International Journal of Integrative Cardiology

Short Communication

DOI: https://doi.org/10.47275/2690-862X-140
Volume 6 Issue 1

An Analysis on the Cardiopulmonary Consequences of Vaping Among Adolescents

Jyotsna Arankkal Jayan[1*], Mohammed Afshar Alam[2], Kasagani Srujana[3]

[1]All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, India
[2]Ayaan Institute of Medical Sciences, Hyderabad, Telangana, India
[3]Govt medical college, Siddipet, Telangana, India

Abstract

Despite not being approved as a cessation aid by the United States (US) Food and Drug Administration (FDA), e-cigarettes have sometimes been presented in this way by the industry as a means to help adults stop smoking cigarettes; however, their novelty and customizability have led them into the hands of unintended users, especially teenagers. The research community is increasingly interested in understanding the respiratory and cardiovascular consequences of e-cigarette use since most new users have never smoked traditional cigarettes. Adult e-cigarette users have been the subject of most studies, but these participants are typically former smokers or those who have switched from traditional smoking to e-cigarettes. In this population, e-cigarette use does not alone cause respiratory and cardiovascular consequences. The health effects of naive e-cigarette use have been studied in preclinical studies; however, almost all of these studies used adult animals, which makes translating results to adolescents difficult. Research into novel therapeutic treatment strategies would be helped by a more comprehensive understanding of the pathways involved in toxicity when inhaled foreign substances can affect the respiratory and cardiovascular systems. This scientific statement aims to provide important background information about the cardiopulmonary consequences of vaping in adolescents, assist in the development of therapeutic and prevention strategies, and inform public policymakers about the risks associated with vaping, both short-term and long-term. With frequent entry and rapid evolution of products in the marketplace, electronic nicotine delivery systems have gained popularity over the past decade. Beyond the nicotine content and ratio of vegetable glycerin (VG) to propylene glycol (PG), the composition of liquids within these devices (commonly called electronic liquids) is not publicly known, making it difficult to predict the health effects, including effects on the lungs and heart. It is difficult to regulate e-cigarettes due to their customizable nature, such as power levels, e-liquid content, and a wide array of flavors, and outbreaks of e-cigarette and vaping product use–associated lung injury have made people aware of the dangers associated with illicit cannabis vapes. E-cigarettes are continuously developing products that are continually evolving. Therefore, reducing their public health burden requires understanding their health effects. As the e-cigarette user group grows, the latest evidence regarding cardiopulmonary effects of e-cigarettes will be reviewed in this scientific statement.

Keywords: E-cigarettes, Cardiopulmonary effects, Adolescents

***Correspondence to**: Jyotsna Arankkal Jayan, All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, India.

Citation: Jyotsna AJ (2024) An Analysis on the Cardiopulmonary Consequences of Vaping Among Adolescents. Int J Integr Cardiol, Volume 6, Issue 1. DOI: https://doi.org/10.47275/2690-862X-140

Received: February 07, 2024; **Accepted:** June 17, 2024; **Published:** June 19, 2024

Overview on the History of E-Cigarettes

Electronic nicotine delivery systems deliver an aerosol (usually containing nicotine) to the user through their lungs. They consist of a battery, an atomizer, and a reservoir for e-liquid. E-cigarettes are the most common electronic nicotine delivery system, resembling pipes, hookahs, cigars, and cigarettes. A number of iterations of e-cigarettes have been released since their introduction to the international market in 2007, but at their core, e-cigarettes remain battery-operated devices that aerosolize e-liquid when touched or puffed. PG/VG is the vehicle in which nicotine, flavors, and other chemical additives are dissolved [1]. Nicotine is increasingly being delivered by e-cigarettes, and now, depending on the user's characteristics and the device, plasma nicotine levels are comparable to those of smokers. E-cigarette pod mods are the latest iteration. In contrast to free-base nicotine, these devices contain e-liquids containing high nicotine content in salt form. E-cigarettes became more popular among adolescents in between 2017 - 2018 as a result of this market shift, which compensated for the lower power and aerosol generation of pod mod devices. Comparing generation 1 to 3 e-cigarettes with combustible cigarettes, generation 1 to 3 e-cigarettes produced lower plasma nicotine levels [2]. The plasma nicotine levels of e-cigarettes of later generation are comparable to those of combustible cigarettes, according to one study. They, however, caused less plasma nicotine than combustible cigarettes in another study. There may have been a greater level of plasma nicotine in the plasma of more experienced vapers, as suggested by the authors, because the test subjects lacked experience with e-cigarette products. The plasma cotinine level was also compared in two studies comparing e-cigarettes to combustible cigarettes in real-life exposure situations over the long term [3]. These studies did not find a difference in cotinine levels between the groups, indicating that vapers may compensate for reduced delivery efficiency by puffing more often over time. It is important to distinguish between tobacco cessation and nicotine cessation. Despite being partially effective at the former, it is debatable whether they are more effective or inferior to other FDA-approved nicotine replacement therapies. The effectiveness of e-cigarettes in reducing nicotine consumption is absent from their effectiveness in reducing nicotine consumption, with 20% efficacy, whereas nicotine patches have 81% efficacy. E-cigarettes are not effective at aiding tobacco cessation in adolescents. A significant change in US federal tobacco regulatory policy, however, is the introduction of e-cigarettes and other less harmful alternatives to nicotine for adults, which will reduce nicotine levels in combustible cigarettes to levels that do not sustain tobacco addiction [4].

A Breakdown of the Compounds Found in E-Cigarettes

It depends on the type and setting of the device that the e-liquid is placed in, when it comes to temperatures. Thermal decomposition of organic compounds can produce smaller chemicals in e-liquids. Many studies have shown that vaping results in the formation of acetaldehyde, acrolein, diacetyl, and formaldehyde. In addition to their potent irritant properties, acrolein and formaldehyde are known carcinogens. Glycidol and acetol have been reported as intermediate breakdown products, suggesting that heated PG/VG is oxidized to produce these carbonyls [5].

Xenobiotics, including those derived from tobacco and electronic cigarettes, are metabolized by enzymes in the cytochrome P450 family. They are expressed in the lungs, though at a much lower level than the liver, and are known to be upregulated when exposed to xenobiotics. The airway epithelia do not metabolize nicotine to cotinine, in accordance with these observations [2, 6-8]. According to research, vapers' lungs are upregulated for cytochrome P450 proteins, suggesting the lung may compensate for the increased chemical exposure caused by vaping. Several studies have shown that vaping may increase toxicity for dual users through the cytochrome P450 aryl hydrocarbon pathway, which produces carcinogenic benzo(a)pyrene metabolites. In the cardiovascular system, cytochrome P450 proteins are not directly examined because there is an unmet need.

How Safe are E-Cigarettes?

There are a few small studies suggesting cardiopulmonary toxicity from e-cigarette vapor, but it remains poorly understood. Generally Regarded as Safe (GRAS) is a list of substances that the FDA has approved for use in e-liquids. Except for nicotine, all other substances are listed on the FDA's list. In spite of this, it is important to remember that the majority of chemicals on the GRAS list were intended as food components, and a key aspect of the GRAS act is that the substance must be 'generally recognized' as safe under the conditions of its intended use under the GRAS act. It is thus unknown what impact GRAS components will have on the pulmonary system since many have not been tested for inhalation toxicology [9-11]. Especially concerning is the use of GRAS products in e-liquids, as stated on the website of the Flavor and Extract Manufacturers Association of the US. Before studies were conducted on the cardiopulmonary effects of e-cigarettes, e-cigarettes were commercially available on the basis that they were covered by GRAS. The development of chronic obstructive pulmonary disease or cardiovascular disease (CVD) usually takes decades for smokers. In light of this, it is premature to argue that e-cigarettes have not caused extensive disease in the past decade. Also, nicotine concentrations, including those found in the systemic circulation after vaping, and PG/VG pharmacokinetics are unknown. Consequently, it is difficult to determine whether the levels of PG/VG used in laboratory settings apply to users of e-cigarettes [12].

The Health Effects of E-Cigarettes

Cardiovascular effects

Clinical studies assessing cardiovascular health effects in adolescents

Research on e-cigarettes and their health effects in adolescents may help us better understand adolescent health. As a result, the patient's blood pressure, heart rate, and sympathetic tone increased. Several acute hemodynamic changes were also observed, including increased arterial stiffness, impaired endothelial function, and elevated blood pressure, heart rate, and sympathetic tone. Using e-cigarettes for a long time can also increase arterial stiffness and sympathetic tone. With exercise, there is an increase in myocardial blood flow, but a decrease in ventricular relaxation. The use of e-cigarettes for a short period of time also increases oxidative stress biomarkers. Tobacco companies have not been interested in removing nicotine from their products, which appears to be responsible for many of the acute vascular effects. Young adults who were former smokers or nonsmokers are the majority of subjects in current studies. Researchers found no long- or short-term effects on endothelial function in young healthy adults who exclusively used e-cigarettes [13]. In contrast to popular e-cigarettes among teenagers, this study predominantly used e-cigarettes with a lower nicotine concentration. Adolescents who use e-cigarettes have higher levels of several potentially harmful volatile organic compounds. There are no extant studies that have directly examined cardiovascular health in adolescents under 18 years of age, who may be more susceptible to acute toxicities. Currently, evidence suggests that long-term e-cigarette users can develop CVD due to acute cardiovascular effects from e-cigarettes [14, 15].

Immune effects and CVD

Long-term cardiovascular risk may be predicted by changes in inflammation associated with e-cigarette use. Young nonusers who smoked e-cigarettes for a short period of time increased their levels of intracellular adhesion molecules and C-reactive protein [16]. The use of e-cigarettes for a long period of time can also increase the expression of systemic inflammatory biomarkers in some studies, but not in all. A study conducted on college students between the ages of 18 and 25 years old found that salivary cytokine levels were elevated among users of pod-based e-cigarettes in comparison to nonusers [17-20]. Researchers have found that e-cigarette users have altered immune responses that may increase their susceptibility to viral and bacterial infections. In young adults, long-term use of e-cigarettes increases levels of proinflammatory white blood cells and oxidative stress. Hence, adolescent e-cigarette users may be at higher cardiovascular risk due to the use of e-cigarettes alone, although further studies are needed.

Pulmonary effects

Different types of inhalants have physiological and pathological effects on the lungs, resulting in a wide variety of lung diseases. The use of e-cigarettes has been associated with higher rates of wheezing, suggesting an increase in airway reactivity as a result of the use of e-cigarettes. The use of e-cigarettes has been identified as a contributing factor to the development of bronchiectasis in one case series. Asthma prevalence and exacerbation may be associated with youth e-cigarette use, according to cross-sectional studies. According to self-reported diagnoses and e-cigarette use, e-cigarette use was also associated with an increase in respiratory disease and worse pulmonary health in chronic obstructive pulmonary disease users. The expression of genes related to immunosuppression was significantly altered in bronchial biopsies taken from vapor subjects. E-cigarette exposure has also been shown to significantly alter bronchial epithelia and airway secretions using proteomic approaches. In spite of the need for longitudinal studies to replicate these findings, these findings are consistent with the findings of the larger population-based studies as well as the laboratory studies that follow [21, 22].

Inhaled pathogens are cleared from the lungs by the pulmonary epithelium, which acts as a barrier against viruses and bacteria. From bench and animal studies, it has been shown that vaping impairs host defenses and increases susceptibility to viral and bacterial pathogens, consistent with the changes seen at the gene and protein levels in vapers' airways [23]. There is a mechanistic link between vaping and an increased risk of bacterial infections in humans due to upregulation of a virulence factor for platelet-activating factor receptor. An innate immune system response to prevent bacterial infection involves the release of proteases from immune cells. According to Ghosh et al. [19], nicotine levels in vapers' lungs were sufficient to elicit protease release from alveolar macrophages and peripheral blood neutrophils, suggesting higher protease levels in both smokers' and vapers' lungs. The data suggest that e-cigarette users are also susceptible to infections of the lungs, just as traditional cigarette smokers are [24].

Effects on lung function/lung structure, including spirometry

As a result of tobacco smoke exposure, indoor wood fires, biomass smoke exposure, and air pollution, airways are inflamed, bronchoreactive, lung cells die, and chronic obstructive pulmonary disease results. Given that the lung consists of thin, delicate cells that form a large surface area for exchanging gas molecules, and is also exposed to environmental pollutants, e-cigarette aerosols included, this makes biological sense. Inhalation of matter outside the normal ambient air leads to changes in lung structure and function, but because e-cigarettes are relatively new, it is unclear whether long-term inhalation of their aerosols will result in lung disease as severe as conventional tobacco or if it will result in the same types of diseases. To date, humans have been exposed to these chemicals only for short periods and have shown only mild changes in spirometry or no changes at all. Other times, the vehicle alone caused the effects without nicotine content (decreased forced expiratory volume in 1 second) [25].

The dose makes the poison, according to an old toxicology adage. However, the chemical concentrations in the lung are not known despite e-cigarettes having fewer chemicals than cigarettes. Almost 70 m^2 of lung surface area is lined by an airway surface liquid film 10 m thick. E-cigarette constituents may reach high levels in the lung before being absorbed into the body. E-cigarette use, however, has been identified as a contributing factor to wheezing and coughing due to increased airway reactivity. Identifying toxic chemicals and factors driving structural and functional changes may enable safer products to be designed [26].

Adolescent vaping and its long-term effects

EVALI has caused severe diseases and deaths in adolescents, so it is important to be concerned about its short-term effects, but it is also important to be concerned about its long-term effects. It took 50 years for tobacco smoking to be linked to a multitude of smoking-related diseases, and smoking became an epidemic during 1900's. Vaping may lead adolescents to become lifelong users of nicotine or tobacco, and it is not yet known what diseases will develop as a result of vaping.

Implications for cardiovascular health

The long-term effects of smoking conventional tobacco as an adolescent can lead to atherosclerosis, heart disease, and stroke during adulthood, but there is no comparable long-term data for e-cigarette use. It is still possible to predict some outcomes by comparing the effects seen in vapers and smokers. According to the evidence, vapers are more likely to have cardiovascular disease due to systemic inflammation and endothelial dysfunction (lower levels of nitric oxide). Adolescent vapers are also more likely to develop CVD once they reach middle age or beyond due to changes in vascular stiffness, blood pressure, and heart rate. It was found that mice that had been exposed to e-cigarette aerosol for a long period of time developed cardiac fibrosis, a decrease in ejection fraction, and atherosclerosis, confirming the findings of the short-term use data in humans. It is clear that e-cigarette aerosols are causing harm to endovascular and myocardial cells, even though adolescents may not feel that vaping affects them at the moment [27]. Over time, these changes may lead to CVD, which can lead to a variety of health problems.

Sleep, addiction, and mental health implications

It is known that vaping adversely affects important components of health, despite its focus on cardiopulmonary damage. By activating dopamine reward pathways, e-cigarette use disrupts sleep quality, potentially affects mental health, and leads to addiction. An individual's set points for addictive behaviors are fundamentally altered when they use addictive substances during their adolescence. In both social and occupational settings, this could lead to lifelong addictions, psychopathology, and dysfunction caused by vaping [28].

Measures Taken to Regulate the Usage of E-Cigarettes

Adults have previously been advised against the use of e-cigarettes and newer tobacco products by the American Heart Association; however, adolescents are becoming more likely to use these products. According to studies, although smoking is declining, e-cigarette use has steadily increased; however, other studies suggest that prior e-cigarette use can contribute to the initiation of traditional tobacco smoking. E-cigarette regulations must address the underlying drivers of youth e-cigarette use, including flavors, advertising, and easy access to high-nicotine–content devices. In the US, tobacco cigarettes are prohibited from having flavors other than menthol, but many e-cigarettes offer flavors. In addition to their primary reason for using e-cigarettes, young users also report that flavors make them more appealing. As well as masking nicotine's aversive sensory effects, flavors facilitate its continued use and dependence. Pod or cartridge-based e-cigarettes flavored with fruit or mint are among the products targeted by the FDA's policy, which prioritizes enforcement against "certain unauthorized flavored e-cigarette products". In two studies, mint-flavored e-cigarettes were found to be highly popular among teens. The removal of flavored e-cigarettes and tobacco products from the marketplace has been proposed in a number of states and municipalities.

As a result of inhibiting transient receptor potential channels in lung neurons, menthol suppresses coughing and irritation. Black individuals are targeted by menthol flavors, which can lead to an increase in smoking uptake in this group, resulting in increased public health harm. In addition, Black vapers are more likely to use e-cigarettes with menthol flavors than other groups. E-cigarettes with flavors have not been banned by the FDA despite this data [29].

E-cigarettes are also available in a variety of flavors and nicotine concentrations. Nicotine concentration in e-liquids is currently not regulated in the US. E-liquid nicotine concentrations in the European Union (EU) are capped at 20 mg/ml on the basis that the EU believes this will deliver nicotine similar to that of standard combustible cigarettes. Nicotine salts, rather than free-base nicotine, are sometimes used in e-cigarettes to reduce the aversive sensory effects of high nicotine concentrations in the aerosols affecting the throat [30]. In human laboratory studies, however, high-nicotine-content pod devices are mixed in terms of their effectiveness for delivering nicotine. The regulation of nicotine concentration in e-cigarettes without concurrent regulation of other characteristics such as power and volume may not result in reliable reductions of nicotine intake. Changing vaping habits or adopting high-power devices can compensate for exposure to toxicants, including carbonyl compounds, emitted in greater quantities by high-power devices [31].

Youth e-cigarette use is also driven by the availability of USB-shaped e-cigarettes. In comparison with larger, higher-power models, these devices have high "tech appeal" aesthetics, are portable and concealable, and produce smaller plumes of aerosol [32]. By combining these features, e-cigarettes can be used inconspicuously in places where smoking is prohibited, thus circumventing smoke-free air laws that have been crucial to reducing smoking. Many e-cigarettes do not resemble cigarettes, unlike cig-a-likes, which were designed to mimic combustible cigarettes, reducing the stigma attached to combustible cigarettes. Additionally, many e-cigarettes are small and shaped in a way that reduces the social stigma previously associated with them.

E-cigarette flavoring should be removed from the market by federal, state, and local policymakers. No tobacco product can be sold to anyone under 21 years of age nationwide. Among the steps taken by the FDA to limit youth access to e-cigarettes have been requiring identification to verify age before attempting to purchase tobacco products; preventing the distribution of free samples of tobacco products; prohibiting tobacco product sales in vending machines (except in facilities that are strictly adult-only); and inspecting e-cigarette manufacturing facilities, including vape shops that manufacture or modify e-cigarettes [2, 33-36].

The tobacco product market landscape offers a variety of flavors to appeal to a broad range of consumers, including youth and certain racial and ethnic groups. A 2016 study found that Black individuals in their cohort had lower rates of e-cigarette use than White or Hispanic individuals but were more likely to continue using them. The vulnerability of Black ever-vapers to maintaining e-cigarette use may therefore be particularly high. Black and Hispanic tobacco users use fewer e-cigarettes than White tobacco users, according to another study. There is, however, a disparity in youth tobacco product use based on race and ethnicity, according to a report by the Centers for Disease Control and Prevention. Nearly a quarter (23.4%) of US teens who currently use tobacco are Native Hawaiians and other Pacific Islanders [37-39].

In order to successfully quit vaping, health care stakeholders (such as medical schools, hospitals, and health insurance providers) must be involved. There should be a curriculum developed for medical schools that explains the long- and short-term risks of vaping. It will enable medical students to have in-depth discussions with future patients about vaping cessation and educate them with the latest information on the impact of vaping. As well as offering vaping cessation programs for adolescents, hospitals can offer programs for parents. It is possible to provide community awareness campaigns and access to support through these programs. A comprehensive cessation program including pharmacotherapy and counseling should be offered without a co-pay by employers and health insurance plans that support cessation. Health care institutions' education and prevention efforts, along with regulatory measures, play an important role in vaping cessation [40].

All jurisdictions must take comprehensive measures to reduce youth access to e-cigarettes, including removing all flavored e-cigarettes from the market. A curfew on the marketing of e-cigarette products to youth, as well as better education on the harms associated with e-cigarettes and tobacco products, is necessary. In order to further de-normalize e-cigarette use among youth, smoke-free air laws must include e-cigarettes [2, 41, 42]. Social media platforms as well as traditional media should be regulated regarding marketing. It is imperative that every effort is made to prevent young people from using e-cigarettes, even though e-cigarettes are available to adults.

Conclusion

There is limited short- and long-term evidence of e-cigarettes' cardiopulmonary effects, although they may help some regular cigarette smokers quit smoking by switching from combustible tobacco to complete cessation. However, their appeal has grown substantially among adolescents. Several major studies have examined the effects of e-cigarette use among adolescents on the lungs and cardiovascular systems. However, this area is clearly of great concern and requires further study. Because vaping in adolescence is likely to have long-term adverse effects, we must determine the short- and long-term consequences.

Acknowledgements

None.

Conflict of Interest

None.

References

1. Yingst JM, Foulds J, Veldheer S, Hrabovsky S, Trushin N, et al. (2019) Nicotine absorption during electronic cigarette use among regular users. PLoS One 14: e0220300. https://doi.org/10.1371/journal.pone.0220300
2. Wold LE, Tarran R, Crotty Alexander LE, Hamburg NM, Kheradmand F, et al. (2022) Cardiopulmonary consequences of vaping in adolescents: a scientific statement from the American Heart Association. Circ Res 131: e70-e82. https://doi.org/10.1161/RES.0000000000000544
3. Hajek P, Pittaccio K, Pesola F, Smith KM, Phillips-Waller A, et al. (2020) Nicotine delivery and users' reactions to Juul compared with cigarettes and other e-cigarette products. Addiction, 115: 1141-1148. https://doi.org/10.1111/add.14936
4. Maloney S, Eversole A, Crabtree M, Soule E, Eissenberg T, et al. (2021) Acute effects of JUUL and IQOS in cigarette smokers. Tob Control 30: 449-452. https://doi.org/10.1136/tobaccocontrol-2019-055475
5. Jain RB (2021) Re-visiting serum cotinine concentrations among various types of smokers including cigarette only smokers: some new, previously unreported results. Environ Sci Pollut Res 28: 3149-3161. https://doi.org/10.1007/s11356-020-10677-4
6. Rapp JL, Alpert N, Flores RM, Taioli E (2020) Serum cotinine levels and nicotine addiction potential of e-cigarettes: an NHANES analysis. Carcinogenesis 41: 1454-1459. https://doi.org/10.1093/carcin/bgaa015
7. Smoking Cessation: A Report of the Surgeon General. [https://www.cdc.gov/tobacco/sgr/2020-smoking-cessation/index.html] [Accessed on April 29, 2024]
8. Przulj D, Hajek P, Phillips-Waller A (2019) E-cigarettes versus nicotine-replacement therapy for smoking cessation. reply. N Engl J Med 380: 1974-1975. https://doi.org/10.1056/NEJMc1903758
9. Hajek P, Phillips-Waller A, Przulj D, Pesola F, Smith KM, et al. (2019) A randomized trial of e-cigarettes versus nicotine-replacement therapy. N Engl J Med 380: 629-637. https://doi.org/10.1056/NEJMoa1808779
10. Kalkhoran S, Glantz SA (2016) E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis. Lancet Respir Med 4: 116-128. https://doi.org/10.1016/S2213-2600(15)00521-4
11. Zeller M (2019) The future of nicotine regulation: key questions and challenges. Nicotine Tob Res 21: 331-332. https://doi.org/10.1093/ntr/nty200
12. Benowitz NL, Fraiman JB (2017) Cardiovascular effects of electronic cigarettes. Nat Rev Cardiol 14: 447-456. https://doi.org/10.1038/nrcardio.2017.36
13. Tarran R, Barr RG, Benowitz NL, Bhatnagar A, Chu HW, et al. (2021) E-cigarettes and cardiopulmonary health. Function 2(2): zqab004. https://doi.org/10.1093/function/zqab004
14. Mull ES, Shell R, Adler B, Holtzlander M (2020) Bronchiectasis associated with electronic cigarette use: a case series. Pediatr Pulmonol 55: 3443-3449. https://doi.org/10.1002/ppul.25062
15. Bein K, Leikauf GD (2011) Acrolein – a pulmonary hazard. Mol Nutr Food Res 55: 1342-1360. https://doi.org/10.1002/mnfr.201100279
16. Gotts JE, Jordt SE, McConnell R, Tarran R (2019) What are the respiratory effects of e-cigarettes? BMJ 366: I5275. https://doi.org/10.1136/bmj.l5275
17. Pavek P, Dvorak Z (2008) Xenobiotic-induced transcriptional regulation of xenobiotic metabolizing enzymes of the cytochrome P450 superfamily in human extrahepatic

tissues. Curr Drug Metab 9: 129-143. https://doi.org/10.2174/138920008783571774

18. Clunes LA, Bridges A, Alexis N, Tarran R (2008) *In vivo* versus *in vitro* airway surface liquid nicotine levels following cigarette smoke exposure. J Anal Toxicol 32: 201-207. https://doi.org/10.1093/jat/32.3.201
19. Ghosh A, Coakley RC, Mascenik T, Rowell TR, Davis ES, et al. (2018) Chronic e-cigarette exposure alters the human bronchial epithelial proteome. Am J Respir Crit Care Med 198: 67-76. https://doi.org/10.1164/rccm.201710-2033OC
20. Sun YW, Kosinska W, Guttenplan JB (2019) E-cigarette aerosol condensate enhances metabolism of benzo(a)pyrene to genotoxic products, and induces CYP1A1 and CYP1B1, likely by activation of the aryl hydrocarbon receptor. Int J Environ Res Public Health 16: 2468. https://doi.org/10.3390/ijerph16142468
21. McConnell R, Barrington-Trimis JL, Wang K, Urman R, Hong H, et al. (2017) Electronic cigarette use and respiratory symptoms in adolescents. Am J Respir Crit Care Med 195: 1043-1049. https://doi.org/10.1164/rccm.201604-0804OC
22. Braymiller JL, Barrington-Trimis JL, Leventhal AM, Islam T, Kechter A, et al. (2020) Assessment of nicotine and cannabis vaping and respiratory symptoms in young adults. JAMA Netw Open 3: e2030189-e2030189. https://doi.org/10.1001/jamanetworkopen.2020.30189
23. Alnajem A, Redha A, Alroumi D, Alshammasi A, Ali M, et al. (2020) Use of electronic cigarettes and secondhand exposure to their aerosols are associated with asthma symptoms among adolescents: a cross-sectional study. Respir Res 21: 300. https://doi.org/10.1186/s12931-020-01569-9
24. Schweitzer RJ, Wills TA, Tam E, Pagano I, Choi K (2017) E-cigarette use and asthma in a multiethnic sample of adolescents. Prev Med 105: 226-231. https://doi.org/10.1016/j.ypmed.2017.09.023
25. Cho JH, Paik SY (2016) Association between electronic cigarette use and asthma among high school students in South Korea. PLoS One 11: e0151022. https://doi.org/10.1371/journal.pone.0151022
26. Wong J, Magun BE, Wood LJ (2016) Lung inflammation caused by inhaled toxicants: a review. Int J Chron Obstruct Pulmon Dis 11: 1391-1401. https://doi.org/10.2147/COPD.S106009
27. Alexander LEC, Shin S, Hwang JH (2015) Inflammatory diseases of the lung induced by conventional cigarette smoke: a review. Chest 148: 1307-1322. https://doi.org/10.1378/chest.15-0409
28. Viegi G, Maio S, Pistelli F, Baldacci S, Carrozzi L (2006) Epidemiology of chronic obstructive pulmonary disease: health effects of air pollution. Respirology 11: 523-532. https://doi.org/10.1111/j.1440-1843.2006.00886.x
29. Makanya A, Anagnostopoulou A, Djonov V (2013) Development and remodeling of the vertebrate blood-gas barrier. Biomed Res Int 2013: 101597. https://doi.org/10.1155/2013/101597
30. Kyung SY, Jeong SH (2020) Particulate-matter related respiratory diseases. Tuberc Respir Dis 83: 116. https://doi.org/10.4046/trd.2019.0025
31. Crotty Alexander L, Fuster M, Montgrain P, Malhotra A (2015) The need for more e-cigarette data: a call to action. Am J Respir Crit Care Med 192: 275-276. https://doi.org/10.1164/rccm.201505-0915ED
32. Brożek GM, Jankowski M, Zejda JE (2019) Acute respiratory responses to the use of e-cigarette: an intervention study. Sci Rep 9: 6844. https://doi.org/10.1038/s41598-019-43324-1
33. Antoniewicz L, Brynedal A, Hedman L, Lundbäck M, Bosson JA (2019). Acute effects of electronic cigarette inhalation on the vasculature and the conducting airways. Cardiovasc Toxicol 19: 441-450. https://doi.org/10.1007/s12012-019-09516-x
34. Pulvers K, Nollen NL, Rice M, Schmid CH, Qu K, et al. (2020) Effect of pod e-cigarettes vs cigarettes on carcinogen exposure among African American and Latinx smokers: a randomized clinical trial. JAMA Netw Open 3: e2026324-e2026324. https://doi.org/10.1001/jamanetworkopen.2020.26324
35. Chaumont M, De Becker B, Zaher W, Culié A, Deprez G, et al. (2018) Differential effects of e-cigarette on microvascular endothelial function, arterial stiffness and oxidative stress: a randomized crossover trial. Sci Rep 8: 10378. https://doi.org/10.1038/s41598-018-28723-0
36. Moheimani RS, Bhetraratana M, Peters KM, Yang BK, Yin F, et al. (2017) Sympathomimetic effects of acute e-cigarette use: role of nicotine and non-nicotine constituents. *J Am Heart Assoc* 6(9): e006579. https://doi.org/10.1161/JAHA.117.006579
37. Fetterman JL, Keith RJ, Palmisano JN, McGlasson KL, Weisbrod RM, et al. (2020) Alterations in vascular function associated with the use of combustible and electronic cigarettes. J Am Heart Assoc 9: e014570. https://doi.org/10.1161/JAHA.119.014570
38. Moheimani RS, Bhetraratana M, Yin F, Peters KM, Gornbein J, et al. (2017) Increased cardiac sympathetic activity and oxidative stress in habitual electronic cigarette users: implications for cardiovascular risk. JAMA Cardiol 2: 278-284. https://doi.org/10.1001/jamacardio.2016.5303
39. Rader F, Rashid M, Nguyen TT, Luong E, Kim A, et al. (2020) E-cigarette use and subclinical cardiac effects. Circ Res 127: 1566-1567. https://doi.org/10.1161/CIRCRESAHA.120.316683
40. Farsalinos KE, Tsiapras D, Kyrzopoulos S, Savvopoulou M, Voudris V (2014) Acute effects of using an electronic nicotine-delivery device (electronic cigarette) on myocardial function: comparison with the effects of regular cigarettes. BMC Cardiovasc Disord 14: 78. https://doi.org/10.1186/1471-2261-14-78
41. Haptonstall KP, Choroomi Y, Moheimani R, Nguyen K, Tran E, et al. (2020) Differential effects of tobacco cigarettes and electronic cigarettes on endothelial function in healthy young people. Am J Physiol Heart Circ Physiol 319: H547-H556. https://doi.org/10.1152/ajpheart.00307.2020
42. Vogel EA, Prochaska JJ, Ramo DE, Andres J, Rubinstein ML (2019) Adolescents' E-cigarette use: increases in frequency, dependence, and nicotine exposure over 12 months. J Adolesc Health 64: 770-775. https://doi.org/10.1016/j.jadohealth.2019.02.019