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Review article

The Potential Short- and Long-Term Health Effects of Post-pandemic Teen Vaping

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Abstract

The COVID-19 pandemic has negatively impacted mental health throughout our society. Despite this, studies report that vaping among teens and young adults has decreased during the pandemic. This paper aims to analyze why COVID-19 impacted vaping in such a way and if that change will remain consistent as we head toward the end of the pandemic. Additionally, using PubMed and Google Scholar, we examined the different mental and physical effects of vaping and what that means for the future. Studies from the early stages of the pandemic show vaping rates among teens and young adults to be decreasing due to health concerns. However, as people become less concerned about COVID-19, vaping rates have begun to increase. The potential future health effects are unknown and need to be evaluated further.

Keywords: ***vaping; e-cigarettes; adolescent; COVID-19; health effects; long-term health effects***

1. Introduction

Over the past ten years, there has been a rapid increase in vaping rates among teens and young adults. For example, between 2011 and 2019, the percentage of high schoolers who vaped went from 1.5% to 27.5% [1]. The COVID-19 pandemic also negatively impacted mental health [2]. Since stress and depression are both key reasons why teens started to vape, the pandemic could have also contributed to an increase in vaping [3]. However, various surveys express conflicting results on the youth vaping trend during the COVID-19 pandemic.

E-cigarettes are marketed as a less harmful alternative to the traditional cigarette [4]. Although this may be the case, that does not mean they are completely harmless. However, evidence shows that vaping may cause harm to physical and mental health due to the toxic metals and chemicals found in vapes [5]. Lung damage caused by e-cigarettes has increased in recent years [6]. For instance, a total of 2807 E-cigarette or Vaping use Associated Lung Injury (EVALI) cases have been reported since just 2020 [6]. Additionally, nicotine, a main component of e-cigarettes, has been shown to harm mental health and cause brain damage [1,7]. Other components of vapes include various heavy metals and carcinogens that have potentially harmful effects [5].

Although e-cigarettes show harmful effects in the short term, the potential long-term effects of vaping haven't been thoroughly researched. Since vapes were only released into the market in 2007, the effects of long-term vaping may become prevalent in a few years. With less than 90% of e-cigarette users having vaped for less than 4 years and 80% that have vaped for less than one year, it may be a while before we see the long-term effects of e-cigarettes [8]. However, this does not mean that the long-term effects are not foreseeable. The purpose of this paper is to determine the magnitude of the short-term and long-term health effects of e-cigarettes by analyzing the effects of the COVID-19 pandemic on the trend of vaping among teens and young adults.

2. Generations of E-cigarettes and their Effects on Health

The first generation of vapes were disposable e-cigarettes (**Figure 1**). This type of e-cigarette was only designed to be used once and to be disposed of, not recharged or refilled. These are often referred to as "cigalikes" since they are designed to mimic the look and feel of traditional cigarettes [9].

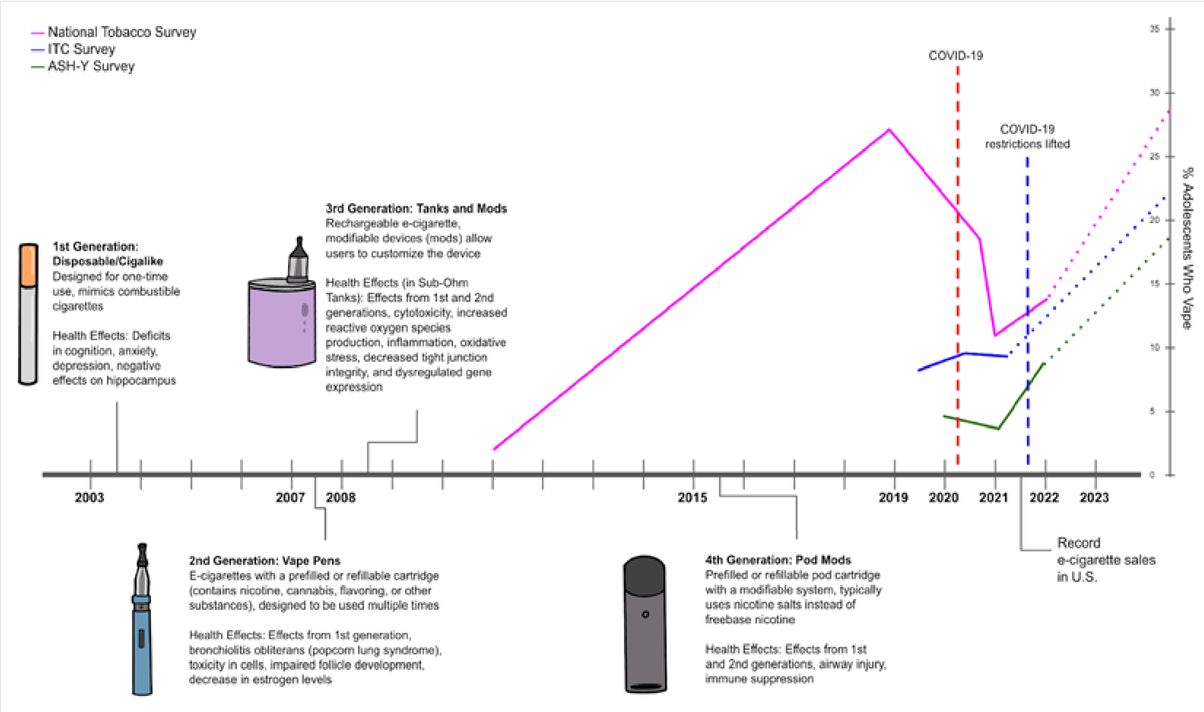

Figure 1: E-cigarette generations' health effects and youth vaping trends from 2003 to 2023. Data from the National Tobacco Survey (purple line), ITC Survey (blue line), and ASH-Y Survey (green line) point to an initial decrease in vaping rates after COVID-19 (indicated by the broken red line) and an increase after COVID-19 restrictions (indicated by the blue broken blue line) were lifted. The dotted lines are the predicted adolescent vaping trends in the near future.

The second generation of e-cigarettes are e-cigarettes that contain a prefilled or refillable cartridge (**Figure 1**). These cartridges can be filled with substances including nicotine, cannabis, flavoring, or solvents. The cartridge is also attached to a battery pen [9]. The flavoring introduced in this generation, such as cinnamaldehyde, benzaldehyde, diacetyl, 3-pentadione, vanillin, acetoin, and triacetin, have shown to be very toxic to cells [10]. For instance, studies have shown that when inhaled, diacetyl produces morphological changes in the liver and toxicity in cells which may cause bronchiolitis obliterans or "popcorn lung syndrome" [10]. Additionally, the introduction of a refillable e-liquid has been shown to pose a threat to follicular development and decrease estrogen concentration in ovaries in rats [11].

The third generation of e-cigarettes is composed of tanks or mods (**Figure 1**). The third generation of e-cigarettes are rechargeable and are designed to be used multiple times, similar to the second generation [9]. Mods are modifiable devices that allow e-cigarette users to customize the substances in the device such as flavoring or delivery. Tanks are the part of an e-cigarette that contains the e-liquid and the coil that vaporizes the e-liquid [9]. One type of tank, a Sub-Ohm tank, contains low-resistance coils. This results in a larger delivery of nicotine or other substances [9,12]. One study showed that cells that were exposed to butter-flavored or cinnamon flavored e-cigarette aerosol in a Sub-Ohm tank displayed significant cytotoxicity, increased reactive oxygen species production, inflammation, oxidative stress, decreased tight junction integrity, and dysregulated gene expression [12].

The fourth generation of e-cigarettes is called Pod Mods, an e-cigarette product with a prefilled or refillable pod cartridge with a modifiable system (**Figure 1**). These prefilled pod cartridges can contain nicotine, tetrahydrocannabinol, or cannabidiol with or without flavoring [9]. Additionally, Pod Mods typically use nicotine salts rather than freebase nicotine used in previous e-cigarette products. Nicotine salts have a lower pH than freebase nicotine, allowing easier inhalation of nicotine [9,13]. Additionally, nicotine salts are more likely to be absorbed into the body than freebase nicotine which may increase the risk of respiratory illness by altering inflammatory responses in the lung epithelium [13]. Fourth-generation e-cigarette users expressed airway injury and had more bronchial epithelial cells in the sputum [13]. Furthermore, fourth-generation e-cigarettes have caused lower concentrations of C-reactive protein, monocyte chemo-attractant protein-1, matrix metalloproteinase 2, uteroglobin, and vascular endothelial growth factor in comparison to third-generation e-cigarettes and resulted in lower concentrations of soluble intracellular adhesion molecular-1 and soluble vascular cell adhesion molecule-1 compared to non-smokers, smokers, and third generation e-cigarette users [14]. This suggests the overall immune suppression caused by fourth-generation e-cigarettes which may be attributable to the inhalation of high concentrations of nicotine salts [14,15].

3. COVID-19's Impacts on Vaping Trends

Vaping rates in teens and adolescents experienced a surge in the last decade. From 2011 to 2019 alone, the percentage of high schoolers who used e-cigarettes increased from 1.5% to 27.5% or 4.11 million high school students who vaped in 2019 [1,16].

However, the COVID-19 pandemic impacted vaping and the reports on the vaping rate are complex. A study conducted in May 2020 showed that 56.4% of those who originally vaped reported a change in their e-cigarette use due to the pandemic. Within those that changed their usage, 32.8% reported they quit vaping and 35.3% reduced their e-cigarette use. On the other hand, 25.4% of the respondents that changed their usage reported increasing their vaping and 43.6% continued to vape at the same rate [1]. Later on, the National Youth Tobacco Survey, released in September 2020, reported that 19.6%, or 3.6 million, of high school students currently vaped compared to the 27.5% of high schoolers vaping before the pandemic [1,17].

A comparison between youth vaping during late 2019 and late 2020 expressed that more teens quit e-cigarettes than initiated use. Out of those who vaped from September to December 2019, 38.7% quit e-cigarettes from September to December 2020. Additionally, 6.3% of non-vapers in 2019 initiated use during 2020. It was also noted that there was a correlation between exposure to COVID-19 news and e-cigarette use [18]. Moreover, out of a survey of 12th-graders in the United States during the fall of 2020, 44.4%

reported decreasing e-cigarette usage whereas 16.8% and 38.9% reported in-creasing and no change respectively [19].

The vaping prevalence in 16-19-year-olds according to the 2021 ITC survey was 9.1% in February 2021. However, the same survey gathered that the prevalence of e-cigarette use was 9.4% in February 2020 and 7.7% in August 2019 [20]. This can be explained because public anxiety about COVID-19 wasn't prominent during February 2020.

Furthermore, national e-cigarette sales in the US hit a record in June 2021, reaching 22.44 million units sold [17]. It is also noted that vaping prevalence in teens has been recently increasing [20,21]. The 2020 ASH-Y survey of 11 to 18-year-olds states that vaping prevalence was 8.6% compared with 4% in 2021 and 4.8% in 2020 which illustrates the initial decrease in e-cigarette usage during the pandemic and the more recent increase [20]. Additionally, the 2022 National Youth Tobacco Survey reports an increase of 14.1% of adolescents who use e-cigarettes compared to 11.3% in 2021 [21]. We can conclude that the COVID-19 pandemic briefly decreased youth vaping rates but youth vaping is continuing to rise.

The COVID-19 pandemic implemented many regulations to stop the spread of the disease. Social distancing, the closure of schools, and businesses (such as vape shops) being shut down are all factors that could potentially affect the number of teens that use e-cigarettes [22]. Since the U.S. Food and Drug Administration requires those who purchase tobacco products (including e-cigarettes although their main ingredient is nicotine) to be above the age of 21, this may decrease vaping rates [23]. According to a study conducted in 2020, 19.5% of participants who decreased their usage over the pandemic stated that it was solely because they could not get products to vape [1]. The COVID-19 pandemic has caused approximately 20% of youth vapers to switch to online stores [1]. However, the impact of legislation and pandemic isolation on e-cigarette use is unclear since studies indicate that underage vaping did not increase more than vaping among those aged 21 and above [1]. Additionally, 15.2% of youth e-cigarette users re-ported that other reasons for their decreased use included that parents would know [1]. Another paper reported that 22% of youth decreased their vaping due to fewer social interactions [3]. Other young adults who decreased vaping over the pandemic were also less likely to vape to get high [19]. This may be due to the limited social interaction during the pandemic, lessening the pressure of influences from friends. 40% of youth reported their reason for vaping was because their friends also used e-cigarettes [24].

COVID-19 negatively impacted teen mental health, increasing anxiety, depression, and stress [25]. As one study conducted in 2021 stated that 36% of youth increasing their e-cigarette use was due to managing stress, there is a correlation between the COVID-19 pandemic and vaping among youth [3]. Furthermore, another study states that those who kept their usage of e-cigarettes the same throughout the pandemic had lower odds of vaping to reduce stress compared to those who increased their usage [19]. This shows that those who increased vaping were more likely to do so because of stress. Similarly, youth that vaped during the pandemic were more likely to report vaping because they were sad, anxious, or bored than before the pandemic [24]. 92% of youth vapers in December 2021 reported feeling stressed with 15% feeling extreme levels of stress, a 10% increase from September [24]. Moreover, e-cigarette use is associated with anxiety and lower self-esteem [26]. Those who use e-cigarettes are more likely to have a health history of attention-deficit/hyperactivity disorder (ADHD), anxiety, and post-traumatic stress disorder (PTSD) [26].

Other reasons for a decrease in e-cigarette use include being concerned about health [1,3,24]. 18% of youth who decreased their vaping reported that it was due to concerns over their health [3]. Another study on youth explanations for decreasing e-cigarette use states that 25% of youth reduced vaping since e-cigarettes may weaken the lungs [1]. In another study, among those who stopped vaping within 3 months of December 2020, 37% quit because they were worried about their health [24]. Addition-ally, a June 2020 survey noted that 64% of youth believed vaping would negatively im-pact their health [24]. A major reason youth quit vaping in 2020 was due to general health concerns moreover, concerns specifically about COVID-19 also directly impacted vaping rates [18,20]. Those who did not vape during late 2019 and started vaping during late 2020 were more likely to have less COVID-19 news exposure [18]. According to the 2021 ITC Youth Survey, 15% of e-cigarette users reported decreasing their usage due to the COVID-19 pandemic [20]. On the contrary, 15% also reported vaping more as a result of the pandemic [20]. Vape companies also exploited the pandemic, encouraging people to buy their vapes by advocating for people to stay home and vape [27]. On top of that, they also offered contactless delivery and curb side pickup during quarantine [27]. This could have contributed to an increase in e-cigarette use due to the companies portraying themselves as safe.

The varying statistics on whether e-cigarette use among youth increased or de-creased over the COVID-19 pandemic is merely due to the fact there was initial anxiety about contracting COVID-19 [3]. Although studies show an initial decrease, more recent information shows that vaping among adolescents is also beginning to increase again [17,20].

4. E-cigarette Health Effects and their Potential Mechanisms

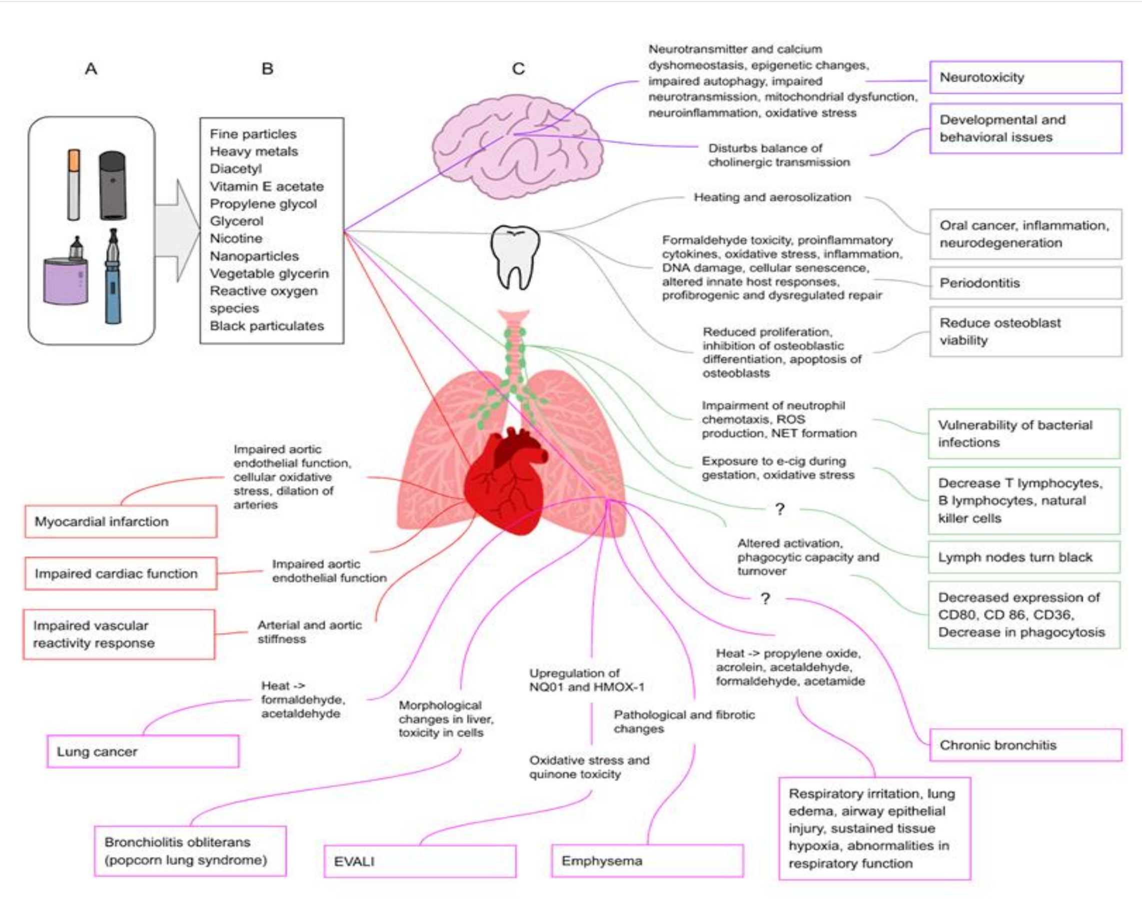

Figure 2. E-cigarette components and their health effects on the body. (A) Different generations of the e-cigarettes; (B) toxic components among different generations; (C) components' effects and the potential underlying mechanisms on the brain (indicated by purple lines and boxes), the lungs (indicated by pink lines and boxes), the heart (indicated by red lines and boxes), the mouth (indicated by grey lines and boxes), and the immune system (indicated by green lines and boxes).

4.1. E-cigarettes' Effects on the Lungs

Two decades before the E-cigarette or Vaping Product Use Associated Lung Injury (EVALI) outbreak, a series of cases of patients with pulmonary diseases who also used e-cigarettes emerged [28]. Most commonly, lung injury with an organizing pattern such as organizing pneumonia or acute fibrinous pneumonitis with organization, hypersensitivity pneumonitis, diffuse alveolar damage, and lipoid pneumonia [28]. Additionally, multiple studies found that e-cigarette smoking causes increased asthma exacerbation, cough, wheezing, and chronic bronchitis in adolescents [29,30].

However, as of February 18, 2020, there have been a total of 2,807 EVALI cases and deaths in the United States [31]. In just 29 states and the District of Columbia, there have been a total of 68 deaths reported to be caused by EVALI [31]. Studies show that EVALI is linked to vapes that contain cannabis emulsified with vitamin E acetate [31,32]. Vit-amin E acetate is a thickening/cutting agent added to vapes by black-market dealers [32]. Vitamin E acetate has been found in the lungs of EVALI patients tested by the CDC as well as in product samples tested by the U.S. Food and Drug Administration. Furthermore, vitamin E acetate hasn't been found in the lung fluid of e-cigarette users without EVALI [31].

Studies show that EVALI symptoms are most likely a result of synergistic interactions between thermal decomposition products of vitamin E acetate [33]. The thermal decomposition products of vitamin E acetate have been shown to cause oxidative stress and quinone toxicity to exposed lung cells since vitamin E acetate emissions were linked to an upregulation of the NQ01, a quinone-metabolizing enzyme, and HMOX-1, an ox-idative stress biomarker, genes [33]. These decomposition products may also have the ability to penetrate the alveolar region in the lungs, having been found to exist at sizes below 100 nm [33].

There are many short-term and long-term effects of vaping on pulmonary health [8]. Irritation of e-cigarette aerosol may cause a short-term increase in flow resistance and an increase in airway reactivity [8]. Pathological and fibrotic changes from e-cigarette use may cause long-term effects such as emphysema, higher airway resistance, airway obstruction, or airway inflammation [8]. Additionally, the heating of the components of e-cigarettes creates new substances. Parts of the e-liquid like propylene glycol, glycerol, nicotine, and flavoring can become substances like propylene oxide, acrolein, acetaldehyde, formaldehyde, and acetamide when heated [34]. These new components can negatively impact the lungs of e-cigarette users by causing problems like respiratory irritation, lung edema, airway epithelial injury, sustained tissue hypoxia, abnormalities in respiratory function, or even EVALI [34].

4.2. E-cigarettes' Effects on the Heart

Studies using carotid-femoral pulse wave velocity and photoplethysmography both show arterial stiffness after vaping [35]. In mice, exposure to e-cigarettes resulted in aortic stiffness and significantly impaired aortic endothelial function which may lead to impaired cardiac function [35]. Arterial and aortic stiffness from e-cigarettes may lead to an impaired vascular reactivity response [35,36].

E-cigarettes have also been linked to myocardial infarctions [28,36,37]. Studies show that daily e-cigarette use is associated with an increased risk of myocardial infarction [28,36]. An analysis of the National Health Interview Surveys of 2014 showed that daily e-cigarette use is independently associated with having a myocardial infarction [36]. E-cigarettes deliver ultrafine particles into the lungs which, in mic, lead to impaired aortic endothelial function which is associated with an increased risk of myocardial infarction [36]. Additionally, heavy metals in e-cigarettes may cause cellular oxidative stress due to the glutathione levels in the lungs, as shown in mice studies, from exposure to e-cigarette aerosols [37]. This oxidative stress as well as the afore-mentioned dilation of arteries are both associated with increased risks for myocardial infarctions [36].

4.3. E-cigarettes' Effects on Oral/Dental Health

Periodontitis is an inflammatory disease that destroys the supporting tissues of the teeth [38]. One study that measured the inflammatory response in traditional cigarette, e-cigarette, and former smokers found elevated levels of proinflammatory cytokines in the crevicular fluid of dental implants of cigarettes and e-cigarette users [38,39]. Substances in e-cigarette aerosols could contribute to oral diseases such as periodontitis by inducing oxidative stress, inflammation, DNA damage, cellular senescence, altered innate host responses, profibrinogenic and dysregulated repair [39]. In rats, periodontium functions were disrupted by formaldehyde toxicity, a substance found in e-cigarettes through the pyrolysis of glycerol, by altering cell growth [34,39,40]. Furthermore, the heating of e-cigarettes results in heavy metals such as nickel, cadmium, chromium, and lead, being transferred from the coil into the e-liquid [39]. Aerosolization of the e-liquid results in exposure to these substances during e-cigarette use which can cause chronic periodontitis, oral cancer, inflammation, and neurodegeneration [39]. These results show that adolescents who smoke e-cigarettes could develop periodontitis among other health effects like oral cancer, inflammation, and neurodegeneration due to the heating of the e-liquid.

Additionally, smoking e-cigarettes may reduce oral osteoblast viability [41,42]. Studies show that e-cigarette vapor is toxic to human osteoblasts and reduce osteoblast viability [41-43]. One study reported that exposure to e-cigarette aerosol extract reduced proliferation and impaired osteoblastic differentiation of bone marrow-derived mesenchymal stem cells [41]. Furthermore, reactive oxygen species released by the e-cigarette induce apoptosis of osteoblasts as well as inhibit osteoblastic differentiation [41]. These results suggest that e-cigarettes may reduce oral osteoblast viability in vapers.

4.4. E-cigarettes' Effects on Mental Health

Particles in e-cigarettes such as nanoparticles, heavy metals, nicotine, and propylene glycol or vegetable glycerin can all cause neurotransmitter and calcium dyshomeostasis, epigenetic changes, impaired autophagy, impaired neurotransmission, mitochondrial dysfunction, neuroinflammation, and oxidative stress, resulting in neuro-toxicity [7]. Nicotine in particular causes various developmental and behavioral issues by disturbing the balance of cholinergic transmission [7].

Nicotine exposure can also negatively affect memory, attention, emotional regulation, executive functioning, reward processing, and even learning [7,44]. Studies report that e-cigarettes also have a bidirectional relationship between vaping and depression [7,45]. Teens who were depressed were more likely to start vaping while the study also showed that depressive symptoms were worse after a 30-day use of e-cigarettes [46]. Another study showed that those who used e-cigarettes were 9.1% more likely to have suicidal thoughts, with 30.7% of vapers reporting experiencing depressive symptoms for over two weeks while 17.3% reported considering committing suicide within the past year [47]. Moreover, vaping is also associated with PTSD, ADHD, and anxiety [24,26]. Reports of vaping due to depression, anxiety, and boredom were common during the pandemic [24]. 92% of youth e-cigarette users reported feeling stressed [24]. E-cigarette use has also been associated with poorer self-esteem and higher rates of impulsivity as measured according to the Barratt Impulsivity Scale [26].

4.5. E-cigarettes' Effects on the Immune Systeem

E-cigarette uses increases the vulnerability of bacterial infections due to the impairment of human neutrophil chemotaxis, reactive oxygen species (ROS) production, and neutrophil extracellular trap (NET) formation [48]. E-cigarette vapor extract, or EVE, inhibits human neutrophil chemotaxis [48]. One study reported that following EVE exposure, neutrophils have significantly reduced their migration [48]. Additionally, Neutrophil ROS production is inhibited by EVE exposure [48]. ROS is a key component of the antimicrobial activity of a neutrophil. A study conducted by quantifying ROS production in humans over a two-hour time period found that EVE significantly reduced baseline levels of ROS production at 50, 75, and 100% exposure [48]. E-cigarette vapor has significantly inhibited NET production at all levels of exposure [48]. This means that neutrophil extracellular trap (NET) production in adolescents who smoke e-cigarettes could be inhibited.

The fine particles released by e-cigarette use may have damaging effects on the immune system [49-51]. Adolescents who vape are exposed to fine particulate matter [49]. One study found that prenatal exposure to particulate matter could decrease T lymphocytes, B lymphocytes, and natural killer cells depending on when the exposure happened. Exposure during early gestation led to an increase in T lymphocytes but de-creased B lymphocytes and natural killer cells, on the other hand, exposure during late gestation resulted in decreased T lymphocytes but increased B lymphocytes and natural killer cells [49]. Since T lymphocytes, B lymphocytes, and natural killer cells play roles in the immune system, exposure to particulate matter through e-cigarettes may harm immune systems in adolescents [50,52]. However, a study on mice found that exposure to fine particulate matter stimulated the immune response in the mice, resulting in an accumulation of immune cells in their lungs after the exposure [51].

Fine particles emitted by e-cigarettes have negative impacts on adolescent immune systems, especially in the lungs [53]. One study showed that black particulates which are present in the atmosphere caused lung-associated lymph nodes to turn black, whereas the mesenteric lymph nodes from the same individual were beige or translucent [53]. This demonstrates how inhaling fine particles from e-cigarettes may result in changes to adolescent lung-associated lymph node function. Additionally, expression of the phagocytic marker CD36 key activation markers CD80 and CD86 decreased as they were more exposed to fine particles in CD28+CD169- macrophages in lung-associated lymph nodes but remained unchanged in mesenteric lymph nodes [53]. Furthermore, imaging in CD68+CD169- macrophages depicted a decrease in CD36 expression in macrophages with particulates as well as a significant decrease in phagocytosis in those macrophages [53]. This is because fine particles alter activation, phagocytic capacity, and turnover which results in a decrease in the expression of phagocytic marker CD36 and key activation markers CD80 and CD86 [53]. This shows that adolescents who are ex-posed to fine particles in e-cigarettes may have negative impacts on their lung immune system.

Vaping may also accelerate non-small cell lung cancer through exposure to carbon black particles [54]. A study found that mice who were exposed to carbon black particles in concentrations equal to those found in the lungs of smokers developed lung tumors at a higher rate (58%) than control mice of the same genotype (15%). Additionally, 21% of the mice exposed to carbon black particles developed distant metastases [54]. This may be because carbon black particles cause metabolic changes and immunosuppression in macrophages which could result in non-small cell lung cancer [54]. These results show that particles, like carbon black, may put adolescents who vape at risk of developing lung cancer.

5. E-cigarette Long-term Health Issues

5.1. The Effects of Nicotine

One of the components of e-cigarettes is nicotine [55]. Nicotine has many long-term health effects on the brain and mental health of adolescents [56].

One study found that young mice treated with nicotine displayed a decreased context-induced freezing and were less sensitive than the control mice to nicotine enhancement of performance, results that were not shown by adult mice treated with nicotine. Additionally, the same study discovered that adult female mice's performance in an object learning task and novel object test decreased if they were exposed to nicotine as adolescents [57]. These results depict the long-term effects of nicotine on the hippocampus, a brain region critical for memory formation and retrieval, processing contextual information, and spatial learning [57,58]. Thus, we could hypothesize that nicotine exposure to adolescents who vape may later impact the functions of their hippocampus.

Furthermore, animal studies have shown a correlation between adolescent nicotine exposure and the long-term effects of anxiety and depression [56,59-62]. These studies tested anxiety by measuring the time the mice spent in the center zone of an open field, forced swim test, sucrose preference, and elevated plus maze [59-61]. Adolescent mice who were treated with nicotine expressed more anxiety later in their life than those who were not [59-61]. Additionally, several studies reported that mice exposed to nicotine as adolescents showed depressive symptoms later in their life as well as social withdrawal and deficits in social cognition [60-62]. For instance, some depressive symptoms in mice exposed to nicotine include immobility in the forced swim test and decreased sucrose preference [60,61]. All these results raise the idea that adolescents exposed to nicotine through vaping could express anxiety and depressive symptoms as adults.

5.2. The Effects of Fine Particles

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5.3. The Effects of Formaldehyde

E-cigarettes also contain many carcinogens, including acetaldehyde and formaldehyde, that form as a result of reactions within the e-cigarette device [40,63]. One study showed that formaldehyde was detected in 6/7 e-liquids due to being formed from the pyrolysis of glycerol [40]. Multiple studies on rats exposed to formaldehyde at up to 15 ppm report squamous cell carcinomas in the nasal cavity [64-66]. Another study on industrial workers exposed to formaldehyde showed that the workers exposed to formaldehyde had an increased mortality rate from several cancers and a deficit of lung cancer among workers exposed to only low levels of formaldehyde [67]. Thus, we can hypothesize that this may have significant effects on the future health of vaping adolescents.

5.4. The Effects of Diacetyl

The buttery-like aroma of e-cigarettes is due to diacetyl [68]. A study on female and male mice has shown that diacetyl promotes metabolomic changes [69]. In both male and female groups that were exposed to diacetyl, the metabolite levels of 5-HT, Ala, Arg, Asn, Cit, Gln, Gly, His, Ile, Leu, Met, Phe, Pro, Sar, Tau, The, Tyr, and Val increased. However, in the female-treated group, the metabolite levels of Asp, Glu, Orn, and T4-OH-Pro decreased and in the male-treated group, Cre, Dopa, Hst, Kyn, Car, and Trp decreased [69]. Additionally, diacetyl caused the mice to express anxiety and fear when treated with diacetyl. This may be because the metabolite 5-HT, which is involved in the pathophysiology of anxiety disorders, increased in both male and female mice treated with diacetyl [69]. This shows that the metabolite levels of adolescents who smoke e-cigarettes containing diacetyl may become altered.

5.5. The Effects of Heavy Metals

The heavy metals in e-cigarettes have negative effects on neurological health [70,71]. A study on the effects of heavy metals on astrocytes showed that under expo-sure to excessive heavy metals, astrocytes, which are crucial for the protection of neurons in the central nervous system, may become the main targets of metal toxicity which could cause damage in cognition, memory, and learning [71-73]. Additionally, heavy metals such as Mn, Pb, Ng, and iron that damage astrocytes can destroy nervous tissue and glial-neuronal interactions [74,75]. Furthermore, heavy metals can alter the pro-duction of glutamate since astrocytes are the only cells in the brain that can produce glutamate [76]. The negative effects of heavy metals on neurological health may appear in adolescents who have been exposed to heavy metals through e-cigarettes.

5.6. The Effects of Proopylene Glycol

E-cigarette users are exposed to propylene glycol, which can be up to 95% of the liquid volume in an e-cigarette [77]. For example, one study using a single brand of e-cigarettes made in Greece found that the e-liquid consisted of at least 60% propylene glycol [78]. Multiple studies on the effects of e-cigarettes on mice have shown that acute exposure to doses with propylene glycol has caused up-regulation of mucins and cyto-kines as well as impaired autophagy while chronic exposure has caused airway inflammation, impairment of neutrophil phagocytosis, and emphysema [79-84]. Additionally, propylene glycol enters cells through aquaporins such as AQP3, causing it to have intracellular effects [85]. One study showed that propylene glycol caused a de-crease in membrane fluidity in airway epithelia which may affect endocytosis, exocytosis, and plasma membrane protein-protein interactions [86]. This shows that adolescents who smoke e-cigarettes and are exposed to propylene glycol may be exposed to negative intracellular effects such as a decrease in membrane fluidity. Furthermore, propylene glycol forms propylene oxide when heated and vaporized, an International Agency for Research on Cancer class 2B carcinogen [87]. This shows that adolescents exposed to vaporized propylene glycol through e-cigarette vapor will most likely be exposed to carcinogens.

5.7. The Effects of Acrolein

Acrolein is formed in the vapor of e-cigarettes through the heating of glycerine [88]. One study reported that of 12 studied e-cigarettes, 11 contained acrolein. The contents of acrolein ranged from 0.7 to 41.9 micrograms in every e-cigarette [88]. Multiple studies have reported that acrolein causes irritation of the nasal cavity, damage to the lining of the lungs, as well as cardiovascular disease [88-90]. Additionally, one study on the effects of acrolein on key regulators of mitochondrial content and function in rat lungs discovered that exposure to acrolein resulted in a decrease in the abundance of multiple subunits of electron transport chain complexes as well as decreased protein levels of important regulators that are involved in mitochondrial biogenesis. Furthermore, acrolein inhalation caused mtDNA damage, an increase in intracellular and mitochondrial ROS production, as well as disturbed mitochondrial metabolism [91]. These results show that adolescents exposed to e-cigarette vapor could be exposed to the harmful effects of acrolein including a decrease in electron transport chain subunits and protein levels, increased ROS production, and disturbed mitochondrial metabolism.

6. Conclusions

In conclusion, the COVID-19 pandemic has had a significant impact on vaping behavior among adolescents. Initially, concerns about the potential health risks of COVID-19, the decrease in the availability of e-cigarettes through business closures, and social distancing led to a decline in vaping rates. However, as restrictions from the pandemic are being lifted, there has been a significant increase in vaping rates among adolescents.

One crucial consequence of the rising vaping rates is the potential short and long-term health effects. This is particularly important in adolescents who have more time to experience these negative effects later in life. Current studies show that e-cigarettes can negatively impact neurological, oral, cardiovascular, pulmonary, and immune health, however, the long-term effects of vaping are still being researched. With these findings, we can conclude that adolescents who smoke e-cigarettes are at an increased risk of experiencing the negative health effects of e-cigarettes in the future.

Given these findings, it is imperative to implement effective policies to reduce vaping rates by limiting the availability of e-cigarettes to adolescents. These policies should focus on stricter regulations on marketing practices that target young individuals, raising awareness about potential health effects associated with e-cigarettes, and ensuring the enforcement of age restrictions for purchasing vaping products. By re-stricting adolescents' access to e-cigarettes, we can mitigate the potential long-term consequences of vaping in the years to come.

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Abbreviations

ADHD - Attention-Deficit/Hyperactivity Disorder
PTSD - Post-Traumatic Stress Disorder
EVALI - E-cigarette or Vaping Product Use-Associated Lung Injury
nm - Nanometer
DNA - Deoxyribonucleic Acid
ROS - Reactive Oxygen Species
NET - Neutrophil Extracellular Trap
EVE - E-cigarette Vapor Extract
ppm - Parts Per Million
5-HT - 5-Hydroxytryptamine (Serotonin)
Ala - Alanine
Arg - Arginine
Asn - Asparagine
Cit - Citrulline
Gln - Glutamine
Gly - Glycine
His - Histidine
Ile - Isoleucine
Leu - Leucine
Met - Methionine
Phe - Phenylalanine
Pro - Proline
Sar - Sarcosine
Tau - Tau Protein
The - Threonine
Tyr - Tyrosine
Val - Valine
Asp - Aspartic Acid
Glu - Glutamic Acid
Orn - Ornithine
T4-OH-Pro - 4-Hydroxyproline
Cre - Creatine
Dopa - Dihydroxyphenylalanine
Hst - Histamine
Kyn - Kynurenine
Car - Carotene
Trp - Tryptophan
Mn - Manganese
Pb - Lead
ng - Nanogram
mtDNA - Mitochondrial DNA

References

[1] Stokes, A.C. Declines in Electronic Cigarette Use Among US Youth in the Era of COVID-19—A Critical Opportunity to Stop Youth Vaping in Its Tracks. JAMA

Netw. Open 2020, 3, e2028221, doi:10.1001/jamanetworkopen.2020.28221.

[2] Usher, K.; Durkin, J.; Bhullar, N. The COVID-19 Pandemic and Mental Health Impacts. Int. J. Ment. Health Nurs. 2020, 29, 315–318, doi:10.1111/inm.12726.

[3] Bennett, M.; Speer, J.; Taylor, N.; Alexander, T. Changes in E-Cigarette Use Among Youth and Young Adults During the COVID-19 Pandemic: Insights into Risk Perceptions and Reasons for Changing Use Behavior. Nicotine Tob. Res. 2022, ntac136, doi:10.1093/ntr/ntac136.

[4] Rom, O.; Pecorelli, A.; Valacchi, G.; Reznick, A.Z. Are E-Cigarettes a Safe and Good Alternative to Cigarette Smoking? Ann. N. Y. Acad. Sci. 2015, 1340, 65–74, doi:10.1111/nyas.12609.

[5] Association, A.L. What's in an E-Cigarette? Available online: https://www.lung.org/quit-smoking/e-cigarettes-vaping/whats-in-an-e-cigarette (accessed on 19 June 2023).

[6] Health, C.O. on S. and Smoking and Tobacco Use; Electronic Cigarettes Available online: https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html (accessed on 19 June 2023).

[7] Ruszkiewicz, J.A.; Zhang, Z.; Gonçalves, F.M.; Tizabi, Y.; Zelikoff, J.T.; Aschner, M. Neurotoxicity of E-Cigarettes. Food Chem. Toxicol. Int. J. Publ. Br. Ind. Biol. Res. Assoc. 2020, 138, 111245, doi:10.1016/j.fct.2020.111245.

[8] Tsai, M.; Byun, M.K.; Shin, J.; Crotty Alexander, L.E. Effects of E-Cigarettes and Vaping Devices on Cardiac and Pulmonary Physiology. J. Physiol. 2020, 598, 5039–5062, doi:10.1113/JP279754.

[9] E-Cigarette, or Vaping, Products Visual Dictionary.

[10] Singh, J.; Luquet, E.; Smith, D.P.T.; Potgieter, H.J.; Ragazzon, P. Toxicological and Analytical Assessment of E-Cigarette Refill Components on Airway Epithelia. Sci. Prog. 2016, 99, 351–398, doi:10.3184/003685016X14773090197706.

[11] Chen, T.; Wu, M.; Dong, Y.; Kong, B.; Cai, Y.; Hei, C.; Wu, K.; Zhao, C.; Chang, Q. Effect of E-Cigarette Refill Liquid on Follicular Development and Estrogen Secretion in Rats. Tob. Induc. Dis. 2022, 20, 36, doi:10.18332/tid/146958.

[12] Noël, A.; Hossain, E.; Perveen, Z.; Zaman, H.; Penn, A.L. Sub-Ohm Vaping Increases the Levels of Carbonyls, Is Cytotoxic, and Alters Gene Expression in Human Bronchial Epithelial Cells Exposed at the Air–Liquid Interface. Respir. Res. 2020, 21, 305, doi:10.1186/s12931-020-01571-1.

[13] Leventhal, A.M.; Madden, D.R.; Peraza, N.; Schiff, S.J.; Lebovitz, L.; Whitted, L.; Barrington-Trimis, J.; Mason, T.B.; An-derson, M.K.; Tackett, A.P. Effect of Exposure to E-Cigarettes With Salt vs Free-Base Nicotine on the Appeal and Sensory Expe-rience of Vaping: A Randomized Clinical Trial. JAMA Netw. Open 2021, 4, e2032757, doi:10.1001/jamanetworkopen.2020.32757.

[14] Hickman, E.; Payton, A.; Duffney, P.; Wells, H.; Ceppe, A.S.; Brocke, S.; Bailey, A.; Rebuli, M.E.; Robinette, C.; Ring, B.; et al. Biomarkers of Airway Immune Homeostasis Differ Significantly with Generation of E-Cigarettes. Am. J. Respir. Crit. Care Med. 2022, 206, 1248–1258, doi:10.1164/rccm.202202-0373OC.

[15] Sullivan, L.; Crotty Alexander, L.E. A Problem for Generations: Impact of E-Cigarette Type on Immune Homeostasis. Am. J. Respir. Crit. Care Med. 206, 1195–1197, doi:10.1164/rccm.202207-1247ED.

[16] Wang, T.W. E-Cigarette Use Among Middle and High School Students — United States, 2020. MMWR Morb. Mortal. Wkly. Rep. 2020, 69, doi:10.15585/mmwr.mm6937e1.

[17] National-E-CigaretteSales-DataBrief-2021-June21.Pdf.

[18] Bennett, B.; Romm, K.F.; Berg, C.J. Changes in Cigarette and E-Cigarette Use among US Young Adults from before to during the COVID-19 Pandemic: News Exposure and Risk Perceptions as Potential Predictors. Tob. Prev. Cessat. 2022, 8, 18, doi:10.18332/tpc/148245.

[19] Parks, M.J.; Fleischer, N.L.; Patrick, M.E. Increased Nicotine Vaping Due to the COVID-19 Pandemic among US Young Adults: Associations with Nicotine Dependence, Vaping Frequency, and Reasons for Use. Prev. Med. 2022, 159, 107059, doi:10.1016/j.ypmed.2022.107059.

[20] Nicotine Vaping in England: 2022 Evidence Update Summary Available online: https://www.gov.uk/government/publications/nicotine-vaping-in-england-2022-evidence-update/nicotine-vaping-in-england-2022-evidence-update-summary (accessed on 24 May 2023).

[21] Products, C. for T. Results from the Annual National Youth Tobacco Survey. FDA 2023.

[22] Coates, B.; Cowgill, M.; Chen, T.; Mackey, W. Shutdown: Estimating the COVID-19 Employment Shock. 2020.

[23] Products, C. for T. This Is Our Watch. FDA 2023.

[24] Youth_vaping_covid19.Pdf.

[25] Meherali, S.; Punjani, N.; Louie-Poon, S.; Abdul Rahim, K.; Das, J.K.; Salam, R.A.; Lassi, Z.S. Mental Health of Children and Adolescents Amidst COVID-19 and Past Pandemics: A Rapid Systematic Review. Int. J. Environ. Res. Public. Health 2021, 18, 3432, doi:10.3390/ijerph18073432.

[26] Grant, J.E.; Lust, K.; Fridberg, D.J.; King, A.C.; Chamberlain, S.R. E-Cigarette Use (Vaping) Is Associated with Illicit Drug Use, Mental Health Problems, and Impulsivity in University Students. Ann. Clin. Psychiatry Off. J. Am. Acad. Clin. Psychiatr. 2019, 31, 27–35.

[27] Ramamurthi, D.; Chau, C.; Jackler, R.K. Exploitation of the COVID-19 Pandemic by e-Cigarette Marketers. Tob. Control 2021, 30, e56–e59, doi:10.1136/tobaccocontrol-2020-055855.

[28] Cao, D.J.; Aldy, K.; Hsu, S.; McGetrick, M.; Verbeck, G.; De Silva, I.; Feng, S. Review of Health Consequences of Electronic Cigarettes and the Outbreak of Electronic Cigarette, or Vaping, Product Use-Associated Lung Injury. J. Med. Toxicol. 2020, 16, 295–310, doi:10.1007/s13181-020-00772-w.

[29] Kim, S.Y.; Sim, S.; Choi, H.G. Active, Passive, and Electronic Cigarette Smoking Is Associated with Asthma in Adolescents. Sci. Rep. 2017, 7, 17789, doi:10.1038/s41598-017-17958-y.

[30] McConnell, R.; Barrington-Trimis, J.L.; Wang, K.; Urman, R.; Hong, H.; Unger, J.; Samet, J.; Leventhal, A.; Berhane, K. Electronic Cigarette Use and Respiratory Symptoms in Adolescents. Am. J. Respir. Crit. Care Med. 2017, 195, 1043–1049, doi:10.1164/rccm.201604-0804OC.

[31] Besaratinia, A.; Tommasi, S. Vaping Epidemic: Challenges and Opportunities. Cancer Causes Control CCC 2020, 31, 663–667, doi:10.1007/s10552-020-01307-y.

[32] Mendelsohn, C.P.; Wodak, A.; Hall, W. Nicotine Vaping Was Not the Cause of E-Cigarette, or Vaping, Product Use-Associated Lung Injury in the United States. Drug Alcohol Rev. 2023, 42, 258–261, doi:10.1111/dar.13533.

[33] Canchola, A.; Ahmed, C.M.S.; Chen, K.; Chen, J.Y.; Lin, Y.-H. Formation of Redox-Active Duroquinone from Vaping of Vitamin E Acetate Contributes to Oxidative Lung Injury. Chem. Res. Toxicol. 2022, 35, 254–264, doi:10.1021/acs.chemrestox.1c00309.

[34] Marques, P.; Piqueras, L.; Sanz, M.-J. An Updated Overview of E-Cigarette Impact on Human Health. Respir. Res. 2021, 22, 151, doi:10.1186/s12931-021-01737-5.

[35] Olfert, I.M.; DeVallance, E.; Hoskinson, H.; Branyan, K.W.; Clayton, S.; Pitzer, C.R.; Sullivan, D.P.; Breit, M.J.; Wu, Z.; Klinkhachorn, P.; et al. Chronic Exposure to Electronic Cigarettes Results in Impaired Cardiovascular Function in Mice. J. Appl. Physiol. 2018, 124, 573–582, doi:10.1152/japplphysiol.00713.2017.

[36] Alzahrani, T.; Pena, I.; Temesgen, N.; Glantz, S.A. Association Between Electronic Cigarette Use and Myocardial Infarction. Am. J. Prev. Med. 2018, 55, 455–461, doi:10.1016/j.amepre.2018.05.004.

[37] Lerner, C.A.; Sundar, I.K.; Yao, H.; Gerloff, J.; Ossip, D.J.; McIntosh, S.; Robinson, R.; Rahman, I. Vapors Produced by Electronic Cigarettes and E-Juices with Flavorings Induce Toxicity, Oxidative Stress, and Inflammatory Response in Lung Epi-thelial Cells and in Mouse Lung. PLOS ONE 2015, 10, e0116732, doi:10.1371/journal.pone.0116732.

[38] Karaaslan, F.; Dikilitaş, A.; Yiğit, U. The Effects of Vaping Electronic Cigarettes on Periodontitis. Aust. Dent. J. 2020, 65, 143–149, doi:10.1111/adj.12747.

[39] Ebersole, J.; Samburova, V.; Son, Y.; Cappelli, D.; Demopoulos, C.; Capurro, A.; Pinto, A.; Chrzan, B.; Kingsley, K.; Howard, K.; et al. Harmful Chemicals Emitted from Electronic Cigarettes and Potential Deleterious Effects in the Oral Cavity. Tob. Induc. Dis. 2020, 18, 41, doi:10.18332/tid/116988.

[40] Kosmider, L.; Cox, S.; Zaciera, M.; Kurek, J.; Goniewicz, M.L.; McRobbie, H.; Kimber, C.; Dawkins, L. Daily Exposure to Formaldehyde and Acetaldehyde and Potential Health Risk Associated with Use of High and Low Nicotine E-Liquid Concentra-tions. Sci. Rep. 2020, 10, 6546, doi:10.1038/s41598-020-63292-1.

[41] Nicholson, T.; Davis, L.; Davis, E.T.; Newton Ede, M.; Scott, A.; Jones, S.W. E-Cigarette Vapour Condensate Reduces Via-bility and Impairs Function of Human Osteoblasts, in Part, via a Nicotine Dependent Mechanism. Toxics 2022, 10, 506, doi:10.3390/toxics10090506.

[42] Rouabhia, M.; Alanazi, H.; Park, H.J.; Gonçalves, R.B. Cigarette Smoke and E-Cigarette Vapor Dysregulate Osteoblast In-teraction With Titanium Dental Implant Surface. J. Oral Implantol. 2019, 45, 2–11, doi:10.1563/aaid-joi-D-18-00009.

[43] Wavreil, F.D.M.; Heggland, S.J. Cinnamon-Flavored Electronic Cigarette Liquids and Aerosols Induce Oxidative Stress in Human Osteoblast-like MG-63 Cells. Toxicol. Rep. 2020, 7, 23–29, doi:10.1016/j.toxrep.2019.11.019.

[44] Dinardo, P.; Rome, E.S. Vaping: The New Wave of Nicotine Addiction. Cleve. Clin. J. Med. 2019, 86, 789–798, doi:10.3949/ccjm.86a.19118.

[45] Javed, S.; Usmani, S.; Sarfraz, Z.; Sarfraz, A.; Hanif, A.; Firoz, A.; Baig, R.; Sharath, M.; Walia, N.; Chérrez-Ojeda, I.; et al. A Scoping Review of Vaping, E-Cigarettes and Mental Health Impact: Depression and Suicidality. J. Community Hosp. Intern. Med. Perspect. 2022, 12, 33–39, doi:10.55729/2000-9666.1053.

[46] Lechner, W.V.; Janssen, T.; Kahler, C.W.; Audrain-McGovern, J.; Leventhal, A.M. Bi-Directional Associations of Electronic and Combustible Cigarette Use Onset Patterns with Depressive Symptoms in Adolescents. Prev. Med. 2017, 96, 73–78, doi:10.1016/j.ypmed.2016.12.034.

[47] Lee, Y.; Lee, K.-S. Association of Depression and Suicidality with Electronic and Conventional Cigarette Use in South Ko-rean Adolescents. Subst. Use Misuse 2019, 54, 934–943, doi:10.1080/10826084.2018.1552301.

[48] Corriden, R.; Moshensky, A.; Bojanowski, C.M.; Meier, A.; Chien, J.; Nelson, R.K.; Crotty Alexander, L.E. E-Cigarette Use Increases Susceptibility to Bacterial Infection by Impairment of Human Neutrophil Chemotaxis, Phagocytosis, and NET For-mation. Am. J. Physiol. Cell Physiol. 2020, 318, C205–C214, doi:10.1152/ajpcell.00045.2019.

[49] Volesky, K.D.; Maki, A.; Scherf, C.; Watson, L.; Van Ryswyk, K.; Fraser, B.; Weichenthal, S.A.; Cassol, E.; Villeneuve, P.J. The Influence of Three E-Cigarette Models on Indoor Fine and Ultrafine Particulate Matter Concentrations under Real-World Conditions. Environ. Pollut. 2018, 243, 882–889, doi:10.1016/j.envpol.2018.08.069.

[50] Johnson, N.M.; Hoffmann, A.R.; Behlen, J.C.; Lau, C.; Pendleton, D.; Harvey, N.; Shore, R.; Li, Y.; Chen, J.; Tian, Y.; et al. Air Pollution and Children's Health—a Review of Adverse Effects Associated with Prenatal Exposure from Fine to Ultrafine Par-ticulate Matter. Environ. Health Prev. Med. 2021, 26, 72, doi:10.1186/s12199-021-00995-5.

[51] Jiao, Z.; Wen, Z.; Yang, W.; Hu, L.; Li, J. Influence of Fine Particulate Matter and Its Pure Particulate Fractions on Pulmonary Immune Cells and Cytokines in Mice. Exp. Ther. Med. 2021, 21, 662, doi:10.3892/etm.2021.10094.

[52] Cano, R.L.E.; Lopera, H.D.E. Introduction to T and B Lymphocytes. In Autoimmunity: From Bench to Bedside [Internet]; El Rosario University Press, 2013.

[53] Ural, B.B.; Caron, D.P.; Dogra, P.; Wells, S.B.; Szabo, P.A.; Granot, T.; Senda, T.; Poon, M.M.L.; Lam, N.; Thapa, P.; et al. Inhaled Particulate Accumulation with Age Impairs Immune Function and Architecture in Human Lung Lymph Nodes. Nat. Med. 2022, 28, 2622–2632, doi:10.1038/s41591-022-02073-x.

[54] Chang, C.-Y.; You, R.; Armstrong, D.; Bandi, A.; Cheng, Y.-T.; Burkhardt, P.M.; Becerra-Dominguez, L.; Madison, M.C.; Tung, H.-Y.; Zeng, Z.; et al. Chronic Exposure to Carbon Black Ultrafine Particles Reprograms Macrophage Metabolism and Ac-celerates Lung Cancer. Sci. Adv. 2022, 8, eabq0615, doi:10.1126/sciadv.abq0615.

[55] Health, C.O. on S. and Smoking and Tobacco Use; Electronic Cigarettes Available online: https://www.cdc.gov/tobacco/basic_information/e-cigarettes/about-e-cigarettes.html (accessed on 10 June 2023).

[56] Leslie, F.M. Unique, Long-Term Effects of Nicotine on Adolescent Brain. Pharmacol. Biochem. Behav. 2020, 197, 173010, doi:10.1016/j.pbb.2020.173010.

[57] Spaeth, A.M.; Barnet, R.C.; Hunt, P.S.; Burk, J.A. Adolescent Nicotine Exposure Disrupts Context Conditioning in Adult-hood in Rats. Pharmacol. Biochem. Behav. 2010, 96, 501–506, doi:10.1016/j.pbb.2010.07.011.

[58] Opitz, B. Memory Function and the Hippocampus. Front. Neurol. Neurosci. 2014, 34, 51–59, doi:10.1159/000356422.

[59] Slawecki, C.J.; Gilder, A.; Roth, J.; Ehlers, C.L. Increased Anxiety-like Behavior in Adult Rats Exposed to Nicotine as Ado-lescents. Pharmacol. Biochem. Behav. 2003, 75, 355–361, doi:10.1016/s0091-3057(03)00093-5.

[60] Holliday, E.D.; Nucero, P.; Kutlu, M.G.; Oliver, C.; Connelly, K.L.; Gould, T.J.; Unterwald, E.M. Long-Term Effects of Chronic Nicotine on Emotional and Cognitive Behaviors and Hippocampus Cell Morphology in Mice: Comparisons of Adult and Adolescent Nicotine Exposure. Eur. J. Neurosci. 2016, 44, 2818–2828, doi:10.1111/ejn.13398.

[61] Iñiguez, S.D.; Warren, B.L.; Parise, E.; Alcantara, L.F.; Schuh, B.; Maffeo, M.L.; Manojlovic, Z.; Bolaños Guzmán, C.A. Nicotine Exposure During Adolescence Induces a Depression-Like State in Adulthood. Neuropsychopharmacol. Off. Publ. Am. Coll. Neuropsychopharmacol. 2009, 34, 1609–1624, doi:10.1038/npp.2008.220.

[62] Jobson, C.L.M.; Renard, J.; Szkudlarek, H.; Rosen, L.G.; Pereira, B.; Wright, D.J.; Rushlow, W.; Laviolette, S.R. Adolescent Nicotine Exposure Induces Dysregulation of Mesocorticolimbic Activity States and Depressive and Anxiety-like Prefrontal Cortical Molecular Phenotypes Persisting into Adulthood. Cereb. Cortex N. Y. N 1991 2019, 29, 3140–3153, doi:10.1093/cercor/bhy179.

[63] Bracken-Clarke, D.; Kapoor, D.; Baird, A.M.; Buchanan, P.J.; Gately, K.; Cuffe, S.; Finn, S.P. Vaping and Lung Cancer – A Review of Current Data and Recommendations. Lung Cancer 2021, 153, 11–20, doi:10.1016/j.lungcan.2020.12.030.

[64] Swenberg, J.A.; Kerns, W.D.; Mitchell, R.I.; Gralla, E.J.; Pavkov, K.L. Induction of Squamous Cell Carcinomas of the Rat Nasal Cavity by Inhalation Exposure to Formaldehyde Vapor. Cancer Res. 1980, 40, 3398–3402.

[65] Kerns, W.D.; Pavkov, K.L.; Donofrio, D.J.; Gralla, E.J.; Swenberg, J.A. Carcinogenicity of Formaldehyde in Rats and Mice after Long-Term Inhalation Exposure. Cancer Res. 1983, 43, 4382–4392.

[66] Swenberg, J.A.; Moeller, B.C.; Lu, K.; Rager, J.E.; Fry, R.; Starr, T.B. Formaldehyde Carcinogenicity Research: 30 Years and Counting for Mode of Action, Epidemiology, and Cancer Risk Assessment. Toxicol. Pathol. 2013, 41, 181–189, doi:10.1177/0192623312466459.

[67] Nelson, N.; Levine, R.J.; Albert, R.E.; Blair, A.E.; Griesemer, R.A.; Landrigan, P.J.; Stayner, L.T.; Swenberg, J.A. Contribution of Formaldehyde to Respiratory Cancer. Environ. Health Perspect. 1986, 70, 23–35, doi:10.1289/ehp.867023.

[68] Langel, S.N.; Kelly, F.L.; Brass, D.M.; Nagler, A.E.; Carmack, D.; Tu, J.J.; Travieso, T.; Goswami, R.; Permar, S.R.; Blasi, M.; et al. E-Cigarette and Food Flavoring Diacetyl Alters Airway Cell Morphology, Inflammatory and Antiviral Response, and Suscep-tibility to SARS-CoV-2. Cell Death Discov. 2022, 8, 1–11, doi:10.1038/s41420-022-00855-3.

[69] Jedlicka, L.D.L.; Silva, J. da C.; Balbino, A.M.; Neto, G.B.; Furtado, D.Z.S.; da Silva, H.D.T.; Cavalcanti, F. de B.C.; van der Heijden, K.M.; Penatti, C.A.A.; Bechara, E.J.H.; et al. Effects of Diacetyl Flavoring Exposure in Mice Metabolism. BioMed Res. Int. 2018, 2018, 9875319, doi:10.1155/2018/9875319.

[70] Farsalinos, K.E.; Voudris, V.; Poulas, K. Are Metals Emitted from Electronic Cigarettes a Reason for Health Concern? A Risk-Assessment Analysis of Currently Available Literature. Int. J. Environ. Res. Public. Health 2015, 12, 5215–5232, doi:10.3390/ijerph120505215.

[71] Li, B.; Xia, M.; Zorec, R.; Parpura, V.; Verkhratsky, A. Astrocytes in Heavy Metal Neurotoxicity and Neurodegeneration. Brain Res. 2021, 1752, 147234, doi:10.1016/j.brainres.2020.147234.

[72] Hussien, H.M.; Abd-Elmegied, A.; Ghareeb, D.A.; Hafez, H.S.; Ahmed, H.E.A.; El-Moneam, N.A. Neuroprotective Effect of Berberine against Environmental Heavy Metals-Induced Neurotoxicity and Alzheimer's-like Disease in Rats. Food Chem. Toxicol. Int. J. Publ. Br. Ind. Biol. Res. Assoc. 2018, 111, 432–444, doi:10.1016/j.fct.2017.11.025.

[73] Mason, L.H.; Harp, J.P.; Han, D.Y. Pb Neurotoxicity: Neuropsychological Effects of Lead Toxicity. BioMed Res. Int. 2014, 2014, 840547, doi:10.1155/2014/840547.

[74] Zheng, Z.; White, C.; Lee, J.; Peterson, T.S.; Bush, A.I.; Sun, G.; Weisman, G.A.; Petris, M.J. ALTERED MICROGLIAL COPPER HOMEOSTASIS IN A MOUSE MODEL OF ALZHEIMER'S DISEASE. J. Neurochem. 2010, 114, 1630–1638, doi:10.1111/j.1471-4159.2010.06888.x.

[75] Verkhratsky, A.; Nedergaard, M. Astroglial Cradle in the Life of the Synapse. Philos. Trans. R. Soc. B Biol. Sci. 2014, 369, 20130595, doi:10.1098/rstb.2013.0595.

[76] Hertz, L.; Dringen, R.; Schousboe, A.; Robinson, S.R. Astrocytes: Glutamate Producers for Neurons. J. Neurosci. Res. 1999, 57, 417–428.

[77] Azimi, P.; Keshavarz, Z.; Lahaie Luna, M.; Cedeno Laurent, J.G.; Vallarino, J.; Christiani, D.C.; Allen, J.G. An Unrecognized Hazard in E-Cigarette Vapor: Preliminary Quantification of Methylglyoxal Formation from Propylene Glycol in E-Cigarettes. Int. J. Environ. Res. Public. Health 2021, 18, 385, doi:10.3390/ijerph18020385.

[78] Flouris, A.D.; Chorti, M.S.; Poulianiti, K.P.; Jamurtas, A.Z.; Kostikas, K.; Tzatzarakis, M.N.; Wallace Hayes, A.; Tsatsakis, A.M.; Koutedakis, Y. Acute Impact of Active and Passive Electronic Cigarette Smoking on Serum Cotinine and Lung Function. Inhal. Toxicol. 2013, 25, 91–101, doi:10.3109/08958378.2012.758197.

[79] Reidel, B.; Radicioni, G.; Clapp, P.W.; Ford, A.A.; Abdelwahab, S.; Rebuli, M.E.; Haridass, P.; Alexis, N.E.; Jaspers, I.; Kesimer, M. E-Cigarette Use Causes a Unique Innate Immune Response in the Lung, Involving Increased Neutrophilic Activation and Altered Mucin Secretion. Am. J. Respir. Crit. Care Med. 2018, 197, 492–501, doi:10.1164/rccm.201708-1590OC.

[80] Hwang, J.H.; Lyes, M.; Sladewski, K.; Enany, S.; McEachern, E.; Mathew, D.P.; Das, S.; Moshensky, A.; Bapat, S.; Pride, D.T.; et al. Electronic Cigarette Inhalation Alters Innate Immunity and Airway Cytokines While Increasing the Virulence of Col-onizing Bacteria. J. Mol. Med. Berl. Ger. 2016, 94, 667–679, doi:10.1007/s00109-016-1378-3.

[81] Shivalingappa, P.C.; Hole, R.; Van Westphal, C.; Vij, N. Airway Exposure to E-Cigarette Vapors Impairs Autophagy and Induces Aggresome Formation. Antioxid. Redox Signal. 2016, 24, 186–204, doi:10.1089/ars.2015.6367.

[82] Lim, H.B.; Kim, S.H. Inhallation of E-Cigarette Cartridge Solution Aggravates Allergen-Induced Airway Inflammation and Hyper-Responsiveness in Mice. Toxicol. Res. 2014, 30, 13–18, doi:10.5487/TR.2014.30.1.013.

[83] Clapp, P.W.; Pawlak, E.A.; Lackey, J.T.; Keating, J.E.; Reeber, S.L.; Glish, G.L.; Jaspers, I. Flavored E-Cigarette Liquids and Cinnamaldehyde Impair Respiratory Innate Immune Cell Function. Am. J. Physiol. - Lung Cell. Mol.

Physiol. 2017, 313, L278–L292, doi:10.1152/ajplung.00452.2016.
[84] Garcia-Arcos, I.; Geraghty, P.; Baumlin, N.; Campos, M.; Dabo, A.J.; Jundi, B.; Cummins, N.; Eden, E.; Grosche, A.; Salathe, M.; et al. Chronic Electronic Cigarette Exposure in Mice Induces Features of COPD in a Nicotine-Dependent Manner. Thorax 2016, 71, 1119–1129, doi:10.1136/thoraxjnl-2015-208039.
[85] Verkman, A.S. Aquaporins in Clinical Medicine. Annu. Rev. Med. 2012, 63, 303–316, doi:10.1146/annurev-med-043010-193843.
[86] Ghosh, A.; Coakley, R.C.; Mascenik, T.; Rowell, T.R.; Davis, E.S.; Rogers, K.; Webster, M.J.; Dang, H.; Herring, L.E.; Sas-sano, M.F.; et al. Chronic E-Cigarette Exposure Alters the Human Bronchial Epithelial Proteome. Am. J. Respir. Crit. Care Med. 2018, 198, 67–76, doi:10.1164/rccm.201710-2033OC.
[87] Laino, T.; Tuma, C.; Moor, P.; Martin, E.; Stolz, S.; Curioni, A. Mechanisms of Propylene Glycol and Triacetin Pyrolysis. J. Phys. Chem. A 2012, 116, 4602–4609, doi:10.1021/jp300997d.
[88] Lukasz, G.M.; Jakub, K.; Michal, G.; Leon, K.; Andrzej, S.; Jolanta, K.; Adam, P.; Magdalena, J.-C.; Czeslawa, R.-D.; Chris-topher, H.; et al. Levels of Selected Carcinogens and Toxicants in Vapor from Electronic Cigarettes. Tob. Control 2014, 23, 133–139, doi:10.1136/tobaccocontrol-2012-050859.
[89] Bekki, K.; Uchiyama, S.; Ohta, K.; Inaba, Y.; Nakagome, H.; Kunugita, N. Carbonyl Compounds Generated from Electronic Cigarettes. Int. J. Environ. Res. Public. Health 2014, 11, 11192–11200, doi:10.3390/ijerph111111192.
[90] Henning, R.J.; Johnson, G.T.; Coyle, J.P.; Harbison, R.D. Acrolein Can Cause Cardiovascular Disease: A Review. Cardio-vasc. Toxicol. 2017, 17, 227–236, doi:10.1007/s12012-016-9396-5.
[91] Tulen, C.B.M.; Snow, S.J.; Leermakers, P.A.; Kodavanti, U.P.; van Schooten, F.J.; Opperhuizen, A.; Remels, A.H.V. Acrolein Inhalation Acutely Affects the Regulation of Mitochondrial Metabolism in Rat Lung. Toxicology 2022, 469, 153129, doi:10.1016/j.tox.2022.153129.