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Vaping Linked with Severe Lung Illnesses

Background

"Vaping" refers to the use of an electronic device (e-cigarette, vape, vape-pen, etc.) with a heating element that, when activated, vaporizes a liquid so that the user of the device can inhale the vapour. The liquid, made for this purpose and commonly called an "e-liquid," contains solvents, additives, water, flavourings and diverse active ingredients, usually liquid nicotine or cannabinoids, such as THC and CBD,* suspended in oils. The vapours, when inhaled by the person who vapes, produces psychoactive effects. While nicotine and cannabinoids are the most common psychoactive drugs consumed through vaping (Jones, Hill, Pardini, & Meier, 2016; Tucker et al., 2019), recent evidence shows that e-cigarettes can also be used as a way to deliver other non-medical psychotropic substances, such as methamphetamine and heroin (Breitbarth, Morgan, & Jones, 2018; Krakowiak, Poklis, & Peace, 2019).

Earlier studies suggested that vaping nicotine is less harmful to the lungs and respiratory system than cigarette smoking (National Academies of Sciences, Engineering, and Medicine, 2018), and consequently vaping has emerged as a common method of inhaling nicotine and cannabinoids. According to the 2017 Canadian Tobacco, Alcohol and Drugs Survey, 15% of Canadians in the general population (aged 15 years and older) reported using an e-cigarette in their life, which represents a significant increase from the 13% reported in 2015 (Statistics Canada, 2017).

Even more concerning is the popularity of vaping among youth and this is a trend that appears to be steadily growing. According to the most recent data obtained by the Youth Tobacco and Vaping Survey of the International Tobacco Control Policy Evaluation Project, 37% of Canadians aged 16 to 19 years old reported lifetime use of a nicotine e-cigarette in 2018, which represents a significant increase from the 29.3% reported in 2017 (Hammond et al., 2019). Vaping has also become a common way of inhaling cannabis among Canadians, with 29% of cannabis-using individuals (aged 15 years and older) indicating that vaping is their preferred method for cannabis use (Statistics Canada, 2017).

Current Developments

While it is believed by consumers that vaping nicotine is a healthier alternative to conventional cigarettes, it has recently been demonstrated that vaping is linked with severe lung and pulmonary illnesses (Layden et al., 2019). The U.S. Centers for Disease Control and Prevention (CDC) has identified 1,888 confirmed and highly probable cases of pulmonary illnesses resulting from vaping in the United States and 37 patients have died from the illnesses (Centers for Disease Control and Prevention, 2019).[†] The CDC analysis showed that 79% of the cases have occurred in adults aged

^{*} Tetrahydrocannabinol (THC) is the main psychoactive cannabinoid in cannabis. Cannabidiol (CBD) is the main non-psychoactive cannabinoid in cannabis

[†] The CDC statistics are updated weekly. The figures used in this report are up to date as of October 31, 2019.



under 35 years old; 70% of the cases were male. To date, Health Canada has reported two confirmed cases in the province of Quebec of a pulmonary illness that has resulted from vaping; two probable cases have been identified in New Brunswick and one probable case in British Columbia (Health Canada, 2019).

The reported symptoms include respiratory dysfunctions (shortness of breath, cough, pleuritic chest pain) and gastrointestinal disorders (diarrhea, nausea, vomiting). A high percentage of patients also showed leukocytosis (high white blood cell count), indicating a strong inflammatory response by the immune system (Layden et al., 2019). Other details of the U.S. cases include:

- All reported cases have used an e-cigarette containing either THC or nicotine or a combination of both within the 90 days before developing symptoms (Layden et al., 2019).
- Most of the cases of emerging lung and respiratory disorders (over 75%) have been linked to vaping products containing THC from cannabis extracts (Layden et al., 2019).
- The THC vape cartridges used in the cases were mostly, but not exclusively, purchased from the illicit market.

To deal with the emergence of lung illnesses associated with vaping in Canada, the Public Health Agency of Canada and the Council of Chief Medical Officers of Health have organized a federal, provincial and territorial task group on severe pulmonary illness related to vaping. The task group aims to develop a uniform approach to identifying and reporting cases, and is working collaboratively to develop technical documents (e.g., a Canadian case definition), data collection tools and information-sharing processes (Health Canada, 2019).

Beside Health Canada's response to the outbreak, the Government of Canada has established a strong regulatory framework for vaping products. Vaping products that do not contain cannabis are regulated by the *Tobacco and Vaping Products Act* and the *Canada Consumer Product Safety Act*. Additional regulatory measures, such as strictly restricting vaping product advertising, packaging and flavours will be applied to further reduce and prevent uptake of nicotine vaping products by youth. Vaping products containing cannabis are regulated separately under the *Cannabis Act*. The purpose of these acts is to protect public health and public safety with regards to the use of any sort of vaping products.

What Is Accounting for Lung and Pulmonary Illnesses in People Who Vape?

Although no substance or product has yet been clearly identified as the cause for the illnesses, the CDC reports that chemical exposure might play a key role. At first, the CDC and FDA were pointing at vitamin E acetate for several cases. According to the CDC, laboratories have identified high levels of vitamin E acetate in many of the vaping product samples they have analyzed. Other toxicants such as flavouring substances and solvents in e-liquids are also being investigated.

Vitamin E Acetate in E-liquids

Vitamin E acetate (also called tocopheryl acetate) is a form of vitamin E usually found in skin care products or dietary supplements. When applied topically or taken orally over a short-term period, vitamin E acetate is harmless. However, long-term oral exposure to high doses of vitamin E acetate can increase the risk of heart failure (Lonn et al., 2005) and all-cause mortality (Miller et al., 2005).

There is a common misconception among people who use cannabinoid oil that the thickness of the oil indicates its quality. To exploit this misconception, illicit market suppliers have used vitamin E acetate as a thickening agent in cannabinoid-infused oils to mimic this characteristic of what users think is high-quality pure oil. In past years, vitamin E acetate was found in small quantities in vape oils (less than 20%), but with the increased popularity of vaping, illicit market suppliers have started to add larger amount of vitamin E acetate in their oil products (more than 50%). The effects of inhaling high doses of vitamin E are currently unknown and more studies are needed. However, the FDA has warned that when inhaled vitamin E could lead to lipoid pneumonia.

E-flavours in E-liquids

There are more than 7,500 e-liquid flavours available (Zhu et al., 2014), and some of them have the potential to be harmful when heated and inhaled (National Academies of Sciences, Engineering, and Medicine, 2018). For instance, saccharides, used to sweeten e-liquid flavours, can produce respiratory irritants such as furans and aldehydes when heated (Soussy et al., 2016; Tierney, Karpinski, Brown, Luo, & Pankow, 2016). Diacetyl, acetylpropionyl and acetoin are chemicals that are added to e-liquids (Allen et al., 2016) to produce various candy flavours. When heated and inhaled, these flavouring substances have been associated with adverse respiratory health consequences including chronic cough, bronchitis, asthma and bronchiolitis obliterans, a severe and irreversible lung illness that can lead to pulmonary scarring and obstruction (Kreiss et al., 2002; National Academies of Sciences, Engineering, and Medicine, 2018). Finally, pulegone, a substance found in high levels in mint and menthol flavoured e-liquids, has possible carcinogenic properties, and preclinical studies showed that oral administration of pulegone in rodents can cause hepatic carcinomas, pulmonary metaplasia and other neoplasms (Jabba & Jordt, 2019). To date, there is little information available about the health effects of flavouring agents in e-liquids and more studies are needed to determine if they are safe to inhale.

Other Potential Toxins in E-liquids

Beside vitamin E acetate, e-liquids contain other chemicals known to have potentially deleterious effects on health. For example, the most popular solvents found in e-liquids to dissolve nicotine or cannabinoids are vegetable glycerin and propylene glycol. The heating process that vaporizes the e-liquid in an e-cigarette is sufficient to induce a thermal decomposition of both vegetable glycerin and propylene glycol into carbonyl compounds, such as formaldehyde, acetaldehyde, acrolein, acetone and propanal, all substances known to have toxic properties and to induce mouth, throat and lung irritation (Goniewicz et al., 2014; Kosmider et al., 2014). For example, formaldehyde is a strong respiratory irritant and is classified by the International Agency for Research on Cancer as a human carcinogen (Jensen, Luo, Pankow, Strongin, & Peyton, 2015). Acrolein can damage the lung lining, irritate the nasal cavity and contribute to cardiovascular disease (Park & Taniguchi, 2008). Acetone is a mucous membrane irritant and inhalation can also lead to hepatotoxic effects (Buron, Hacquemand, Pourie, & Brand, 2009).

The release of toxicants into the lungs from e-cigarettes can vary depending of the model of vaping device, the material from which a device is made (e.g., plastic, metal, glass) and the heating-coil. For instance, using a vaping device with a higher battery output that will increase the heat generated by the heating coil can produce and release more chemicals and toxicants (Geiss, Bianchi, & Barrero-Moreno, 2016; Kosmider et al., 2014). However, it is important to note that the amount of chemicals and contaminants in aerosols from e-cigarettes is found at lower levels than in tobacco or cannabis cigarette smoke (National Academies of Sciences, Engineering, and Medicine, 2018).



Key Considerations

Rigorous testing of vaping products for toxic substances is essential to ensuring the health and safety of people who vape. Studies are needed to evaluate the presence of potentially toxic and hazardous compounds in e-liquids and the vapours generated from them by vaping devices. While cannabinoid e-liquids in newly legalized products that will soon be appearing on the market will be strictly tested and regulated, concerns about the health effects of vaping remain. Due to the lack of epidemiological studies and large clinical trials, the short- and long-term health effects of vaping and vaping products are unknown and more studies are required to determine their health impacts.

While additional scientific information is gathered, the following suggestions are made to protect the health of those considering vaping or who already vape:

- For health reasons, people should not vape.
- People who do vape should avoid doing so until there is more conclusive evidence of a specific agent causing the illnesses.
- People who vape should not buy any e-cigarettes or vaping products from the illicit market.
- People who vape should closely monitor themselves and seek medical attention for any symptoms of cough, shortness of breath, chest pain, nausea, diarrhea or vomiting.





References

- Allen, J.G., Flanigan, S.S., LeBlanc, M., Vallarino, J., MacNaughton, P., Stewart, J.H., & Christiani, D.C. (2016). Flavoring chemicals in e-cigarettes: Diacetyl, 2,3-pentanedione, and acetoin in a sample of 51 products, including fruit-, candy-, and cocktail-flavored e-cigarettes. *Environmental Health Perspectives*, 124(6), 733–739.
- Anic, G.M., Sawdey. M.D., Jamal, A., & Trivers, K.F. (2018). Frequency of use among middle and high school student tobacco product Users – United States, 2015–2017. *Morbidity and Mortality Weekly Report*, 67(49), 1353–1357.
- Breitbarth, A.K., Morgan, J., & Jones, A.L. (2018). E-cigarettes An unintended illicit drug delivery system. *Drug and Alcohol Dependence*, 192, 98–111.
- Buron, G., Hacquemand, R., Pourié, G., & Brand, G. (2009). Inhalation exposure to acetone induces selective damage on olfactory neuroepithelium in mice. *Neurotoxicology*, 30(1), 114–120.
- Centers for Disease Control and Prevention. (2019, Oct. 17). Outbreak of lung injury associated with e-cigarette use, or vaping. Retrieved from https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html.
- Drugs Forum. (2017). how to use a Vape to smoke meth! *Drugs Forum* [Online forum discussion]. Retrieved from https://drugs-forum.com/threads/how-to-use-a-vape-to-smoke-meth.280002/
- Food and Drug Administration. (2018). Results from 2018 National Youth Tobacco Survey show dramatic increase in e-cigarette use among youth over past year [FDA news release]. U.S. Food and Drug Administration. Retrieved from https://www.fda.gov/news-events/press-announcements/results-2018-national-youth-tobacco-survey-show-dramatic-increase-e-cigarette-use-among-youth-over
- Geiss, O., Bianchi, I., & Barrero-Moreno, J. (2016). Correlation of volatile carbonyl yields emitted by ecigarettes with the temperature of the heating coil and the perceived sensorial quality of the generated vapours. *International Journal of Hygiene and Environmental Health*, 219(3), 268–277.
- Goniewicz, M.L., Knysak, J., Gawron, M., Kosmider, L., Sobczak, A., Kurek, J., . . . Benowitz, N. (2014). Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tobacco Control,* 23(2), 133–139.
- Hammond, D., Reid, J.L., Rynard, V.L., Fong, G.T., Cummings, K.M., McNeill, A., . . . White, C.M. (2019). Prevalence of vaping and smoking among adolescents in Canada, England, and the United States: Repeat national cross sectional surveys. *BMJ*, 365(8204), 12219.
- Health Canada. (2019, Sept. 4). Information Update Health Canada warns of potential risk of pulmonary illness associated with vaping products. Retrieved from https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2019/70919a-eng.php
- Jabba, S.V., & Jordt, S.E. (2019). Risk analysis for the carcinogen pulegone in mint- and mentholflavored e-cigarettes and smokeless tobacco products. *JAMA Internal Medicine*. Advance online publication. Retrieved from https://jamanetwork.com/journals/jamainternalmedicine/articleabstract/2751245
- Jensen, R.P., Luo, W., Pankow, J.F., Strongin, R.M., & Peyton, D.H. (2015). Hidden formaldehyde in ecigarette aerosols. *New England Journal of Medicine*, 372(4), 392–394.



- Jones, C.B., Hill, M.L., Pardini, D.A., & Meier, M.H. (2016). Prevalence and correlates of vaping cannabis in a sample of young adults. *Psychology of Addictive Behaviors*, 30(8), 915–921.
- Kosmider, L., Sobczak, A., Fik, M., Knysak, J., Zaciera, M., Kurek, J., & Goniewicz, M.L. (2014). Carbonyl compounds in electronic cigarette vapors: effects of nicotine solvent and battery output voltage. *Nicotine and Tobacco Research*, 16(10), 1319–1326.
- Krakowiak, R.I., Poklis, J.L., & Peace, M.R. (2019). The analysis of aerosolized methamphetamine from e-cigarettes using high resolution mass spectrometry and gas chromatography mass spectrometry. *Journal of Analytical Toxicology*, *43*(8), 592–599
- Kreiss, K., Gomaa, A., Kullman, G., Fedan, K., Simoes, E. J., & Enright, P. L. (2002). Clinical bronchiolitis obliterans in workers at a microwave-popcorn plant. *New England Journal of Medicine*, 347(5), 330–338.
- Layden, J.E., Ghinai, I., Pray, I., Kimball, A., Layer, M., Tenforde, M., . . . Meiman, J. (2019). Pulmonary illness related to e-cigarette use in Illinois and Wisconsin – preliminary report. *New England Journal of Medicine*. Advance online publication. Retrieved from https://www.nejm.org/doi/full/10.1056/NEJMoa1911614
- Lonn, E., Bosch, J., Yusuf, S., Sheridan, P., Pogue, J., Arnold, J. M., . . . HOPE and HOPE-TOO Trial Investigators. (2005). Effects of long-term vitamin E supplementation on cardiovascular events and cancer: A randomized controlled trial. *JAMA*, 293(11), 1338–1347.
- Miller, E.R., 3rd, Pastor-Barriuso, R., Dalal, D., Riemersma, R.A., Appel, L.J., & Guallar, E. (2005). Meta-analysis: High-dosage vitamin E supplementation may increase all-cause mortality. *Annals of Internal Medicine*, *142*(1), 37–46.
- National Academies of Sciences, Engineering, and Medicine (2018). *Public Health Consequences of E-Cigarettes*. Washington, D.C.: National Academies Press.
- Park, Y.S., & Taniguchi, N. (2008). Acrolein induces inflammatory response underlying endothelial dysfunction: A risk factor for atherosclerosis. *Annals of the New York Academy of Sciences*, 1126, 185–189.
- Peace, M.R., Krakowiak, R.I., Wolf, C.E., Poklis, A., & Poklis, J.L. (2017). Identification of MDMB-FUBINACA in commercially available e-liquid formulations sold for use in electronic cigarettes. *Forensic Science International*, 271, 92–97.
- Quora Questions. (2016). Can I mix meth with e-liquid? *Quora*. [Online forum discussion]. Retrieved from https://www.quora.com/Can-I-mix-meth-with-e-liquid-1
- Reddit Drugs Forum. (2015). Heroin e-cig. *Reddit*. [Online forum discussion]. Retrieved from https://www.reddit.com/r/Drugs/comments/2ujswv/heroin_ecig/
- Soussy, S., El-Hellani, A., Baalbaki, R., Salman, R., Shihadeh, A., & Saliba, N.A. (2016). Detection of 5-hydroxymethylfurfural and furfural in the aerosol of electronic cigarettes. *Tobacco Control*, 25(Suppl 2), ii88–ii93.
- Statistics Canada. (2017). Canadian Tobacco, Alcohol and Drugs Survey (CTADS): Summary of results for 2017. Ottawa, Ont.: Author.
- Tierney, P.A., Karpinski, C.D., Brown, J.E., Luo, W., & Pankow, J.F. (2016). Flavour chemicals in electronic cigarette fluids. *Tobacco Control*, 25(e1), e10–15.



- Tucker, J.S., Pedersen, E.R., Seelam, R., Dunbar, M.S., Shih, R.A., & D'Amico, E. (2019). Types of cannabis and tobacco/nicotine co-use and associated outcomes in young adulthood, *Psychology of Addictive Behaviors*, 33(4), 401–411.
- Zhu, S.H., Sun, J.Y., Bonnevie, E., Cummins, S.E., Gamst, A., Yin, L., & Lee, M. (2014). Four hundred and sixty brands of e-cigarettes and counting: implications for product regulation. *Tobacco Control, 23*(Suppl 3), iii3–iii9.

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