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PATHOLOGICAL CHANGES IN LUNG TISSUE UNDER THE INFLUENCE OF ELECTRONIC CIGARETTES. LITERATURE REVIEW.

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Abstract

Background: Electronic cigarettes (e-cigarettes) have gained substantial popularity worldwide, particularly among adolescents and young adults. Their aerosols contain nicotine, flavoring agents, propylene glycol, glycerol, and thermal degradation by-products capable of reaching the distal airways and inducing inflammatory, fibrotic, and potentially precancerous alterations. Coordinated public health measures are necessary to mitigate the global burden of e-cigarette–related respiratory disease.

Aim: To synthesize current evidence on morphological changes in lung tissue following exposure to e-cigarette aerosols.

Search strategy: A literature review was conducted using PubMed, Scopus, Google Scholar, and e-Library databases for studies published between from 2015 to March 2025. Search terms included “electronic nicotine delivery systems,” “vaping,” “lungs,” “morphology,” and “oxidative stress.” Eligible publications comprised systematic reviews and original research in English and Russian.

Results: Data analysis revealed a marked increase in e-cigarette use over the last decade. Given the direct inhalation route, pathological changes predominantly occur in lung tissue, including acute epithelial injury, chronic inflammation, and fibrotic remodeling.

Conclusions: E-cigarette aerosols exert deleterious effects on the respiratory system, with potential mechanisms involving oxidative stress, pro-inflammatory cytokine activation, and suppression of DNA repair. Further morphological and immunohistochemical studies are warranted to elucidate long-term pulmonary consequences.

Keywords: *electronic nicotine delivery systems; vaping; lung pathology; inflammation; fibrosis; oxidative stress.*

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Резюме

ПАТОМОРФОЛОГИЧЕСКИЕ ИЗМЕНЕНИЯ ЛЁГОЧНОЙ ТКАНИ ПРИ ВОЗДЕЙСТВИИ ЭЛЕКТРОННЫХ СИГАРЕТ. ОБЗОР ЛИТЕРАТУРЫ.

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Актуальность. В современном мире электронные сигареты, или вейпы, стали очень популярными, особенно среди лиц молодого возраста. Аэрозоль электронных сигарет содержит никотин, ароматизаторы, пропиленгликоль, глицерин и продукты термического разложения, способные проникать в глубокие отделы легких и способны вызывать воспалительные и даже предраковые изменения. Международные и национальные усилия по профилактике курения электронных сигарет необходимы для снижения заболеваемости и смертности от болезней дыхательной системы во всем мире.

Цель исследования: Обобщить данные о морфологических изменениях в легочной ткани, выявленных при воздействии аэрозоля электронных сигарет

Стратегия поиска: Мы проанализировали систематические обзоры и оригинальные исследования с использованием международных англо- и русскоязычных баз данных, включая PubMed, Scopus, Google Scholar и eLibrary. Поиск охватывал публикации с 2015 по март 2025 года и проводился с использованием ключевых слов: «электронные системы доставки никотина», «вейпинг», «лёгкие», «морфология», и «оксидативный стресс».

Результаты: Анализ литературы позволил сделать выводы о значительном росте употребления электронных сигарет за последнее десятилетие. Учитывая что аэрозоли электронных сигарет попадают сначала в дыхательную систему, основные повреждения наблюдаются в легочной ткани.

Выводы: Проведенный нами обзор научной литературы указывает на негативное влияние употребления электронных сигарет на дыхательную систему, включая острые повреждения, хронические воспалительные и фиброзные изменения в легких. Возможными молекулярными механизмами повреждения являются оксидативный стресс, активация провоспалительных цитокинов, подавление репарации ДНК. Подчеркивается необходимость дальнейших морфологических и иммуногистохимических исследований для оценки долгосрочных последствий использования электронных сигарет.

Ключевые слова: *электронные системы доставки никотина, вейпинг, лёгкие, морфология, воспаление, фиброз, оксидативный стресс.*

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Түйіндеме

ЭЛЕКТРОНДЫҚ ТЕМЕКІЛЕРДІҢ ӘСЕРІНЕН ӨКПЕ ТІНІНДЕГІ ПАТОМОРФОЛОГИЯЛЫҚ ӨЗГЕРІСТЕР. ӘДЕБИЕТТІК ШОЛУ.

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Өзектілігі. Қазіргі уақытта электрондық темекілер немесе вейптер, әсіресе жастар арасында, кеңінен таралған. Электрондық темекінің аэрозолі никотинді, хош иістендіргіштерді, пропиленгликольді, глицеринді және жылулық ыдырау өнімдерін қамтиды, олар өкпенің терең бөлімдеріне еніп, қабыну және тіпті обырға дейінгі өзгерістер тудыруы мүмкін. Дүниежүзілік деңгейде тыныс алу жүйесі ауруларының сырқаттанушылығын және өлім-жітімін төмендету үшін электрондық темекі шегудің алдын алуға бағытталған халықаралық және ұлттық шаралар қажет.

Зерттеу мақсаты: Электрондық темекі аэрозолінің әсерінен анықталған өкпе тініндегі морфологиялық өзгерістер жөніндегі мәліметтерді жинақтау.

Іздеу стратегиясы: PubMed, Scopus, Google Scholar және eLibrary сияқты халықаралық ағылшын- және орыс тіліндегі деректер базасын пайдалана отырып, жүйелі шолулар мен түпнұсқа зерттеулер талданды. Іздеу 2015 жылдан 2025 жылдың март айына дейінгі жарияланымдарды қамтыды және келесі кілт сөздер қолданылды: «никотинді жеткізуге арналған электрондық жүйелер», «вейпинг», «өкпе», «морфология», «оксидативтік стресс».

Нәтижелер: Әдебиеттерді талдау соңғы он жылдықта электрондық темекіні қолданудың айтарлықтай өскенін көрсетті. Электрондық темекі аэрозолі алдымен тыныс алу жүйесіне түсетіндіктен, негізгі зақымданулар өкпе тінінде байқалады.

Қорытындылар: Ғылыми әдебиеттерге жүргізілген шолу электрондық темекі қолданудың тыныс алу жүйесіне теріс әсерін көрсетеді, оған жедел зақымданулар, созылмалы қабыну және өкпедегі фиброздық өзгерістер жатады.

Зақымданудың ықтимал молекулалық механизмдері — оксидативтік стресс, қабынуға қарсы цитокиндердің белсенуі, ДНҚ репарациясының тежелуі. Электрондық темекіні қолданудың ұзақ мерзімді салдарын бағалау үшін морфологиялық және иммуногистохимиялық зерттеулерді жалғастыру қажеттілігі атап өтіледі.

Түйінді сөздер: *никотинді жеткізуге арналған электрондық жүйелер, вейпинг, өкпе, морфология, қабыну, фиброз, оксидативтік стресс.*

Дәйексөз үшін:

Татыкаева У.Б., Абдуллаева А.А., Садыкова К.Ж., Апбасова С.А., Апбасова М., Нускабаева Г.О., Нұрдинов Н.С. Электрондық темекілердің әсерінен өкпе тініндегі патоморфологиялық өзгерістер. Әдебиеттік шолу. // Ғылым және Денсаулық сақтау. 2025. Vol.27 (4), Б. 187-195. *doi 10.34689/SH.2025.27.4.020*

Introduction

In the modern world, the frequent use of electronic cigarettes (e-cigarettes) and vaping devices has become commonplace, especially among adolescents and young adults. In 2011, there were approximately 7 million users worldwide; however, this number steadily increased to 68 million in 2020, and by 2021 it had already reached 82 million adult users [1; 16].

Survey data on e-cigarette users were available for 49 countries, covering 2.8 billion adults, but were unavailable for another 2.9 billion. Given that information on vaping was provided for only half of the world's population, it can be assumed that the actual number of e-cigarette users is significantly higher. Moreover, the pronounced annual growth rate raises concerns regarding their adverse effects on the respiratory system and other organ systems [1; 16].

Key reasons for the active spread of vaping among young people include the perception of e-cigarettes as fashionable, high-tech accessories, as well as the widespread belief that they are less harmful than traditional tobacco products. Additionally, such devices are often used as a means of reducing dependence on conventional cigarettes during smoking cessation attempts [14].

Search strategy: A comprehensive literature review was conducted using international English- and Russian-language databases, including PubMed, Scopus, Google Scholar, and eLibrary. The search strategy covered publications from 2015 to March 2025, using the keywords "electronic nicotine delivery systems," "vaping," "lungs," "morphology," and "oxidative stress." Articles were systematically analyzed, and 42 studies meeting predefined criteria were selected for in-depth analysis from the PubMed database (Figure 1).

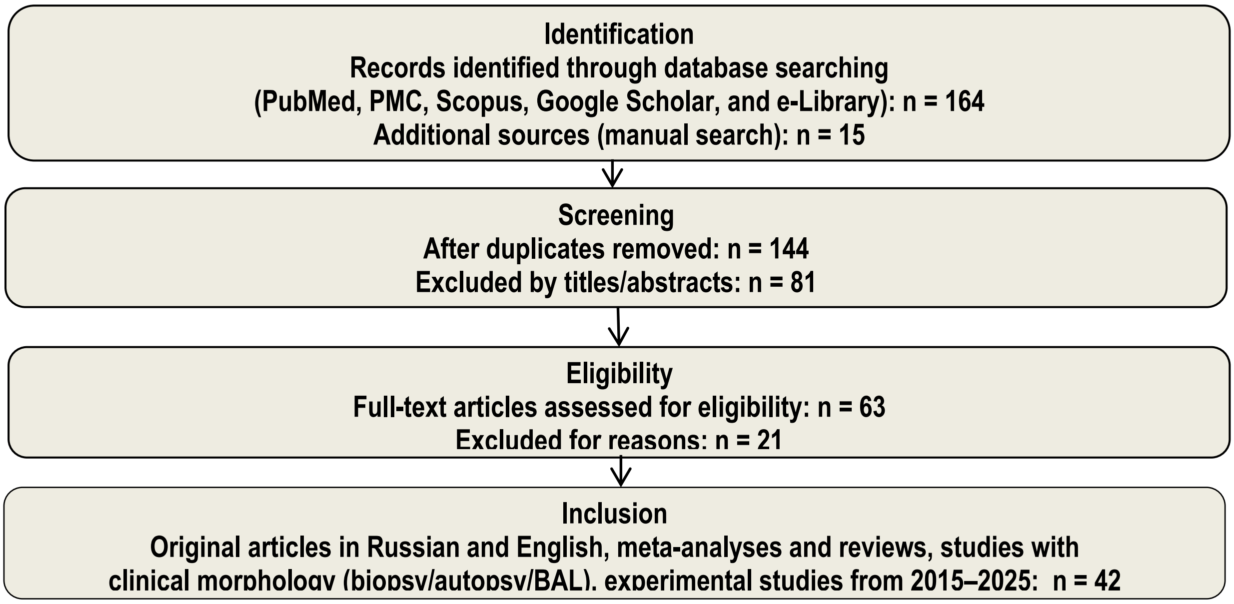

Figure 1. Selection table of articles included in the analysis.

Inclusion criteria: original articles in Russian and English, meta-analyses, and reviews; both clinical morphological studies and experimental animal research assessing morphological changes in lung tissue.

Exclusion criteria: articles without full text, duplicate publications, or studies lacking relevant abstracts; articles exclusively focused on conventional smoking.

The number of publications directly related to the topic under study is relatively limited. In preparing this review we have only included sources from international databases, which explains the relatively small number of sources. During the preparation of this review, we focused on relevant publications from recent years in order to provide a current understanding of issue. Despite this limited literature, our analysis has allowed us to identify key trends and gaps in existing knowledge.

Discussion

Global and Regional Trends in E-Cigarette Use

In recent years, the use of e-cigarettes and vaping among the general population has been growing rapidly.

According to the Global Youth Tobacco Survey (GYTS), conducted in 68 countries from 2012 to 2019, the average prevalence of e-cigarette use in the past 30 days among adolescents aged 12–16 years was 9.2%, with the lowest rate recorded in Kazakhstan (1.9%) and the highest in Guam (33.2%) (Figure 2) [32].

The latest GYTS data for Kazakhstan (2018) report that approximately 3.1% of adolescents aged 11–15 had used e-cigarettes in the past month, with 4.6% among boys and 1.6% among girls. Additionally, 9.4% had tried e-cigarettes at least once [17].

In Europe, according to a review encompassing data from 75 countries, the average prevalence of e-cigarette use among adolescents aged 13–15 years was 10.9%, while 20.2% had tried them at least once [31]. Rates varied widely, from 5.5% in Serbia to 41.4% in Monaco [2]. In England, up to 30% of 15-year-old girls had used e-cigarettes, compared with an EU average of approximately 21% [41].

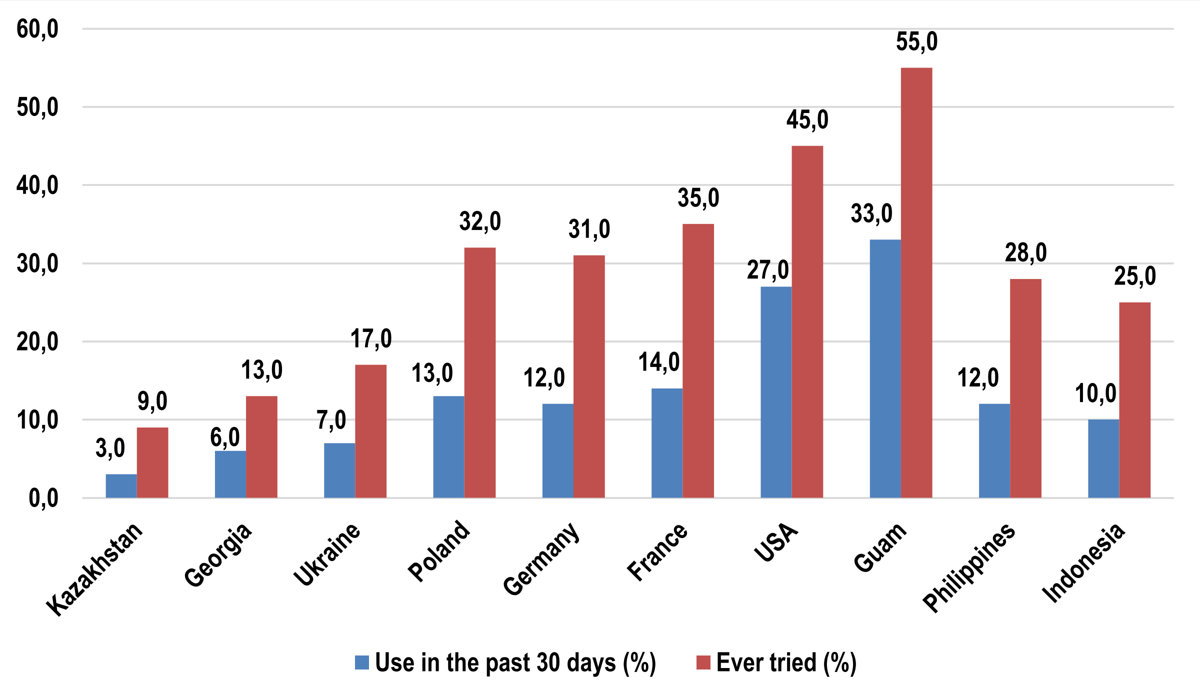

Figure 2. Prevalence of e-cigarette use among adolescents (GYTS) [32].

In the United States, the 2024 National Youth Tobacco Survey (NYTS) reported that 5.9% of middle and high school students had used e-cigarettes in the past 30 days. Of these, 38.4% used the device on ≥20 days per month, and 26.3% used them daily [34]. Among older cohorts, the rates were even higher: among high school students who had ever tried vaping, 49.5% had used e-cigarettes in the past 30 days, and 22.8% used them regularly (≥20 days) [29].

Thus, despite regional differences, e-cigarettes are currently one of the most common forms of nicotine products among adolescents. These trends require special attention, as vaping is associated with the risk of developing a range of pathological changes in the respiratory system, including acute and chronic lung injury.

Composition of E-Cigarette Aerosols

E-cigarettes are portable devices that heat and vaporize liquids, allowing the user to inhale aerosols [12]. The liquid typically consists of propylene glycol, glycerol, flavorings, and—most often—nicotine [19]. In some cases, the liquid may contain tetrahydrocannabinol (THC), the primary psychoactive compound of cannabis.

When heated, the liquid produces an inhalable aerosol. Studies have shown that e-cigarette aerosols contain heavy metals and volatile organic compounds, which may originate from both the liquid and the metallic heating elements of the device. Notably, except for cadmium, metal levels in e-cigarettes often exceed those in conventional tobacco products.

Toxic substances identified in aerosols include acenaphthylene, acetone, benzene, formaldehyde, nitrosonornicotine, and specific tobacco-specific nitrosamines. The long-term effects of these components on human health remain incompletely understood and are the subject of ongoing research [8; 24].

The composition of aerosols varies considerably depending on the manufacturer, device brand, and liquid source. This is especially relevant for homemade mixtures or products purchased on the illicit market, including online sources. E-cigarettes are also frequently used to inhale psychoactive substances, most commonly THC and cannabidiol (CBD) oils, but sometimes also hazardous narcotic compounds such as synthetic cathinones, cocaine (benzoylmethylecgonine), GHB (gamma-hydroxybutyric acid), heroin, fentanyl, MDA, MDMA, and methamphetamine [4; 28].

Acute Lung Injury (Clinical Studies)

Since the early 2010s, e-cigarettes and vaping devices have been actively promoted as a less harmful alternative to conventional smoking. However, as early as 2014, experts from the World Health Organization (WHO) warned that the level of scientific evidence regarding their safety and their effectiveness in combating nicotine addiction remained insufficient. The WHO officially stated that electronic devices cannot be considered a safe replacement for conventional cigarettes [40].

As these devices gained popularity, studies began to emerge that questioned their relative harmlessness. For example, in May 2019, results from an in vitro laboratory experiment showed that exposure to aerosols from smokeless devices (such as IQOS) exerted a negative impact on lung epithelial cells, comparable to the harm caused by tobacco smoke [30].

Particular concern arose with a sharp increase in cases of acute respiratory illness recorded in the summer of 2019 in the United States. At that time, the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) reported the first cases of severe lung injury in e-cigarette and vaping users. This condition was later given the official name **EVALI** (E-cigarette or Vaping product use-Associated Lung Injury), marking the beginning of a new area of clinicopathological research [26].

According to CDC data, by December 2019, there had been 2,409 confirmed cases of EVALI (also known as VAPI — Vaping-Associated Pulmonary Injury) in the United States. A significant proportion of these cases exhibited severe disease, and in 52.2% a fatal outcome was recorded. The epidemic encompassed a broad spectrum of vaping-related lung pathologies, prompting active study of both clinical manifestations and mechanisms of lung injury associated with e-cigarette use [9].

In most cases, morphological and imaging findings in vaping-associated lung injury indicate the development of organizing pneumonia and diffuse alveolar damage [10;11;18]. The morphological pattern varies depending on the stage of the disease at the time of biopsy. In addition to these common patterns, other less frequent types of injury have been described in the literature, such as acute eosinophilic pneumonia and diffuse alveolar hemorrhage [11;18].

Reagan-Steiner S. et al. (2020) examined autopsy material (n = 13) and biopsy specimens (n = 10) from individuals with a history of e-cigarette or vaping use. Of these, 21 cases met the criteria for EVALI, while the remaining two were considered clinically suspected EVALI. Histological examination revealed that all lung biopsies and 9 of the 13 autopsies demonstrated patterns of acute and subacute lung injury, including diffuse alveolar damage or organizing pneumonia [27].

In 2020, *Mukhopadhyay S. et al.* analyzed lung biopsies from 8 patients with vaping-related lung disease. Histological features were characterized by acute lung injury patterns, such as diffuse alveolar damage and organizing pneumonia, evidenced by fibrinous exudates, hyaline membranes, fibroblastic plugs, type II pneumocyte hyperplasia, and interstitial organization. Notably, there were no signs typical of exogenous lipoid pneumonia. In isolated cases, a mild interstitial chronic inflammatory infiltrate was observed [22].

In patients with chronic obstructive pulmonary disease (COPD), e-cigarettes stimulate neutrophilic inflammation and lung injury, accelerating disease progression [3; 23].

According to a 2019 study conducted in Wisconsin and Illinois, bronchoalveolar lavage (BAL) from 43 patients revealed lipid-laden macrophages (endogenous lipoid pneumonia). However, this finding is nonspecific, as it can also be observed in other conditions such as lung cancer, pulmonary tuberculosis, and fungal pneumonia. Histological examination of biopsy material showed mild nonspecific inflammation, organizing pneumonia, bronchiolitis with organizing pneumonia, acute diffuse alveolar damage, foamy macrophages, and interstitial and peribronchiolar granulomatous pneumonitis [20].

Most cases of lung injury were associated with products containing THC or other cannabinoids. Biopsies revealed nonspecific signs of acute lung injury with accumulation of foamy macrophages, predominantly in the small airways. Lipid-laden macrophages are often present in BAL but are nonspecific and should not be used for definitive diagnosis. There are no specific morphological markers for EVALI; diagnosis requires clinicopathological correlation and exclusion of other etiologies [5].

Thus, EVALI is diagnosed by exclusion: there must be a documented history of e-cigarette use within the past 90 days, no alternative cause of lung injury (including infectious, toxic, and autoimmune diseases), and pathological changes on chest CT [10; 11; 18].

Pathomorphological variants of lung changes associated with e-cigarette use, according to histological studies, are presented in Table 1 [11;26].

Table 1.

Pathomorphological changes in the lungs of patients with vaping-associated lung injury [11, 26].

BAL cytological findings	Histological findings (transbronchial biopsy)	Histological findings (surgical biopsy)
• Lipid-laden alveolar macrophages • Foamy macrophages • Predominant neutrophils • Predominant eosinophils • Hemorrhagic secretions / hemorrhagic exudate	• Acute alveolitis with intra-alveolar fibrosis • Diffuse alveolar damage (DAD) • Organizing pneumonia (OP)	• Organizing pneumonia (OP) • Respiratory bronchiolitis–associated interstitial pneumonitis (RB-associated pneumonitis) • Desquamative interstitial pneumonia (DIP) • Diffuse alveolar damage (DAD) • Lipoid pneumonia • Липоидная пневмония

Experimental Animal Studies

According to experimental research, e-cigarettes lead to infiltration of lung tissue by eosinophils, erythrocytes, and mononuclear cells, thickening of interalveolar septa, and hyperemia. Collagen deposition is also observed within interalveolar septa and in the peribronchial region. It is most likely that exposure to nicotine in the form of e-cigarettes induces degeneration of lung tissue, collagen deposition, activation of eosinophils and myofibroblasts, and angiogenesis. These architectural changes impair gas exchange in specific areas [37].

Exposure to nicotine-free e-cigarette liquid composed of glycerol and propylene glycol may result in areas of emphysematous alveolar enlargement, thickening of interalveolar septa, and the phenomenon of plasma imbibition, leading to consolidation of lung tissue [35].

Pikalyuk V.S. et al. (2016) studied the lung structure of Wistar rats exposed to aerosol from nicotine-free e-cigarette liquid in acute (7 days), subacute (30 days), and chronic (60 days) periods. In the acute stage, lung tissue exhibited signs of atelectasis, pronounced inflammatory changes in the bronchi, swelling of interalveolar septa, and accumulation of serous fluid in alveolar spaces. In the subacute stage, an increase in emphysematous transformation of alveoli was noted, along with persistent septal edema and inflammatory response from the bronchial tree. In the chronic stage, morphological changes were dominated by emphysema: thinning of interalveolar septa and expansion of terminal and respiratory bronchioles [25].

In a mouse study, inflammatory cytokine levels and morphological changes in lung tissue were analyzed after three weeks of exposure to e-cigarette aerosol (ECA) and cigarette smoke (CS) separately. Both ECA and CS exposure led to an increase in BAL cellularity; however, pronounced morphological changes—such as infiltration and thickening of interalveolar septa—were more pronounced with CS exposure. In addition, the authors recorded an increase in fibrotic changes in lung tissue, which potentially worsens the course of chronic obstructive pulmonary disease (COPD) due to a decrease in its elasticity and deterioration of external respiratory function. Overall, both exposures caused inflammation and morphological deterioration of the lungs, but the degree of negative change was less pronounced with ECA compared to CS [7].

Research has shown that in COPD, e-cigarette aerosol exacerbates inflammation and promotes pulmonary fibrosis [13].

One-month exposure to e-cigarettes resulted in dystrophic changes in epithelial and endothelial cells, accompanied by reduced collagen and elastin fibers in the extracellular matrix. With prolonged exposure (three months), marked structural alterations were observed: the alveolar membrane became anucleate, endothelial cells were absent, indicating destruction of the extracellular framework. Alveolar spaces were dilated and filled with edematous exudate, and alveolar walls lost their integrity. These changes caused stretching and deformation of interalveolar septa [42].

Molecular and immune mechanisms

In a mouse study, levels of inflammatory cytokines and morphological changes in lung tissue were analyzed after three weeks of exposure to e-cigarette aerosol and to cigarette smoke. Both exposures produced increases in IL-6 and TNF-α in bronchoalveolar lavage fluid (BALF), as well as increased IL-6 in serum; a significant rise in serum TNF-α was observed predominantly in the CS group [7].

Studies indicate that in chronic obstructive pulmonary disease (COPD) models, e-cigarette aerosol modulates pulmonary immune responses and cytokine production. In mice with COPD, exposure to e-cigarette aerosol was associated with elevated levels of several anti-inflammatory cytokines and an increased number of macrophages of the M2 phenotype, which are linked to inflammation regulation. Increased production of multiple cytokines—including M-CSF, IL-1 receptor antagonist (IL-1rα), IL-10 and TGF-β1—was detected in BALF of mice exposed to e-cigarette aerosol, suggesting a shift toward an anti-inflammatory/regulatory microenvironment under certain exposure conditions [13].

Rats exposed to e-cigarette vapor for six weeks showed significantly higher serum concentrations of inflammatory markers (including IL-2, IL-6, IL-9, IL-22, GM-CSF and TNF-α) compared with animals exposed to tobacco smoke or with controls. These findings indicate differences in systemic immune responses that may be important for understanding mechanistic distinctions between vaping and conventional smoking in terms of pulmonary and systemic inflammation [38].

Lee H.W. et al. reported that chronic exposure to e-cigarette aerosol can reduce DNA repair activity and the expression of DNA repair proteins XPC and OGG1/2 in lung tissue, which may have implications for genomic stability and carcinogenesis risk [21].

Acute exposure to e-cigarette aerosol induces oxidative stress in the lung without necessarily producing immediate structural alterations or a marked inflammatory infiltrate. Redox-proteomic analyses have revealed site-specific oxidation of protein thiols caused by acute e-cigarette exposure [36].

Ween M.P. et al., using cultured bronchial epithelial cells, found evidence of airway epithelial cell death, apoptosis, and macrophage efferocytosis mediated by alterations in receptor expression [39].

In an in vitro model of small-airway epithelium exposed to aerosols from capsule-type ENDS (electronic nicotine delivery systems), prolonged device use or device aging was associated with increased oxidative stress, cellular senescence, and DNA damage—likely related to heightened exposure to hazardous aerosols and metal particulates [15].

The principal data on exposure doses and durations and corresponding morphological changes are summarized in the following table (Table 2).

Conclusions

Taken together, the results of preclinical and clinical studies indicate that e-cigarette aerosol produces structural and inflammatory alterations in the lungs that are similar to those observed after exposure to tobacco smoke, while also exhibiting distinct features. The presence of oils, flavoring agents and other additives contributes to the development of lipoid pneumonia and to impaired function of alveolar macrophages. It is particularly concerning that even nicotine-free liquids may provoke inflammation and oxidative stress.

Based on the reviewed evidence, it is advisable that adolescents, young adults and pregnant women refrain from using e-cigarettes. This review synthesizes current data on the morphological characteristics of EVALI and underscores the need for further research to clarify pathogenic mechanisms, improve differential diagnosis, and develop therapeutic approaches for this condition.

Table 2.

Morphological changes in the lungs of animals after exposure to e-cigarette aerosols.

No.	Reference (selected)	Animal model	Duration	Dose / aerosol parameters	Main morphological changes
1	Pikalyuk V.S. et al. (2016) [25]	Rats	7 / 30 / 60 days	4 min once/day; 0.005 mL nicotine-free liquid	Alveolar enlargement, macrophage infiltration
2	Lee H.W. et al. (2018) [22]	Mice (FVB/N)	12 weeks	3 h/day; liquid with 10 mg/mL nicotine	DNA damage, reduced repair activity, preneoplastic changes
3	Tang M.S. et al. (2019) [33]	Mice (FVB/N)	54 weeks	4 h/day; 36 mg/mL nicotine, flavored liquid	22.5% lung adenocarcinoma, 57.5% bladder urothelial hyperplasia
4	Wang Q. et al. (2019) [36]	Mice	3 days	3 h/day; PG/VG 50:50, 25 mg/mL nicotine	Foci of inflammatory infiltrates
5	Wawryk-Gawda E. et al. (2020) [37]	Wistar rats	6 weeks	2×10 inhalations/day; 12 mg/mL nicotine; PG/VG 50:50	Chronic inflammation, fibrosis, epithelial destruction, apoptosis
6	Crotty-Alexander L.E. et al. (2021) [6]	Mice	3 and 6 months	1 h/day; PG/VG 50:50, 24 mg/mL nicotine	Barrier dysfunction, multi-organ fibrosis
7	Han H. et al. (2021) [13]	Mice (COPD model)	8 weeks	30 min/day; 50 mg/mL nicotine	Alveolar enlargement, increased mucus production, fibrogenesis
8	Yanina I.Y. et al. (2023) [35]	Rats	5 days	1×10 min/day; 0.6 mL nicotine-free flavored liquid	Emphysematous alveolar enlargement, septal thickening, plasma-imbibition phenomenon
9	Day Y. et al. (2023) [7]	Mice (BALB/c)	3 weeks	30 min, twice/day; nicotine liquid 10 mg/mL	Respiratory dysfunction, inflammatory cell infiltration, septal widening
10	Wiriansya E.P. et al. (2023) [42]	Rats	1 and 3 months	1 h/day; PG/VG 50:50, 3 mg/mL nicotine	Epithelial and endothelial degeneration, septal damage, edema

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