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Vaping-Associated Acute Lung Injury: A Clinical Narrative Review

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1. Abstract

E-cigarette or vaping product use-associated lung injury (EVALI) emerged as a distinct clinical entity in the United States in mid-2019, culminating in thousands of cases and dozens of deaths within months. This narrative review synthesizes the epidemiology, pathophysiology, clinical presentation, diagnostic approach, and management of EVALI, and situates it within the broader landscape of vaping-related acute lung injury. Vitamin E acetate, used as a diluent in illicit tetrahydrocannabinol (THC)-containing vaping cartridges, was identified as the primary causative agent, though other constituents and device factors likely contribute to a spectrum of inhalational lung injuries. Diagnosis remains one of exclusion, relying on a compatible history, characteristic imaging findings, and elimination of infectious and other causes. Corticosteroids form the mainstay of treatment for moderate-to-severe disease. Despite a marked decline in reported cases following public health interventions and regulatory action, vaping-related lung injury persists as an under recognized entity, and clinicians should maintain a high index of suspicion in patients presenting with respiratory symptoms and a history of e-cigarette or vaping product use.

2. Introduction

Electronic cigarettes and other vaping devices were introduced to the market as reduced-harm alternatives to combustible tobacco, marketed on the premise that removing combustion would eliminate the toxic byproducts associated with traditional smoking. This premise proved incomplete. Beginning in the spring of 2019, clinicians across the United States began reporting clusters of previously healthy young people presenting with severe, rapidly progressive respiratory illness following e-cigarette or vaping product use. The Centers for Disease Control and Prevention (CDC) and state health departments subsequently coordinated a national investigation, formally naming the condition EVALI in October 2019.

By February 2020, the CDC had confirmed over 2,800 hospitalized cases and 68 deaths across all 50 states, the District of Columbia, and two U.S. territories. While the acute outbreak has since subsided, sporadic cases continue to be reported, and the episode exposed significant gaps in the regulation of vaping products, the surveillance of novel inhalational exposures, and clinician awareness of vaping as a cause of acute lung disease. This review outlines what is known about the pathogenesis, clinical features, and management of EVALI, and considers its implications for ongoing vaping-related pulmonary morbidity.

3. Epidemiology

The 2019 EVALI outbreak disproportionately affected young, otherwise healthy individuals, with a median patient age in the early twenties and a strong male predominance. Case investigations consistently linked illness to vaping products containing THC, particularly those obtained from informal or illicit sources such as friends, family members, or unregulated dealers, rather than licensed dispensaries. A minority of cases involved nicotine-only products or reported dual use of THC and nicotine devices, suggesting that while THC-containing products were the dominant driver, they were not the exclusive cause.

Geographic and temporal clustering of cases tracked closely with the introduction of vitamin E acetate as a cutting agent in the illicit THC vaping supply chain, particularly in markets responding to increased demand and supply-chain adulteration. The rapid decline in case counts following public health messaging, product seizures, and vitamin E acetate's removal from many illicit supply chains further supported this causal link, though it does not exclude contributions from other additives, flavoring compounds, or device-related factors such as overheating and thermal degradation of vaping liquid.

4. Pathophysiology

The precise mechanism of lung injury in EVALI is not fully elucidated, but converging lines of evidence point to a chemical pneumonitis pattern rather than an infectious or classic hypersensitivity process. Broncho-alveolar lavage fluid from affected patients has demonstrated vitamin E acetate in the vast majority of samples tested in CDC-led investigations, a finding not replicated in comparison groups without vaping-associated lung injury. Vitamin E acetate is oily at room temperature and is hy-

pothesized to interfere with pulmonary surfactant function and to be directly cytotoxic to airway epithelium when aerosolized and inhaled, particularly at the high heating temperatures generated by some vaping devices.

Histopathologic findings across case series have been heterogeneous but frequently show acute fibrinous pneumonitis, diffuse alveolar damage, organizing pneumonia, or a foamy, lipid-laden macrophage response—patterns broadly consistent with an inhalational chemical injury rather than a single unifying histologic signature. This heterogeneity suggests that EVALI may represent a final common clinical pathway resulting from multiple toxic or irritant exposures rather than a single-agent, single-mechanism disease, a conceptualization that has led some authors to favor "vaping-associated lung injury" as a broader descriptive term encompassing EVALI and related presentations.

5. Clinical Presentation

EVALI typically presents subacutely, with symptoms evolving over days to a few weeks before medical presentation. The clinical picture combines respiratory, gastrointestinal, and constitutional features:

- Respiratory: dyspnea, cough (often nonproductive), pleuritic chest pain
- Gastrointestinal: nausea, vomiting, diarrhea, abdominal pain present in a majority of cases and sometimes dominating the initial presentation
- Constitutional: fever, chills, fatigue, unintentional weight loss

The prominence of gastrointestinal symptoms is a distinctive feature that can mislead initial diagnostic reasoning toward a primary gastrointestinal or infectious process, delaying recognition of the underlying lung injury. Physical examination findings are often nonspecific and may include tachypnea, tachycardia, and hypoxemia; auscultatory findings can be surprisingly unremarkable relative to the degree of hypoxemia and radiographic abnormality.

6. Diagnostic Evaluation

EVALI is a diagnosis of exclusion, and the CDC case definition requires:

1. Use of an e-cigarette or vaping product in the 90 days prior to symptom onset
2. Pulmonary infiltrates on chest radiograph or ground-glass opacities on computed tomography (CT)
3. Absence of pulmonary infection on initial workup, or a clinical course not consistent with infection alone
4. No alternative plausible diagnosis (e.g., cardiac, rheumatologic, or other identifiable cause)

6.1. Imaging: Chest CT is more sensitive than plain radiography and typically reveals bilateral, often diffuse ground-glass opacities, sometimes with subpleural sparing a finding that has been proposed as relatively characteristic of EVALI, though not pathognomonic. Consolidation, centrilobular nodularity, and pleural effusions may also be seen.

6.2. Laboratory studies: Findings are nonspecific and typically include leukocytosis (often with neutrophil predominance), elevated inflammatory markers (C-reactive protein, erythrocyte sedimentation rate), and elevated transaminases in a subset of patients. A thorough infectious workup including respiratory viral panel, blood and sputum cultures where indicated, and consideration of atypical pathogens is essential to exclude alternative causes before attributing illness to vaping.

6.3. Bronchoscopy: Not required in all cases but may be pursued in diagnostic uncertainty or severe disease, both to exclude infection via bronchoalveolar lavage and, in research or referral settings, to identify lipid.

6.4. History-taking:laden macrophages or vitamin E acetate on specialized lavage fluid analysis.

Given the social stigma and legal status of THC in many jurisdictions, patients may underreport vaping history, particularly THC use. A nonjudgmental, specific line of questioning—asking separately about nicotine vaping, THC vaping, product source, and recent changes in product or supplier improves diagnostic yield substantially over a single general query about "vaping."

7. **Management**

Management is largely supportive and stratified by severity:

- Mild disease (adequate oxygenation, reliable follow-up, no comorbidities): outpatient management with close follow-up within 24–48 hours may be appropriate, with strict counseling to cease all vaping product use.
- Moderate-to-severe disease (hypoxemia, significant comorbidities, or diagnostic uncertainty): hospitalization is generally warranted.
- Severe disease: a subset of patients progress to acute respiratory distress syndrome (ARDS) requiring high-flow oxygen, noninvasive ventilation, mechanical ventilation, or, in the most severe cases, extracorporeal membrane oxygenation (ECMO).

Empiric antimicrobial coverage is often initiated pending exclusion of infection, given overlapping presentations with atypical pneumonia. Systemic corticosteroids have emerged as the primary disease-modifying therapy, with observational data and clinical experience suggesting more rapid clinical improvement in patients treated with steroids compared to supportive care alone, though this has not been validated in randomized controlled trials given the outbreak's abrupt emergence and equally abrupt decline. Typical regimens have used methylprednisolone in the range of 1 mg/kg/day (or higher in severe disease), with tapering guided by clinical response.

All patients diagnosed with EVALI should receive counseling on smoking and vaping cessation resources, given the clear causal association and the risk of recurrence with continued or resumed use.

8. Outcomes and Long-Term Considerations

The majority of hospitalized EVALI patients survive to discharge, with clinical improvement typically evident within days of corticosteroid initiation and cessation of the causative exposure. However, the outbreak was associated with substantial morbidity, including prolonged intensive care unit stays and a nontrivial number of deaths, predominantly in patients with delayed diagnosis or underlying comorbidities. Long-term pulmonary outcomes remain incompletely characterized; some patients demonstrate residual radiographic abnormalities or reduced diffusion capacity on follow-up pulmonary function testing, raising concern for lasting parenchymal injury in a subset of survivors, though systematic long-term follow-up data are limited.

9. Public Health and Regulatory Response

The EVALI outbreak prompted a coordinated response spanning public health messaging discouraging vaping product use (particularly THC-containing products from informal sources), enhanced state and federal surveillance case definitions, and regulatory actions targeting flavored e-cigarette products and vitamin E acetate specifically. Several states and jurisdictions restricted or banned vitamin E acetate as a vaping additive, and federal guidance explicitly named it as a chemical of concern. These interventions coincided with a sharp decline in reported EVALI cases through late 2019 and into 2020, although the concurrent onset of the COVID-19 pandemic complicates disentangling the relative contributions of public health messaging, supply-chain changes, and reduced case ascertainment or surveillance capacity during that period.

10. Limitations of Current Evidence

Much of the EVALI literature derives from outbreak-era case series, retrospective cohorts, and public health surveillance data rather than prospective controlled studies, reflecting the emergent nature of the crisis. Causal attribution to vitamin E acetate, while well supported, does not exclude synergistic or independent contributions from other diluents, flavoring chemicals, heavy metals leached from device coils, or thermal degradation products—an area requiring continued toxicological and clinical research as vaping product formulations continue to evolve. Additionally, because vaping product composition is poorly regulated and highly variable, particularly in illicit markets, findings from any given cohort may not generalize to all vaping-associated lung injury going forward.

11. Conclusion

EVALI represents a striking example of a novel, environmentally mediated acute lung injury syndrome that emerged rapidly, caused substantial morbidity and mortality, and was ultimately traced to a specific toxic exposure vitamin E acetate in illicit THC vaping products through coordinated clinical and public health investigation. While the acute outbreak has waned, vaping-associated lung injury has not disappeared, and the underlying conditions that enabled it largely unregulated product formulations, illicit supply chains, and incomplete clinician and patient awareness persist. Continued clinical vigilance, nonjudgmental and specific substance use history-taking, and ongoing toxicological surveillance of vaping product constituents remain essential to preventing future outbreaks of this kind.

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