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Immediate Respiratory Response to Electronic Cigarette Use

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Abstract

Background: Electronic cigarettes were originally designed to reduce adult dependency on normal cigarettes and as a tobacco cessation tool to substitute traditional cigarettes. But it has become the most popular among teenagers. **Rationale:** To investigate the immediate adverse respiratory effect of short-term electronic cigarette vapor inhalation. **Method:** Twenty-five subjects were randomly selected and used in this study. The respiratory resistance values were evaluated and used for comparison. The subjects were asked to breathe into the Airflow Perturbation Device (APD) for evaluation of their respiratory resistance before vaping (in triplicate). The same subjects, a minute later, were then asked to use one poke (3 seconds) of the e-Cigarette device to inhale e-Cigarette vapor with nicotine from a pod with 59 mg/ml nicotine. Immediately following the e-Cigarette use, their respiratory resistance was measured again (in triplicate). **Results:** Comparing the respiratory resistance values before and immediately after exposure to e-Cigarette vapor showed that their respiratory resistance increased almost immediately. **Conclusion:** Although there are long-term studies showing that the e-Cigarette is as harmful as regular cigarettes, this study showed a nearly immediate effect of using the e-Cigarette that significantly increased the respiratory resistance of the user. Very short exposure time to e-Cigarette vapor (3 seconds only), caused an immediate adverse physiologic effect in respiratory resistance.

Keywords

E-Cigarette, Respiratory Resistance, JUUL, E-Cigarette Vapor, Nicotine Pod, Airflow Perturbation Device (APD)

1. Introduction and Background

1.1. Tobacco Cigarette

Recreational use of tobacco has centuries of history. The adverse effects of tobacco smoke have long been associated with damage and disease of nearly every organ in the body. The most common diseases associated with tobacco smoke are a variety of cancers, as well as cardiovascular and respiratory diseases [1]-[7].

It is interesting to note that tobacco is the only legal drug that kills many of its users when used exactly as intended by its manufacturers. According to a World Health Organization (WHO) report, tobacco use is responsible for the death of nearly six million people across the world each year [7]. Recognizing this devastating smoking-related death rate, the western world has witnessed a drastic decline in cigarette use over the last few decades [8]. In this regard, in the US, one should not ignore the efforts made by the US Food and Drug administration (FDA). It should also be noted that the rate of smokers among the young population was in sharp increase at the time [9] [10] [11]. While the FDA and other advocacy groups were fairly successful in reducing tobacco smoking, another smoking alternative, the "electronic cigarette", rapidly gained popularity at the global scale.

1.2. Electronic Cigarette

As an alternative to the traditional smoking, in 2006 the electronic cigarette has been introduced to the market [12].

Electronic cigarettes are also known as "e-Cigarettes", "e-cigs", "vapes", "e-hookahs", "tank systems", "mods", "e-pipes", "Cigalikes", "APVs (Advanced Personal Vaporizers)", "electronic nicotine delivery systems (ENDS)", etc. They come in a variety of shapes, such as regular cigarettes, cigars, pipes, and some even look like USB flash drives, cigarette lighters, flashlights, pens, and other forms. Some include nicotine, but some don't. Some even include marijuana. One of the latest versions of the e-Cigarettes is known as the "JUUL". There are over 460 brands of e-Cigarettes available in the market [13].

An electronic cigarette is a battery-operated device that dispenses nicotine aerosol without burning tobacco and is easily available everywhere despite lack of quality control of their manufacturing process, and their health effects [14] [15] [16] [17]. As soon as manufacturing started, they rapidly gained popularity in many countries.

Although this device was originally designed to reduce adult dependency on normal cigarettes and as a tobacco cessation tool, it has become the most popular among teenagers. According to the manufacturers of JUULs, they were meant for smokers and are not recommended for non-smokers. Despite this, many adolescent non-smokers picked up JUUL for recreational purposes [18] [19] [20] [21].

Although use of combustible cigarettes among young population showed significant decline since the late 1990's, the use of electronic cigarettes of all types is

increasing globally. Even as soon as the introduction of the e-Cigarette to the market and despite lack of valid clinical data some scientists warned the public that the side effects of the e-Cigarettes may be even more devastating than from traditional cigarettes. Because of the lack of persuasive clinical data on potential negative health effects, authorities were not in a position to declare laws and regulations to this new smoking alternative. Until very recently, the FDA's authority to regulate nicotine in tobacco products was limited to tobacco-derived nicotine. Then, in March 2022, Congress closed the loophole that manufacturers were exploiting. The new law allows the FDA to regulate nicotine regardless of the source, and further prohibits menthol in cigarettes and prohibiting flavors in cigars [22].

Also because of its short history and novelty, only recently a few scientists and clinicians-initiated studies to investigate the possible harm that e-Cigarettes may cause to users. Here we briefly summarize the results of some of these investigations. Due to the short history of the e-Cigarettes, long term effects of e-Cigarette smoking have not yet been definitively established.

In an extensive study, Antoniewicz, *et al.* [23] looked at the acute effects of e-Cigarette aerosol inhalation with and without nicotine on the vasculature and the conducting airways of healthy subjects. The findings showed that the e-Cigarette aerosol with nicotine significantly increased blood pressure, heart rate, and arterial stiffness, It also caused obstruction of conducting airways which may cause acute impact on vascular and pulmonary functions. Chronic usage may lead to long term adverse health effects.

Vardavas, *et al.* [24], in their short-term study showed that short term exposure to e-Cigarette aerosol exposure rapidly increased the FeNO (fractional exhaled nitric oxide), respiratory impedance, and respiratory resistance.

A recent longitudinal analysis investigated the association of chronic respiratory disease (chronic obstructive pulmonary disease, chronic bronchitis, emphysema or asthma) with e-Cigarette use. When compared for combustible tobacco smoking, current e-Cigarette use was associated with incidence of respiratory disease by a factor of 1.29 [25].

In addition, a conclusive study by Cho and Paik [26] demonstrated that, among teenagers, more subjects with e-Cigarette use had asthma compared to those who did not use e-Cigarette, indicating that among the high school student group, e-Cigarette use can be a risk factor for asthma.

Qasim, *et al.* [27] demonstrated that short term e-Cigarette exposure increases the risk of thrombogenesis and enhances platelet function in rats. Although their short-term exposure was defined as 2 exposures of 200 puffs per day for 5 days, they demonstrated that e-Cigarette exposures alter physiological hemostasis and increase the risk of thrombogenic events. They attributed this, at least in part, to the hyperactivation state of platelets. Taken together, the data demonstrate for the first time that e-Cigarettes alter physiological hemostasis and increase the risk of thrombogenic events. This is attributable, at least in part, to the hyperactive state of platelets. Thus, the negative health consequences of e-Cigarette exposure

should not be underestimated and warrant further extensive investigation.

Rankin, *et al.* [28] assessed the toxic potential of e-Cigarettes and concluded that the e-Cigarette aerosol can alter the viability, inflammation, oxidative stress and genotoxicity of the human lung epithelial cell lines. In particular, they found that e-Cigarette aerosol containing nicotine, volatile organic compounds, aldehydes and polycyclic aromatic hydrocarbons decreased cell viability and increased DNA damage.

Hedman, *et al.* [29], in their extensive study of over 30,000 subjects, found that respiratory symptoms were more common among e-Cigarette users compared to cigarette smokers.

In the most recent study, Adzrago, *et al.* [30], looked at behavioral associations of e-Cigarette use. Their results indicate that moderate or severe anxiety or depression symptoms were more likely for current e-Cigarette users compared to former e-cigarette users.

In the last few years there has been growing evidence of the harmful effects of e-Cigarettes in pulmonary health including reports of "e-Cigarette or vaping use associated lung injury (EVALI)", originally known as "vaping associated pulmonary illness (VAPI)", gas exchange disturbance, reduced lung function, increased airway inflammation and oxidative stress, downregulation of immunity and increased risk of respiratory infection [31].

The aim of this study is to investigate whether the use of e-Cigarette could have an immediate effect on respiratory mechanics.

2. Methods

Using a University of Maryland IRB approved protocol, respiratory resistance of 25 subjects was measured before and after using the e-Cigarette, so that in this case each subject was his/her own control. This included 24 male and one female subjects, 21 were Caucasian, three were Hispanic and one was Asian. The subjects were between 19 to 55 years of age (with only one 53 and one 55 years old). Subjects were selected regardless of their race, sex, and history of regular cigarette or e-Cigarette use.

For this work the respiratory resistance value of the subjects before and after the use of the e-Cigarette was used. The respiratory resistance was measured using the Airflow Perturbation Device (the APD). All subjects were tested with the same e-Cigarette device as well as the same APD unit. All e-Cigarettes had a similar nicotine pod with 59 mg/ml nicotine.

2.1. Brief Description of the APD

The Airflow Perturbation Device (APD) was initially developed as a simple, noninvasive, inexpensive, portable, and effortless respiratory diagnostic device for adults [32]-[38].

The APD measures resistance of the respiratory system by periodically inserting a known added resistance in the flow path by means of a rotating wheel with open and screened segments. The added resistance causes a slight decrease in

airflow and a change in mouth pressure. The magnitudes of the flow and pressure perturbations depend on the relative resistance inside the patient's respiratory system and resistance of the APD itself. By measuring mouth pressure and airflow rate, with and without the APD resistance inserted into the path of the airflow, external resistance becomes known, and the internal respiratory resistance can then be easily determined noninvasively. The resistance (in $cmH_2O/l/s$) is calculated by simply dividing the mouth pressure change, or perturbation, by the flow perturbation. In general, respiratory resistance in exhalation is slightly higher than respiratory resistance in inhalation.

APD measurements were favorably compared with spirometry, body plethysmograph, and IOS in adults [39]-[44]. It was used in exercising subjects [45], and on subjects with paradoxical vocal fold motion [46] [47] [48] [49] [50]. The APD has also been used in a variety of other research projects, such as: Influence of nasal congestion on respiratory resistance [51]; testing low doses of caffeine on respiratory resistance [52]; comparison with esophageal balloon [53]; diurnal effects of respiratory resistance [54]; identification of patients with reactive airways [55]; optimization of airway caliber [56]; results using nasal strips [57]; and induced anxiety [58]. Recently the APD was also used in assessment of bronchodilator response in children with asthma exacerbation [59].

2.2. Details of the Measurements

To use the APD, a disposable antimicrobial filter was attached to the pneumotachometer of the APD. This antimicrobial filter is a standard antimicrobial filter used at many Pulmonary Function Test clinics. A nose clip was also used to assure mouth only breathing. The users were instructed to seal the antimicrobial filter with their lips to avoid any air leak. Each subject was asked to sit in an upright position against the back of a chair and normally breathe in-and-out of the APD. They were also asked to make sure to keep their tongue flat on the base of the mouth in order not to block or reduce the air flow while breathing. Because this was a research project, each respiratory resistance measurement was repeated in triplicates. The APD is set to measure the respiratory resistance for one minute, after which the device automatically stops, and 3 separate values of the respiratory resistance (in inhalation, exhalation, and the mathematical average) were displayed on the screen of the APD. The measurements were consistently repeated after one minute wait time.

Exactly the same measurements were performed before the use of the e-Cigarette (baseline control), and a minute later after using the e-Cigarette (experimental). For the experimental condition subjects were asked to use the e-Cigarette vapor (inhale) for one poke (3 seconds) only. This was monitored by the person who was conducting the experiment, and at the 3-second timeline the subject was asked to stop using the e-Cigarette. After each measurement the data from the APD screen were copied into an Excel spreadsheet for further analysis. A total of 6 measurements (one minute apart) were recorded.

3. Analysis and Results

The database was a simple one. Figure 1 shows average Respiratory Resistance values in inhalation and exhalation for the 25 subjects. Respiratory resistance in exhalation is, as expected, slightly higher than Inhalation respiratory resistance for all subjects except two that were reversed. Resistance changes after vaping for six subjects were negligible (perhaps within the sensitivity of the APD measurement). For the two subjects for whom the respiratory resistance reduced, this can be due to the existence of a disorder called "Paradoxical Vocal Fold Motion (PVCM)" [46] [47] [48] [49] [50]. This, however, may not be true here because our sample size is fairly small and also other tests such as laryngoscopy is needed to definitively identify the existence of PVCM [46].

Figure 2 shows the average Respiratory Resistance vales for all 25 subjects before the use of e-Cigarette (Avg), and after exposure to the e-Cigarette (JAvg). As can be seen, in general the Respiratory resistance values increased significantly for all subjects after e-Cigarette use (only for 3 seconds), except for 2 that slightly decreased; 4 also showed no change.

We have also looked at the inhalation and exhalation resistance values before and after e-Cigarette exposure to see which resistance (inhalation or exhalation) was responsible for the changes seen in Figure 2. Comparing Figure 3 and Figure 4 may indicate that e-Cigarette exposure affects inhalation somewhat more than exhalation.

4. Statistical Analysis

Table 1 shows the averages of the Respiratory Resistance Values (with Standard Error of the Mean, SEM) for both cases, before and after e-Cigarette smoking. Although this study was based on a small number of subjects, a student t-test was conducted and indicated that the 3 seconds exposure to e-Cigarette vapor significantly increased the Respiratory Resistance value (at $p = 0.0001$ level).

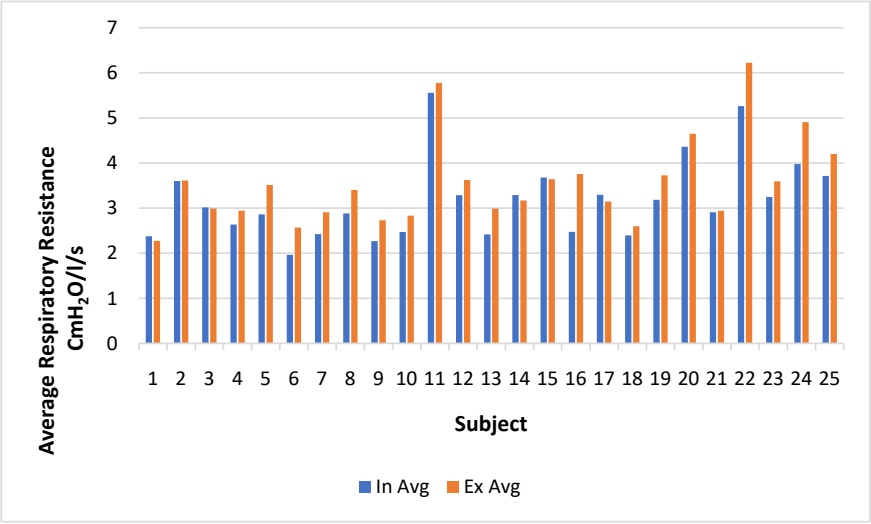

Figure 1. Respiratory resistance values in inhalation and exhalation.

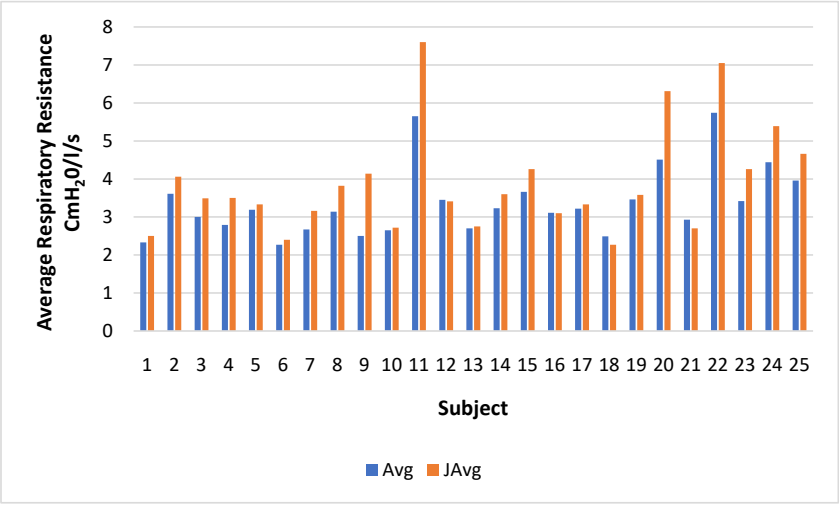

Figure 2. Average respiratory resistance values before and after e-Cigarette use.

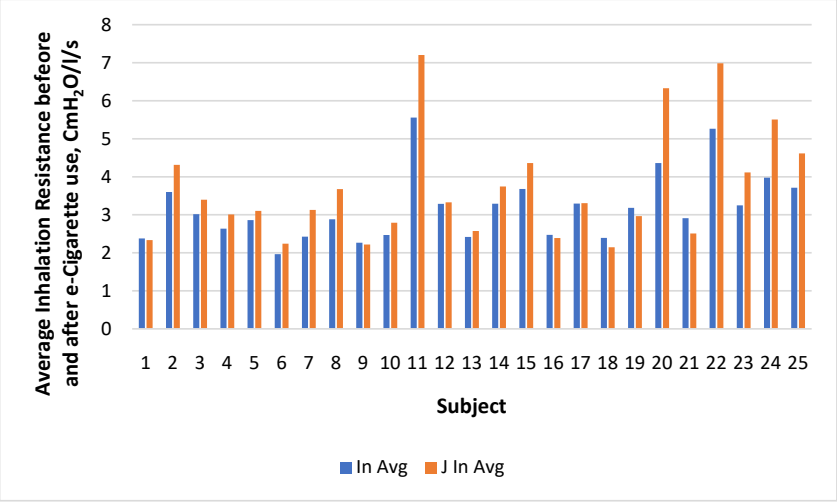

Figure 3. Inhalation respiratory resistance values before and after e-Cigarette use.

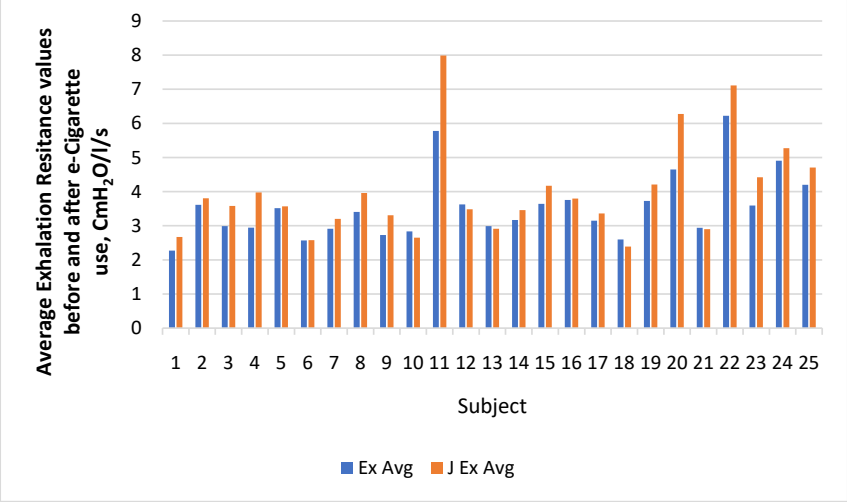

Figure 4. Exhalation respiratory resistance values before and after e-Cigarette use.

Table 1. Respiratory Resistance values before and after e-Cigarette smoking.

	Average Respiratory Resistance before smoking	Average Respiratory Resistance after e-Cigarette smoking
Average ± SEM $cmH_2O/l/s$	3.365 ± 0.282	3.896 ± 0.430

5. Discussion

To our knowledge, this is the first study to investigate an immediate physiologic response after inhalation from an e-Cigarette. Based on the findings of this small sample study, the use of even one poke e-Cigarette inhalation for 3 seconds demonstrated a statistically significant increase in respiratory resistance. Increased resistance has been shown to precede changes in pulmonary function of patients with obstructive airway diseases such as COPD and asthma. It is possible that this measurable effect on respiratory system may indicate a similar health effect. Given that e-Cigarette users typically use the device longer than 3 seconds several times a day may have a greater respiratory health impact. Future studies with a large number of subjects and longer e-Cigarette exposure time will be needed to determine short and long term effects of e-Cigarette in pulmonary mechanics and respiratory health.

In smoking the inhaled nicotine entered the body is rapidly distributed through the bloodstream and crosses the blood-brain barrier and reaches the brain within 10 - 20 seconds after inhalation [60]. In this work we have shown that the inhaled nicotine starts adversely affecting the pulmonary system in only 3 seconds.

6. Conclusion

Very short exposure time to e-Cigarette vapor (3 seconds only), caused an immediate adverse physiologic effect in respiratory resistance. Further research on the effects of short and long term usage of e-Cigarette in respiratory physiology and pulmonary health will be worthy of investigation.

Acknowledgements and Disclosures

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Authors' Contributions

All authors contributed to the study conception and design; Jake Morales and Jafar Vossoughi contributed to the subject data collection; Jafar Vossoughi and Arthur Johnson conducted the data analysis; all four authors contributed to the manuscript preparation and editing.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] US Department of Health and Human Services (2014) The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. National Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, Atlanta.

[2] US Department of Health and Human Services (2010) How Tobacco Smoke Causes Disease: What It Means to You. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, Atlanta.

[3] US Department of Health and Human Services (2014) The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. US Department of Health and Human Services, CDC, Atlanta. https://www.ncbi.nlm.nih.gov/books/NBK179276/pdf/Bookshelf_NBK179276.pdf

[4] Gentzke, A.S., Wang, T.W., Cornelius, M., *et al.* (2022) Tobacco Product Use and Associated Factors among Middle and High School Students—National Youth Tobacco Survey, United States, 2021. *Morbidity and Mortality Weekly Report* (*MMWR*), **71**, 1-29. https://doi.org/10.15585/mmwr.ss7105a1

[5] Centers for Disease Control and Prevention (2013) QuickStats: Number of Deaths from 10 Leading Causes—National Vital Statistics System, United States, 2010. *Morbidity and Mortality Weekly Report*, **62**, 155.

[6] Lim, S.S., Vos, T., Flaxman, A.D., *et al.* (2012) A Comparative Risk Assessment of Burden of Disease and Injury Attributable to 67 Risk Factors and Risk Factor Clusters in 21 Regions, 1990-2010: A Systematic Analysis for the Global Burden of Disease Study 2010. *Lancet*, **380**, 2224-2260. https://doi.org/10.1016/S0140-6736(12)61766-8

[7] World Health Organization (2008) WHO Report on the Global Tobacco Epidemic, 2008. The MPOWER Package. WHO, Geneva.

[8] World Health Organization (2015) WHO Global Report on Trends in Prevalence of Tobacco Smoking 2015. WHO Library Cataloguing-in-Publication Data. WHO, Geneva.

[9] US Department of Health and Human Services (2016) E-Cigarette Use among Youth and Young Adults: A Report of the Surgeon General. US Department of Health and Human Services, CDC, Atlanta.

[10] U.S. Department of Health and Human Services (2012) Preventing Tobacco Use among Youth and Young Adults: A Report of the Surgeon General. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, Atlanta.

[11] Park, L.E., Ren, C., Cooper, M., Cornelius, M., Jamal, A. and Cullen, K.A. (2022) Tobacco Product Use among Middle and High School Students—United States, 2022. *Morbidity and Mortality Weekly Report*, **71**, 1429-1435. https://doi.org/10.15585/mmwr.mm7145a1

[12] The Evolution and Impact of Electronic Cigarettes, 2006. https://nij.ojp.gov/topics/articles/evolution-and-impact-electronic-cigarettes#:~:text=Electronic%20cigarettes%2C%20first%20introduced%20in,a%20range%20of%20illicit%20drugs

[13] Zhu, S.-H., Sun, J.Y., Bonnevie, E., *et al.* (2014) Four Hundred and Sixty Brands of E-Cigarettes and Counting: Implications for Product Regulation. *Tobacco Control*, **23**, iii3-iii9. https://doi.org/10.1136/tobaccocontrol-2014-051670

[14] Laugesen, M. (2008) Safety Report on the Ruyan E-Cigarette Cartridge and Inhaled Aerosol. Health New Zealand, Christchurch, 1-22.

[15] Trtchounian, A. and Talbot, P. (2010) Electronic Nicotine Delivery Systems: Is There a Need for Regulation? *Tobacco Control*, **20**, 47-52. https://doi.org/10.1136/tc.2010.037259

[16] Flouris, A.D. and Oikonomou, D.N. (2010) Electronic Cigarettes: Miracle or Menace? *BMJ*, **340**, Article No. c311. https://doi.org/10.1136/bmj.c311

[17] Goniewicz, M.L., Gupta, R., Lee, Y.H., *et al.* (2015) Nicotine Levels in Electronic Cigarette Refill Solutions: A Comparative Analysis of Products from the US, Korea, and Poland. *International Journal of Drug Policy*, **26**, 583-588. https://doi.org/10.1016/j.drugpo.2015.01.020

[18] QuickStats: Cigarette Smoking Status among Current Adult E-Cigarette Users, by Age Group—National Health Interview Survey, United States, 2015. *Morbidity and Mortality Weekly Report*, **65**, 1177. https://doi.org/10.15585/mmwr.mm6542a7

[19] Schraufnagel, D.E., Blasi, F., Drummond, M.B., *et al.* (2014). Electronic Cigarettes. A Position Statement of the Forum of International Respiratory Societies. *American Journal of Respiratory and Critical Care Medicine*, **190**, 611-618. https://doi.org/10.1164/rccm.201407-1198PP

[20] Ayers, J.W., Ribisl, K.M. and Brownstein, J.S. (2011) Tracking the Rise in Popularity of Electronic Nicotine Delivery Systems (Electronic Cigarettes) Using Search Query Surveillance. *American Journal of Preventive Medicine*, **40**, 448-453. https://doi.org/10.1016/j.amepre.2010.12.007

[21] Noel, J.K., Rees, V.W. and Connolly, G.N. (2011) Electronic Cigarettes: A New 'Tobacco' Industry? *Tobacco Control*, **20**, Article No. 81. https://doi.org/10.1136/tc.2010.038562

[22] Sircar, N. and Attorney, S. (2022) 8/25/22-2022 FDA Updates—E-Cigarettes, Synthetic Nicotine, & Flavors. Public Health Law Center. https://www.publichealthlawcenter.org/commentary/220825/8/25/22-2022-fda-updates-e-cigarettes-synthetic-nicotine-flavors

[23] Antoniewicz, L., Brynedal, A., Hedman, L., Lundbäck, M. and Bosson, J.A. (2019) Acute Effects of Electronic Cigarette Inhalation on the Vasculature and the Conducting Airways. *Cardiovascular Toxicology*, **19**, 441-450. https://doi.org/10.1007/s12012-019-09516-x

[24] Vardakas, C.I., Anagnostopoulos, N., Kougias, M., *et al.* (2012). Short-Term Pulmonary Effects of Using an Electronic Cigarette: Impact on respiratory Flow Resistance, Impedance, and Exhaled Nitric Oxide. *Chest*, **141**, 1400-1406. https://doi.org/10.1378/chest.11-2443

[25] Bhatta, D.N. and Glantz, S.A. (2019) Association of E-Cigarette Use with Respiratory Disease among Adults: A Longitudinal Analysis. *American Journal of Preventive Medicine*, **58**, 182-190. https://doi.org/10.1016/j.amepre.2019.07.028

[26] Cho, J.H. and Paik, S.Y. (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

[27] Qasim, H., Karim, Z.A., Silva-Espinoza, J.C., *et al.* (2018) Short-Term E-Cigarette Exposure Increases the Risk of Thrombogenesis and Enhances Platelet Function in Mice. *Journal of the American Heart Association*, **7**, e009264. https://doi.org/10.1161/JAHA.118.009264

[28] Rankin, G.D., Wingfors, H. Uski, O., *et al.* (2019). The Toxic Potential of a Fourth-Generation E-Cigarette on Human Lung Cell Lines Tissue and Tissue Ex-

plants. *Journal of Applied Toxicology*, **39**, 1143-1154. https://doi.org/10.1002/jat.3799

[29] Hedman, L., Backman, H., Stridsman, C., *et al.* (2018). Association of Electronic Cigarette Use with Smoking Habits, Demographic Factors, and Respiratory Symptoms. *JAMA Network Open*, **1**, e180789. https://doi.org/10.1001/jamanetworkopen.2018.0789

[30] Adzrago, D., Fujimoto, K., Harrell, M.B., Jones, A. and Wilkerson, M. (2023) Association between E-Cigarette Use Behaviors and Perceived Harmfulness of E-Cigarettes and Anxiety/Depression Symptoms among Black/African American Adults. *Preventive Medicine Reports*, **31**, Article ID: 102080. https://doi.org/10.1016/j.pmedr.2022.102080

[31] E-Cigarette or Vaping Use-Associated Lung Injury (EVALI). American Lung Association. https://www.lung.org/lung-health-diseases/lung-disease-lookup/evali

[32] Lausted, C.G. and Johnson, A.T. (1999) Respiratory Resistance Measured by an Airflow Perturbation Device. *Physiological Measurement*, **20**, 21-35. https://doi.org/10.1088/0967-3334/20/1/002

[33] Johnson, A.T., Lin, C.S. and Hochheimer, J.N. (1984) Airflow Perturbation Device for Measuring Airways Resistance of Humans and Animals. *IEEE Transactions on Biomedical Engineering*, **31**, 622-626. https://doi.org/10.1109/TBME.1984.325306

[34] Silverman, N.K., Johnson, A.T., Scott, W.H. and Koh, F.C. (2005) Exercise-Induced Respiratory Resistance Changes as Measured with the Airflow Perturbation Device. *Physiological Measurement*, **26**, 29-38. https://doi.org/10.1088/0967-3334/26/1/003

[35] Vossoughi, J., Johnson, A.T., Silverman, N.K. (2006) In-Home Hand-Held Device to Measure Respiratory Resistance. 1*st Transdisciplinary Conference on Distributed Diagnosis and Home Healthcare*, Arlington, 2-4 April 2006, 12-15. https://doi.org/10.1109/DDHH.2006.1624785

[36] Johnson, A.T., Scott, W.H., Russek-Cohen, E., *et al.* (2007) Resistance Values Obtained with the Airflow Perturbation Device. *International Journal of Medical Implants and Devices*, **2**, 45-58.

[37] Lopresti, E.R., Johnson, A.T., Koh, F.C., *et al.* (2008) Testing Limits to Airflow Perturbation Device (APD) Measurements. *BioMedical Engineering Online*, **7**, Article No. 28. https://doi.org/10.1186/1475-925X-7-28

[38] Shade, D.M. and Johnson, A.T. (2010) Design of Respiratory Devices. In: Kutz, M., Ed., *Standard Handbook of Biomedical Engineering and Design*, 2nd Edition, McGraw-Hill, New York, 111-142.

[39] Goldman, M.D., Lemert, J., Vossoughi, J., *et al.* (2006) Airflow Perturbation Device Reflects Forced Oscillation Indices of Peripheral Airway Obstruction. *Chest*, **130**, 160S. https://doi.org/10.1378/chest.130.4_MeetingAbstracts.160S-e

[40] Lemert, J., Goldman, M.D., Johnson, A., *et al.* (2006) Portable Hand-Held Airflow Perturbation Device Reflects Forced Oscillation Resistance in Children with Asthma. *Chest*, **130**, 241S. https://doi.org/10.1378/chest.130.4_MeetingAbstracts.241S-c

[41] Whitesell, P., Whitesell, J., Vossoughi, J. and Johnson, A. (2012) Comparison of Airflow Perturbation Device and Impulse Oscillometry Measurements of Airway Resistance. *Chest*, **142**, 783A. https://doi.org/10.1378/chest.1388780

[42] Haque, T., Vossoughi, J., Johnson, A.T., *et al.* (2013) Resistance Measured by Airflow Perturbation Compared with Standard Pulmonary Function Measures. *Journal of Respiratory Diseases*, **3**, 63-67. https://doi.org/10.4236/ojrd.2013.32010

[43] Holley, A.B., Boose, W.D., Perkins, M., *et al.* (2018) A Rapid, Handheld Device to

Assess Respiratory Resistance: Clinical and Normative Evidence. *Military Medicine*, **183**, e370-e377. https://doi.org/10.1093/milmed/usx224

[44] Pan, J., Saltos, A., Smith, D., Johnson, A. and Vossoughi, J. (2013) Comparison of Respiratory Resistance Measurements Made with an Airflow Perturbation Device with Those from Impulse Oscillometry. *Journal of Medical Engineering*, **2013**, Article ID: 165782. https://doi.org/10.1155/2013/165782

[45] Johnson, A.T., Chapain, P., Slaughter, D., Gallena, S. and Vossoughi, J. (2013). Inspiratory and Expiratory Resistances during Exercise. *British Journal of Medicine & Medical Research*, **3**, 1222-1232. https://doi.org/10.9734/BJMMR/2013/2409

[46] Gallena, S.J.K., Tian, W., Johnson, A.T., *et al.* (2013) Validity of a New Respiratory-Resistance Measurement Device to Detect Glottal-Area Change. *Journal of Voice*, **27**, 299-304. https://doi.org/10.1016/j.jvoice.2013.01.006

[47] Gallena, S.J.K., Solomon, N.P., Johnson, A.T., Vossoughi, J. and Tian, W. (2014) The Effect of Exercise on Athletes with and without Paradoxical Vocal Fold Motion Disorder. *American Journal of Speech-Language Pathology*, **24**, 470-479. https://doi.org/10.1044/2015_AJSLP-14-0110

[48] Gallena, S.J.K., Solomon, N.P., Johnson, A.T., Vossoughi, J. and Tian, W. (2014) Test-Retest Reliability of Respiratory Resistance Measured with the Airflow Perturbation Device. *Journal of Speech, Language, and Hearing Research*, **57**, 1323-1329. https://doi.org/10.1044/2014_JSLHR-S-13-0246

[49] Gallena, S.J.K., Johnson, A.T. and Vossoughi, J. (2018) Short-Term Intensive Therapy and Outcomes for Athletes with Paradoxical Vocal Fold Motion Disorder. *The American Journal of Speech-Language Pathology*, **28**, 83-95. https://doi.org/10.1044/2018_AJSLP-17-0223

[50] Solomon, N.P., Pham, A., Gallena, S., *et al.* (2022) Resting Respiratory Resistance in Female Teenage Athletes with and without Exercise-Induced Laryngeal Obstruction. *Journal of Voice*, **36**, 734.E1-734.E6. https://doi.org/10.1016/j.jvoice.2020.09.002

[51] Awowale, A., Johnson, A. and Vossoughi, J. (2015) Influence of Nasal Congestion on Respiratory Resistance Values. *Journal of Pulmonary & Respiratory Medicine*, **5**, Article No. 228. https://doi.org/10.4172/2161-105X.1000228

[52] Montgomery, M.K., Luk, A., Johnson, A.T. and Vossoughi, J. (2017) Testing Low Doses of Caffeine on Respiratory Resistance Using the Airflow Perturbation Device. *Open Journal of Respiratory Diseases*, **7**, 53-61. https://doi.org/10.4236/ojrd.2017.72006

[53] Coursey, D.C., Scharf, S.M. and Johnson, A.T. (2011) Comparison of Expiratory Isovolume Pressure-Flow Curves with the Stop-Flow versus the Esophageal-Balloon Method. *Respiratory Care*, **56**, 969-975. https://doi.org/10.4187/respcare.01037

[54] Rausch, N.Z., Johnson, A.T. and Vossoughi, J. (2018) Diurnal Effects of Respiratory Resistance Using an Airflow Perturbation Device. *Archives of Pulmonology*, **1**, 41-48.

[55] Patel, S.U., Rosen, R., Johnson, A.T. and Vossoughi, J. (2018) Identification of Patients with Reactive Airways at Ambient Temperatures. *Archives of Pulmonology*, **1**, 23-29.

[56] Johnson, A.T., Jones, S.C., Pan, J.J. and Vossoughi, J. (2012) Variation of Respiratory Resistance Suggests Optimization of Airway Caliber. *IEEE Transactions on Biomedical Engineering*, **59**, 2355-2361. https://doi.org/10.1109/TBME.2012.2204055

[57] Wong, L.S. and Johnson, A.T. (2004) Decrease of Resistance to Air Flow with Nasal Strips as Measured with the Airflow Perturbation Device. *BioMedical Engineering OnLine*, **3**, Article No. 38. https://doi.org/10.1186/1475-925X-3-38

[58] Bohensky, M., Johnson, A.T. and Vossoughi, J. (2017) Effect of Induced Anxiety on Respiratory Resistance Using Virtual Reality Simulation. *Open Journal of Respiratory Diseases*, **7**, 68-82. https://www.scirp.org/journal/paperinformation.aspx?paperid=76455

[59] Bautista, M.V., Vossoughi, J., Johnson, A.T. and Keszler, M. (2021) Assessment of Bronchodilator Response in Children with Asthma Exacerbation Using the Respiratory Resistance Values. *Open Journal of Respiratory Diseases*, **11**, 117-132. https://doi.org/10.4236/ojrd.2021.114011

[60] Le Houezec, J. (2003) Role of Nicotine Pharmacokinetics in Nicotine Addiction and Nicotine Replacement Therapy: A Review. *The International Journal of Tuberculosis and Lung Disease*, **7**, 811-819.