, according to Burstyn, albeit at low enough levels not to be considered a health concern.

The initial report of diethylene glycol and ethylene glycol in the FDA sample, at a level of 1% of TLV, did not rise to a level of a health concern, and the finding has not been replicated. However, Burstyn did recommend monitoring the respiratory effects of long-term exposure to propylene glycol and glycerin by vaping, since these data do not exist. These compounds are not known to create health problems, he explained, but besides nicotine and water vapor, propylene glycol and glycerin are the main ingredients in e-cigarettes. The exposure to nicotine is no more than what occurs for regular cigarettes.

What about the fear that e-cigarettes will increase tobacco addiction? Will teens...
who try vaping then take up smoking regular cigarettes? A review by Dominic L. Palazzolo, PhD, at the department of physiology and pharmacology at Lincoln Memorial University in Harrogate, Tenn., in the November Frontiers in Public Health, finds little evidence to support this fear. For example, one national online survey of 228 males, aged 11–19 years, showed that although 67% were aware of e-cigarettes, less than 1% had tried them, and smokers were more likely to try them (Pepper et al., J. Adolesc. Health, 2013). Another Web-based survey of 4,444 college students (average age, 21 years) reported that e-cigarette use was more common among smokers (Sutfin et al., Drug Alcohol Depend., 2013). Of the 20,240 students polled in Polish high schools and universities, only 3.2% of those who tried e-cigarettes were non-smokers (Gioniewicz et al., Pediatr J., 2012). Palazzolo found in general that young smokers are more likely to experiment with e-cigarettes than are nonsmokers.

Evidence is emerging that many current smokers use e-cigarettes as nicotine replacement therapy to help them reduce use or quit, whereas others use them as a less harmful alternative to smoking. A survey of e-cigarette users, which included 5,939 current and former smokers from four countries, showed that use of e-cigarettes was highest among both nondaily and heavy smokers. A total of 79.8% used e-cigarettes because they were less harmful, 75.4% said they used them to help reduce smoking, and 85.1% said they used them to help quit (Adkison et al., Am. J. Prev. Med., 2013). Likewise, another cohort of 1,347 e-cigarette users from mostly European countries used them primarily for smoking cessation, but for a longer period than nicotine replacement therapy. Seventy-four percent did not smoke for at least a few weeks while using e-cigarettes, and 70% reported a reduced urge to smoke. Average time used was 10 months. They considered them safe to use and found improvements in coughing and breathing and levels of craving (Dawkins et al., Addiction, 2013).

A few clinical trials using e-cigarettes as a quit tool with smokers have been completed. A study in New Zealand compared the quit rates of smokers using e-cigarettes with and without nicotine to a nicotine patch. After 6 months, 7.3% of smokers using e-cigarettes with nicotine had quit, compared with 5.8% using patches and 4.1% using e-cigarettes without nicotine. The authors concluded that use of e-cigarettes and patches had statistically equivalent quit rates (Bullen et al., The Lancet, 2013). In an Italian trial with 40 smokers again using e-cigarettes as a quit tool, researchers found at the end of 2 years, 32% of the smokers had reduced their smoking by 50%, 12.5% reduced their smoking by 80%, and 22% had quit (Polosa et al., BMC Public Health 2011). Another Italian trial evaluated 300 smokers for reducing and stopping smoking with the help of e-cigarettes. For 1 year, 100 smokers received e-cigarettes at two different strengths of nicotine, and a third group received no-nicotine cartridges. At 12 weeks, smoking had decreased in 22.7% of smokers and 10.7% had quit. At 1 year, 10.3% of smokers had reduced their smoking and 8.7% had quit. No consistent difference was apparent among the three groups (Caponnetto, PLoS One, 2013).

So do e-cigarettes pose a danger? At this point, we have more questions than answers. Some argue that the availability of another method of becoming addicted to nicotine is dangerous. Certainly the 24 states that have restricted sales of e-cigarettes to minors and the 10 others that have introduced legislation to do likewise think so. Scott Leischow, PhD, at the Mayo Clinic in Scottsdale, AZ, who has been working in tobacco control for more than 20 years, predicts and hopes that FDA will restrict marketing and sale of e-cigarettes to minors. While it is not clear at this point whether the use of e-cigarettes will lead to more or less tobacco addiction in either adults or minors, the possibility that e-cigarettes may actually help some of the 40 million smokers in this country quit excites many in the field. “Hooray!” said Shields, “We need more and better alternatives for people struggling to quit.” A product that may prevent any of the 440,000 deaths in the U.S. every year related to tobacco use would be welcome. About 70% of the 40 million smokers in the U.S. want to stop smoking.

Even though the contaminants in e-cigarettes may not pose serious health effects, unanswered questions remain. Both Goniewicz and Burystyn point to the need to find out whether long-term health risks are associated with exposure to e-cigarette vapors, particularly propylene glycol and glycerin. And a more basic need, according to Burystyn, is to standardize the laboratory procedures to evaluate these products; to develop protocols for extracting compounds from aerosols and liquids, to identify core compounds that need to be quantified; and to create a standard vaping machine.

Clinical trials currently under way are addressing many of these questions. Some are looking at long-term health risks, others at the effectiveness of e-cigarettes as a quitting device in several different populations (http://clinicaltrials.gov). A large government-sponsored, 3-year observational trial—the PATH (Population Assessment of Tobacco and Health) study involving 59,000 people, smokers and nonsmokers, aged 12 years and older—is looking at how and why people start using tobacco, how they quit, and why some people who quit start using tobacco again. As these data become available, the role that e-cigarettes play in starting, stopping, or restarting smoking will, it is hoped, become clearer.