Cancer Prevention and Control RESEARCH PROGRAM

In December 2018, the U.S. Attorney General

announced, "I am officially declaring e-cigarette use among youth an epidemic in the United States." He noted that the number of 12th graders who had used e-cigarettes had doubled in just one year. "Now is the time to take action."

In 2019 the statistics grew more alarming. The Centers for Disease Control and Prevention (CDC) reported that more than five million middle and high schoolers had vaped within the past 30 days—27.5 percent of all high school students and 10.5 percent of all middle schoolers.

These figures represent a startling reversal. By 2010, thanks to stringent regulations and effective anti-smoking campaigns, the percentage of teenagers using tobacco products had plummeted. Health officials hoped this trend would eventually lower the incidence of the many diseases caused by tobacco, including cancer.

Then came e-cigarettes. They deliver their nicotine load into the lungs and include appealing flavors, and the cool high-tech devices that produce an odorless sweet-tasting aerosol were easily hidden. Recent studies suggest that teenagers who would not otherwise have started smoking have been enticed back to tobacco products by e-cigarettes.

"What I'm most worried about," said Suchitra Krishnan-Sarin, PhD, Professor of Psychiatry and Co-Leader of the Yale Tobacco Center for Regulatory Science (TCORS), "is that we have all these kids now using nicotine, sometimes at very high levels, and there is evidence that some of them are moving on to cigarettes. Then there's the toxicity of the nicotine itself. It changes the functioning of almost every organ, and the teen brain is particularly sensitive to its effects."

"It takes years to see the consequences of any epidemic," said Stephanie O'Malley, PhD, Elizabeth Mears and House Jameson Professor of Psychiatry, who co-leads TCORS. "There's a huge uncontrolled experiment going on."

"Some flavors, like menthol, are soothing and may make it easier to vape higher concentrations of nicotine," added Dr. Krishnan-Sarin, "and therefore may make it easier to get addicted."

She points out that no studies have yet linked vaping to cancer, most likely because e-cigarettes are young and cancer trends need time to emerge. But she adds that "vaping liquids" contain solvents such as glycerin and propylene glycol, as well as flavor chemicals called aldehydes—all known inflammatory agents. "Repeated inflammation and repeated injury," she explained, "can potentially lead to cancer."

A study in 2019 by Yale TCORS found that when flavor additives are combined with solvents and then heated, the process generates a chemical reaction that creates previously undetected byproducts called acetals. The effects of inhaling acetals are unknown.

To date, the makers of e-cigarettes have not been required to list the ingredients in their products or to prove their safety. That is supposed to change by May 2020, the FDA's long-delayed deadline for requiring manufacturers to submit scientific evidence about the contents and health effects of their products. But the vaping industry—a \$7 billion business in the United States—has vigorously resisted deadlines and transparency. The public has also been alarmed by reports that vaping has caused respiratory illnesses that killed more than 40 people and sickened 2,000.

"The kind of science being generated by tobacco centers such as ours," said Dr. Krishnan-Sarin, "is intended to support decisions that the FDA will continue to make around how these products will be regulated."

A good start might be to treat e-cigarettes like other tobacco products. It seems sensible to require additives to be identified and tested for their effects on health. Tobacco companies are not allowed to market their products toward youth, but youth is the focus of the packaging and marketing used by many e-cigarette companies. Special taxes on cigarettes have raised their price so high that many young people never buy a pack, but e-cigarettes and liquids have been exempted and are affordable by teens.

"If you look historically," said Dr. O'Malley, "flavors were banned from cigarettes because kids were using them. I think there may be some good rationale for taking some of these flavors off the market because of who they appeal to. We also might want to limit the concentration of nicotine the way they do in Europe."

Neither Dr. Krishnan-Sarin nor Dr. O'Malley advocates banning e-cigarettes, because the devices might still deliver on their original purpose—to help wean smokers off of cigarettes by giving them an alternative source of nicotine, minus the carcinogenic particulates of tobacco smoke.

"I hope we can regulate these products in such a way that they continue to be helpful to people who want to use them to quit smoking," said Dr. Krishnan-Sarin, "but without having the appeal to youth."

