

MAYO CLINIC
PROCEEDINGSE-Cigarettes: An Asset or Liability in Efforts to
Lessen Tobacco Smoking and Its Consequences

Every physician should agree that tobacco control and a reduction of smoking-related deaths is a desirable outcome. Holford et al¹ have recently reported the dramatic reductions in premature deaths and the years of life already saved by successful tobacco control. However, much remains to be done. No single US Food and Drug Administration–approved cessation aid works for more than a small fraction of smokers. Despite the availability of varenicline, bupropion, and various nicotine replacement therapy products, getting current smokers to quit remains a challenge.

In this month's issue of *Mayo Clinic Proceedings*, 2 articles focus on yet another method of nicotine replacement therapy: electronic cigarettes, also known as e-cigarettes or electronic nicotine delivery systems (ENDS). In their Concise Review, Ebbert et al² present a somewhat negative view of ENDS, perhaps flavored by their exhaustive work in the field of smoking cessation and the immense challenges associated with getting patients to end tobacco and nicotine addiction. Kadimpati et al,³ in a report on their pilot study, discuss attitudes of current smokers about to undergo elective surgery and report that those who have never tried ENDS have a higher interest in their perioperative use (as a method of diminishing dependence on smoking) than those who have previously tried ENDS.

There are several issues at the core of these articles. For example, the study by Kadimpati et al³ addresses the fact that a formal preoperative evaluation with surgical patients tends to cause those patients to focus on their health. Coaching patients about their health in this setting exploits "surgery as a teachable moment" in patient education. As Warner, a coauthor of the Kadimpati et al report, has previously proposed, when physicians take optimal advantage

of this period, there is a potential for reducing the incidence of postoperative medical and surgical complications as a result of preoperative smoking cessation.⁴ Shi and Warner⁵ have also clarified that the once-feared risks of increasing pulmonary symptomatology when smoking cessation is commenced immediately before surgery is a flawed concept based on a misinterpretation of the literature. As such, from the perspective of Kadimpati et al,³ Warner,⁴ and Shi and Warner,⁵ all efforts to have patients cease smoking, or transfer to a smokeless form of nicotine replacement, should be pursued before surgery, even immediately before surgery. This concept has been supported by others.⁶⁻⁸

With respect to using surgery as a "teachable moment," the patients studied by Kadimpati et al³ are clearly not like my own. Specifically, my own patients are very anxious before surgery; so anxious, in fact, that they often forget almost everything I tell them, including many more imminently important matters than advice about smoking. This perception on my part is consistent with that reported in the indexed literature, in which patients more commonly than not forget physician instructions about medical conditions, medications, and the reasons for taking those medications.⁹ Perhaps these differences in experience relate to the fact that Mayo Clinic, where Kadimpati et al practice, has a unique surgical practice, and I suspect that their patients are seen by anesthesiologists even closer to the time of surgery than my own patients are. In most US medical environments, the time from a perioperative visit with the anesthesiologist to the time of surgery is 2 weeks or less. I question whether this is sufficient lead time to substantially impact smoking-related complications, even if smokers "buy in" to the idea of using ENDS.



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As Kadimpati et al³ eloquently elaborate, there are many deleterious effects of smoking before elective surgery, including cardiac, respiratory, and wound complications. A vaporized nicotine product could conceivably reduce some of these problems. Many plastic and reconstructive surgeons have long refused to perform cosmetic procedures or operations involving the use of tissue flaps in patients who are smokers because of the relative tissue hypoxia caused by both the vasoconstrictive effects of nicotine and cigarette smoke—associated carbon monoxide.^{10,11} My plastic surgery colleagues specifically instruct patients that they must be abstinent from all forms of nicotine (including ENDS) before surgery. With respect to wound complications, further research is needed to determine to what extent these complications are due to carbon monoxide and what portion is due to nicotine-associated vasoconstriction. Interestingly, these aforementioned surgeons do not have the same aggressive stance against caffeine, which will similarly cause vasoconstriction. The duration of the vasoconstriction with respect to the withdrawal time of the stimulus also needs further examination. Nicotine itself has been shown to have notable effects on skin in in vitro studies.¹² The use of nicotine vapor might not be associated with a reduction in wound complications. Although such a product would not contain carbon monoxide and would therefore eliminate the effects of that substance on wound healing, clinically important nicotine-associated vasoconstriction might still be present. As Ebbert et al² note, the effect of ENDS on pulmonary function and their impact on respiratory complications is uncertain. One study, however, found improvement in peripheral vascular tone with nicotine replacement therapy in the form of nicotine gum and patches, as measured by an improvement in the augmentation index and stability of the pulse wave velocity.¹³

Several prospective, randomized trials have evaluated the positive effect of preoperative smoking cessation on reducing the incidence of postoperative complications overall and wound complications in particular.^{14,15} In one study, however, a 2- to 3-week period of smoking cessation was inadequate for a substantial reduction in the frequency of postoperative complications such as wound complications, anastomotic leak, pneumonia, or need for ventilator support.¹⁶ This finding again highlights the concern that a

preoperative visit with the anesthesiologist may be too late to produce any meaningful improvement in the smoker's postoperative course.

Ebbert et al² highlight different, yet important, issues regarding ENDS: regulatory and safety issues and the issue of the efficacy of nicotine replacement therapy as a method of smoking cessation. The recent statements by the World Health Organization¹⁷ and a recent article in *The New York Times*¹⁸ discuss the warnings that tobacco companies (whatever their real motive) have placed on these products in the absence of government mandates; these warnings may cause many physicians to not recommend such products for their patients as an aid for smoking cessation. It is, however, important to note that the World Health Organization's opposition to ENDS has been criticized by a prestigious group of tobacco research and policy experts.¹⁹ One must also realize that no therapy is entirely without risk, the US Food and Drug Administration's black box warning on varenicline being a case in point.²⁰

Another real concern is the marketing of ENDS and the vast array of liquid humectant flavors, which many rightly or wrongly feel specifically target the young and underage consumer.²¹ This concern is expressed in an excerpt from a website that focuses on childhood smoking: "It's not surprising that youth use of e-cigarettes has gone up at the same time that e-cigarettes are being promoted using many of the same tactics long used to market regular cigarettes to kids. These include celebrity endorsements, slick TV and magazine ads that portray e-cigarette use as glamorous and rugged, sponsorships of race cars and music festivals, and sweet flavors such as gummi bear and cotton candy."²² In addition, there have been increasing reports of accidental poisoning due to nicotine liquid used in ENDS.²³ Many have urged the introduction of child-resistant packaging for these products as well as many others.

I treat a large cohort of patients with Crohn disease, and extensive research has revealed that cigarette smoking aggravates the severity of Crohn disease.²⁴ Despite this finding, in a prospective clinical trial, we were unsuccessful in getting patients to switch from smoking to a smokeless tobacco product. It is hard to overestimate the satisfaction patients derive from inhaling, puffing, and handling cigarettes. I was, however, very impressed recently when one of

my patients with Crohn disease told me of her successful attempt to quit smoking using ENDS. She initially began using products with the highest nicotine liquid concentration and gradually weaned herself down until she was only using what was essentially propylene glycol. This is a real success story, and it is far from an isolated case.²⁵ The comparative efficacy of other types of nicotine replacement therapy and varenicline in smoking cessation has already been discussed in this journal.²⁶ In that UK study, the agents were nearly equally effective, and overall, approximately 40% of patients were carbon monoxide-validated abstinent from smoking at 4 weeks. If ENDS or other recreational nicotine products can add to those numbers, their use may be justified. However, we must ensure that they are appropriately regulated as tobacco products and are not marketed to children.

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Susan Galandiuk, MD

Hiram C. Polk Jr, MD, Department of Surgery
University of Louisville
Louisville, KY

Correspondence: Address to Susan Galandiuk, MD, Hiram C. Polk Jr, MD, Department of Surgery, University of Louisville, 550 S Jackson St, Louisville, KY 40202 (susan.galandiuk@louisville.edu).

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