

# A Burning Question

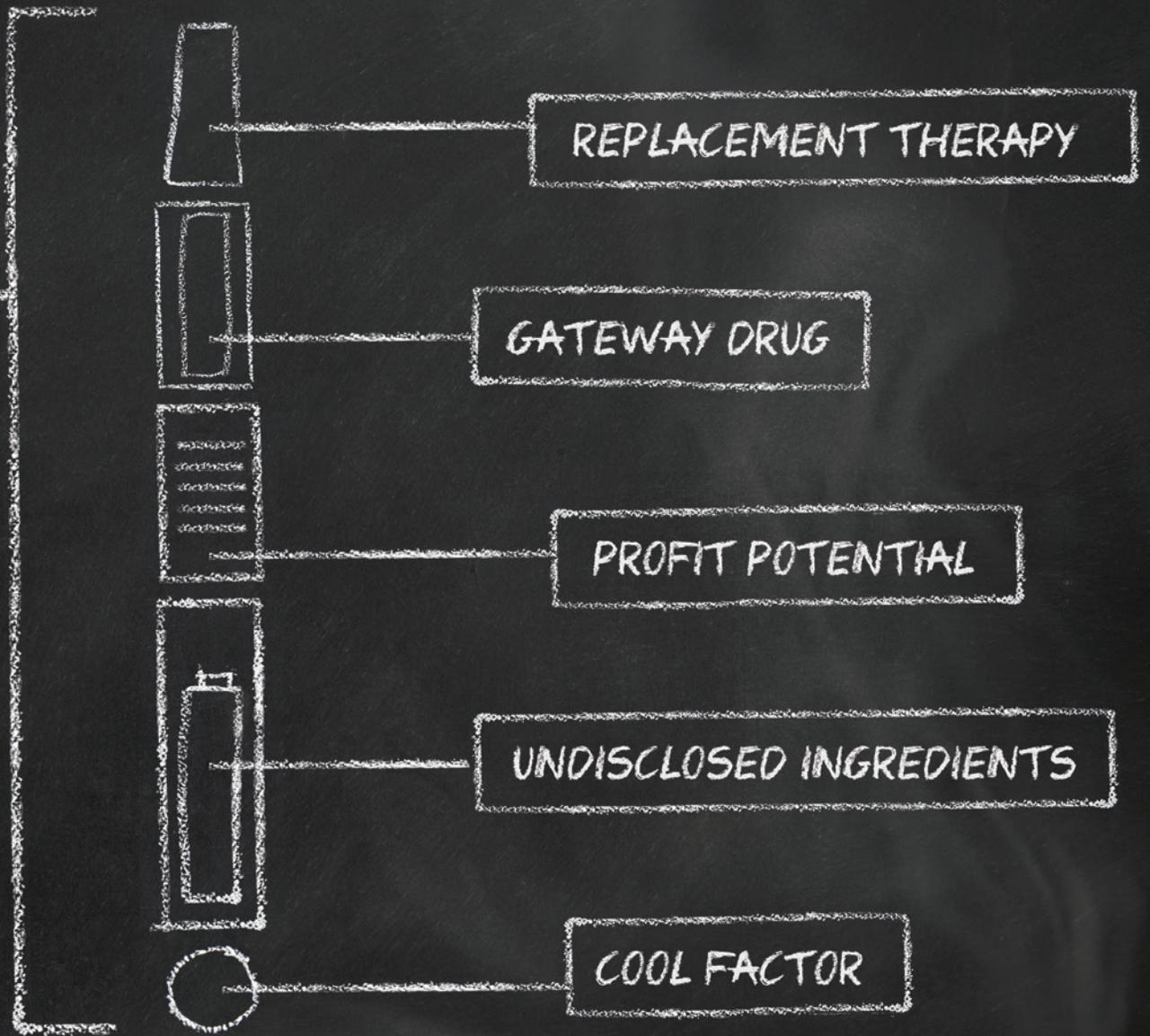
The Debate  
Over E-Cigarettes

by Joe Miksch

In 2010, 43 percent of cigarette smokers quit for a day or more. More than 60 percent relapsed.

The biochemistry of nicotine addiction is, of course, at the heart of the matter. And then there's the pull of the habit, the ritual: slide a smoke from the pack, ignite it, tuck it between the lips, inhale. E-cigarettes—unlike the patch, nicotine gum, or prescription pills—furnish a proxy for the experience of lighting up, without the same level of harmful chemicals and tar found in conventional smokes.





For many, it's the verisimilitude of these battery-powered liquid nicotine vaporizers and their alluring flavors that fuel concern. Will "vaping" reel in young people? Should e-cigarettes be banned due to the risk of abuse or embraced as a less harmful alternative to cigarettes? And how harmful is that nicotine, anyway?

This spring, the Food and Drug Administration announced plans to regulate e-cigarettes. The proposed rules would limit purchases to those 18 and older and mandate warning labels. The public comment period on the proposal ended August 8. Soon after, the debate intensified: The World Health Organization, American Heart Association, American Lung Association, and American Cancer Society each released statements declaring their concerns about the hazards of e-cigarettes. Then a Centers for Disease Control and Prevention report confirmed that a growing number of non-smoking teens have tried vaping and that the experience predisposes them to experimentation with conventional smokes. Smoking cessation researchers, however, continued to champion a nuanced approach to regulation.

## HARM REDUCTION

In January, anticipating the FDA proposal, faculty members Amy L. Fairchild, MPH '90, PhD '97; Ronald Bayer, PhD; and James Colgrove, MPH '01, PhD '04, published an essay in the *New*

*England Journal of Medicine* advocating that regulators use a light hand. "Given the magnitude of tobacco-related deaths—some 6 million globally every year and 400,000 in the United States, disproportionately among people at the lower end of the socioeconomic spectrum," they write, "an unwillingness to consider e-cigarette use until all risks or uncertainties are eliminated strays dangerously close to dogmatism."

E-cigarettes hold great promise for smokers. Vaping offers the possibility of a less toxic, tar-free nicotine buzz and—for those intent on weaning themselves from the habit—a tool for stepping down. E-cigs also clearly pose risks—from undisclosed ingredients to the hazard of recruiting new users—especially for kids.

## THE ROAD TO ADDICTION

Professor of Sociomedical Sciences Denise B. Kandel, PhD '60, has devoted four decades to studying the use of nicotine and other drugs among adolescents. In September, the *New England Journal of Medicine* published her analysis—with her husband and research collaborator, Nobel laureate Eric Kandel, MD, a University Professor and the Kavli Professor of Brain Science at Columbia—of the molecular basis for nicotine as a gateway drug and its implications for the debates over legalized marijuana and e-cigarettes. "While e-cigarettes eliminate some of the health

# BUTTING OUT



**WHEN IT COMES TO CONVENTIONAL CIGARETTES, THERE'S NOT MUCH TO DEBATE.** Finding anyone who'd advocate smoking would be tough, probably impossible—even among smokers.

As giant retailers go, however, no entity has gone as far as CVS Health, the nation's largest pharmacy chain, to discourage it. In September, CVS stopped selling all tobacco products in its 7,000 retail stores. The company's chief medical officer is Troyen Brennan, MD, JD, MPH, a member of the Mailman School Board of Overseers.

CVS, he says, is becoming less a convenience store with a pharmacy attached than a healthcare provider. Then why ban tobacco sales yet allow space on the store's

shelves for sugary drinks and fatty foods?

"Tobacco is unalterably bad; the calories in junk food or soft drinks, in and of themselves, aren't bad," Brennan says. "You can drink a coke and it's not necessarily going to have any ill effects on you. You can't say that about smoking a cigarette, as regards yourself or those around you. In many ways, tobacco is a category of one."

As for those pharmacies that have not or will not follow CVS's lead, Brennan says, "Others talk that talk [of being a healthcare provider], but over time I think it will become corrosive if they don't walk the walk. Some may still feel that they're a retailer, but we are committed to being a healthcare provider."

effects associated with combustible tobacco,” she says, “they are still nicotine-delivery devices.”

Denise Kandel originated the “gateway hypothesis”—the idea that use of illicit drugs like cocaine or heroin is preceded by exposure to such substances as alcohol, tobacco, and marijuana—in a 1975 *Science* paper. Three decades later, she issued a call to action in *JAMA*. “A developmental sequence of involvement in drugs is one of the best-replicated findings in the epidemiology of drug use,” she wrote. Scientists, she urged, must turn their attention to the biological underpinnings of the gateway hypothesis, bringing light to the heated policy debates in which it has featured for decades.

The scientist has since embraced her own charge. Working with Eric Kandel and Columbia psychiatrist Amir Levine, MD, she developed animal models to explore the behavioral, electrophysiological, and molecular genetic effects of particular drug-use sequences. Using these specially engineered mice, the team was able to delve into the mechanisms by which nicotine, in particular, fuels addiction. In a series of experiments, the researchers demonstrated that mice exposed first to nicotine exhibited a heightened response to cocaine. Exposure first to cocaine had no effect on nicotine response.

In 2011, *Science Translational Medicine* published the team’s report, which also details the molecular mechanism underlying the data: nicotine has an irreversible effect on the FosB gene, known to promote addiction. The Kandel team had demonstrated how nicotine primes the cocaine-addiction pump. “In addition to the flavoring and other factors that make e-cigarettes more attractive to youth, people don’t take into account that nicotine affects brain biology,” she says. “E-nicotine use will increase the risk of addictive behavior.”

## HARD EVIDENCE

Based on their own research, the Kandels would have the FDA take a much harder line than the agency does in its 2014 rules and make e-cigarettes available, by prescription only, exclusively to smokers weaning themselves from the habit. Fairchild, a professor of Sociomedical Sciences who has detailed her position in op-eds for *The New York Times* and *The Huffington Post*, favors more permissive regulation.

“There is evidence suggesting that [e-cigarettes] are at least as good as other nicotine-replacement therapies, if not better,” says Fairchild, who advocates an approach on a par with the over-the-counter availability of smoking-cessation products—such as patches or gums—that decouples nicotine exposure from the behavioral elements of addiction. “There’s this assumption that [vaping] is going to lead people to tobacco cigarettes or sustain people who smoke tobacco cigarettes as something they do in lieu

of smoking in public. I tend to think not. Even among smokers who have no intention of quitting, using e-cigarettes causes their tobacco smoking to go down.”

Yet the possibility that e-cigarettes might swell the ranks of conventional smokers bears further investigation, says Bayer, a professor of Sociomedical Sciences and co-director of the Mailman School’s Center for the History and Ethics of Public Health. While the market has ballooned to \$2.5 billion annually (among 466 brands) and new vaping shops are popping up throughout major metropolitan markets, the product only entered the public consciousness about a decade ago; its medium- and long-term effects are unknown.

Bayer, who has also analyzed the effect of warning labels for conventional tobacco products and investigated the extent to which science informs regulations banning cigarette smoking in public venues, advocates more thorough studies. To exceed the FDA’s proposal and aggressively constrain access to the product without that hard evidence, he says, would be to deny the public a tool to limit tobacco-related deaths among smokers.

“No one thinks [e-cigarettes] shouldn’t be regulated,” says Bayer. “The question is whether these regulations are going to be used as a pretext for banning e-cigarettes or whether they’re going to serve their two stated goals: trying to prevent toxins from being included in the liquid nicotine and not making them available to children.”

Stopping short of prohibition still leaves plenty for regulators to sink their teeth into. At the moment, pretty much anyone can whip up a batch of e-cig “juice” in the bathtub, ensuring that consumers are none the wiser about exactly what’s in there, including contaminants and carcinogens. Anyone can buy them; in many states, there’s no age-related regulation at all. And some of the flavors—cotton candy, bubblegum, and gummy bear—seem tailored to beguile youthful consumers. The same goes for the ads, which make “vaping” look pretty cool.

“E-cigarettes are used by two very different populations,” says Denise Kandel. “The issues are very different, depending on the population you focus on—chronic smokers who want to stop smoking or young people, who are using the product at a time when their brains are very vulnerable.”

Considering the undeniably pernicious effects of tobacco use, says Fairchild, the public interest might best be served if vaping remains broadly available to current smokers—even if all the information is not yet in. “The harm-reduction potential of e-cigarettes is going to be debated for decades, but conventional cigarettes are already out there in the open,” she says. “Tobacco is probably the greatest man-made killer of all time, and that’s the harm we’re talking about reducing.”

---

JOE MIKSCH writes about science and medicine in Pittsburgh.