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## Is it Cool to Juul?

### A Case of Vaping Induced Lung Injury

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## Introduction

"Vaping" is the inhalation of an aerosolized substance produced through heating a solution that typically contains nicotine, cannabis, or other substances. There are many products available commercially used as devices for vaping such as the electronic cigarette, vape, or "JUUL." Vaping has become especially popular among teens and young adults likely due to marketing these devices as "safe" when compared to the traditional cigarette, and there are a wide variety of flavors.<sup>1</sup>



Figure 1<sup>1</sup>

According to the CDC, more than 3.5 million teens reported using e-cigarettes in 2018. The number of vapers globally has been increasing rapidly - from about seven million in 2011 to 41 million in 2018. The use of vaping products has been associated with an outbreak of "E-cigarette or vaping product use associated lung injury (EVALI)," which started in the United States in the summer of 2019. According to the CDC, as of January 14, 2020, there have been a total of 2668 hospitalized EVALI cases, reported in all 50 states, with sixty confirmed deaths. While the CDC, FDA, and state health authorities are still collecting data, research is suggesting that THC-containing products are most often linked to EVALI cases. Data has also been collected that suggest Vitamin E acetate is strongly linked to EVALI cases, and the compound has been found in bronchoalveolar lavage fluid.<sup>2</sup>

#### Symptoms of EVALI include<sup>3</sup>:

- Shortness of Breath (85%)
- Cough (85%)
- Chest pain (52%)
- Hemoptysis (8%)
- Constitutional Symptoms like Fever (84%) and Chills (60%)
- GI symptoms: Nausea (66%), Vomiting (61%), Diarrhea (44%)

Patients can present to the emergency department or physician's office with many of the above symptoms. Upon examination 58% of people are hypoxemic, fever is present in 33% of cases, and can be seen with both tachycardia and tachypnea. On chest x-ray, 83% of patients can be expected to have diffuse hazy or consolidative opacities.<sup>3</sup>

Formal diagnostic criteria for EVALI have not been totally established, and the diagnosis is typically a diagnosis of exclusion. Clinicians should specifically rule out lung infection. It is recommended to order testing for Influenza, a viral respiratory panel, and urine antigen tests for *Legionella* and *S. pneumoniae*, in addition to blood cultures, sputum culture. If HIV is clinically suspected testing for opportunistic infections is appropriate. Once infection has been ruled out, and alternative diagnoses (ie cardiac, neoplastic, or rheumatologic) have also been ruled out, clinicians may then think about a diagnosis of EVALI. Criteria to establish a diagnosis of EVALI include use of an e-cigarette or related product in the previous 90 days, and lung opacities on CT or chest x-ray.<sup>3,4</sup>

Treatment of EVALI has not yet been well established. One study has shown that approximately 95% of patients with EVALI have required hospitalization. The mainstay of treatment is supportive care including supplemental oxygen if required with a target pulse oximetry reading from 88-92%. In most EVALI patients, it is recommended not to overlook the diagnosis of community acquired pneumonia, so empiric antibiotics to cover for CAP are recommended.

Systemic glucocorticoids are often used in the treatment of EVALI, though there are no formal studies. There have been several small scale studies that may show a benefit of systemic glucocorticoids. Long term effect of EVALI are unknown. With regards to follow up, it is recommended to follow clinically until resolution of symptoms. It is also recommended to follow radiographically to ensure resolution of the illness process.<sup>3,4,5</sup>



(Illustration/Pascal Kison, iStock)

## Case

### History

17-year-old male with no significant PMH who presented to Reading hospital with a nonproductive cough, SOB, chest tightness, vomiting, diarrhea and fever to 103 at home. Fever did improve with Tylenol at home. Started with URI symptoms about a week ago which acutely became worse over the last few days. Seen in ED 4 days prior to admission, CXR at that time unremarkable, vital signs within normal limits at the time and sent home with supportive care. Also endorsed pain with deep inspiration. 9/10 severity with deep breaths. Location was over the middle of the chest. Endorsed daily vaping with tobacco and near daily vaping with Marijuana, last use 3 days prior to admission. Also endorsed recent weight loss, did not have exact weight but dropped 4 pant sizes in the last month, however, may patient believe it may have been due to not playing rugby. NO recent travel, NO sick contacts, NO animal exposure

**ROS** – decreased activity level & appetite, fever, chills, unexpected weight change, congestion, shortness of breath, abdominal pain, and headache

### Physical Exam

Vitals : BP 122/72 // Pulse 109 // Temp 38.4C or 101.1F // RR 48 // SpO2 87% // Wt 57.6kg

**Constitutional:** Normal appearance.

**HEENT:** unremarkable, moist mucous membranes without erythema, exudates or petechiae, tonsils: 2+ and cryptic, PERRL

**Cardiovascular:** RRR, no MGR, no chest wall tenderness

**Pulmonary:** scattered wheezing. Course bibasilar rales (L>>R), Increased resp effort requiring O2 NC

**Abdominal:** Soft, nontender, normal bowel sounds in all 4 quadrants

**Neurological:** Alert and oriented x3, no focal neurological deficit

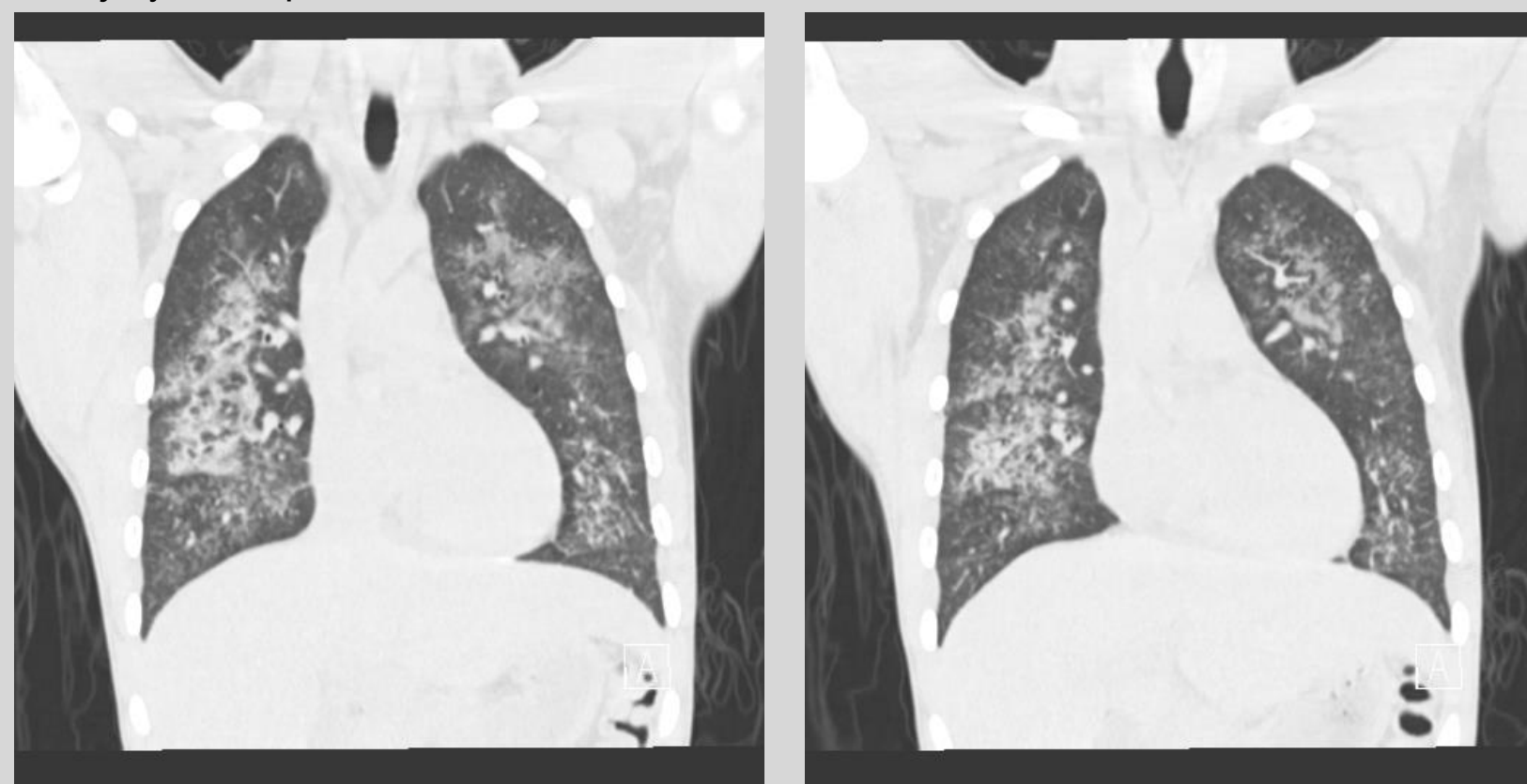
**Skin:** warm, no rashes, no ecchymosis

<b>Labs:</b>	131	98	16	94	15.5	12.7
	4.2	20.5	0.90		355	

Anion gap 13	MCV 86.3
Calcium 9.0	Lymphocyte% 7.4
Total Protein 7.2	CRP 33.0
Albumin 3.7	Sed Rate 68
Total Bilirubin 0.7	Lactic Acid 0.8
AST 27, ALT 9, alkaline phosphatase 67	Neutrophil % 75.9
	Eosinophil% 13.6
	Basophils% 0.3

**Imaging: CXR:** Fairly diffuse bilateral infiltrates are now demonstrated suggesting atypical pneumonia or possibly inhalational lung injury. Pulmonary edema or hemorrhage is considered less likely.

**CT:** Extensive, diffusely scattered, and partially consolidated alveolar densities throughout the upper lungs bilaterally with areas of **subpleural sparing**. Negative for pleural effusion, pneumothorax, or pneumomediastinum. Findings are nonspecific but given clinical history and age vaping associated pulmonary injury is suspected.



## Treatment Course

### TIMELINE

**09/21/2019:** Patient presents to the ED for fever and persistent non-productive cough for a week. Chest x-ray obtained shows no acute cardiopulmonary activity. Based on reported symptoms etiology thought to be viral illness by ED provider. Patient's vaping habits were discussed prior to discharge from the ED

**09/23-9/25/2019:** Despite follow-up visit with PCP on 09/23 there were multiple telephone encounter between PCP's office and mother of patient for persistent fevers, as high as 103 F, dyspnea and excessive coughing with episodes of post-tussive emesis.

**09/25/2019:** patient returns to the ED febrile, tachypneic, hypoxic and tachycardic. Chest x-ray obtained was significant for diffuse bilateral infiltrates. Based on chest x-ray atypical pneumonia versus inhalation injury was considered as the etiology. RSV PCR, influenza PCR, blood and urine cultures were collected, and he was given azithromycin and dexamethasone by ED provider. His SpO2 improved (>92%) with 3L nasal cannula. Once stable, patient was admitted on the pediatric unit under Family Medicine Residency Service for acute hypoxemic respiratory failure.

Pulmonary intensivist was consulted. High-Resolution CT chest, streptococcal pneumoniae and Legionella urinary antigens were ordered by the specialist. CT imaging showed extensive bilateral alveolar/interstitial infiltrates consistent with vaping induced lung injury. Treatment regimen recommended: azithromycin 250 daily X5 days, prednisone 40 mg daily, DuoNeb q.4hr p.r.n., albuterol q.2hr p.r.n., and O2 therapy as needed.

**9/26/2019:** Patient continues to have dyspnea, hypoxemia and tachypnea with minimal exertion. The case was reported to Pennsylvania Department of Health who then requested that vaping devices and solutions would be sent to DOH for further investigation into the potential substance abuse substances causing the syndrome.

**09/27/2019:** Dyspnea and intermittent tachypnea with minimal exertion unchanged. Hypoxemia resolved. Repeat chest x-ray showed minimal improvement of airspace consolidation.

**09/28/ 2019-** Day of discharge. Patient continues to have SpO2 greater than 90% on room air. There is resolution of tachypnea with minimal exertion. dyspnea, lesser intensity when compared to admission, persists. Urinary antigens resulted negative. Blood and urine cultures were negative. HIV study negative. Patient completed 4/5 days of azithromycin 250 daily prior to discharge. He was discharged with his final dose azithromycin and prednisone 40 mg to take q.daily until follow-up with Pulmonary outpatient.

**10/04/2019-** patient evaluated by PCP. No respiratory distress or hypoxia noted. Per chart review, patient continued to have intermittent episodes of dyspnea with moderate exertion and persistent fatigue. Documented resolution of these symptoms were on 10/28/2019.

**10/24/2019-** chest x-ray ordered by CHOP pulmonology group. Impression read: "Interval resolution of the bilateral pulmonary opacities. The lungs are now clear".

## Discussion

New device on commercial markets. New pathology. Unlike tobacco and marijuana cigars, the delivery system of the E-cigarettes provides higher concentration of substances at a higher temperature. Often the oils used as a vehicle for delivery of THC or nicotine contain other various solvents and solutions which are not FDA approved. All components, including THC and nicotine, are aerosolized and delivered directly into the lung alveoli. In a few of the case reports available since early 2019 the duration of use to presentation of symptoms is a range between 6 to 12 months. There were a few outliers who became symptomatic after 2 years of use. Severity of presentation various as does length of hospital stay. Per Characteristics of a Multistate Outbreak of Lung Injury Associated with E-cigarette Use, or Vaping — United States, M&M report, the median duration between symptom onset and hospitalization was 6 days<sup>9</sup>.

Mechanism of injury to the lung parenchyma is due to inflammation which isn't a novel concept, but the type inflammation that predominates the lung parenchyma is something that is looked at among researchers. Most of the information available are through case studies where bronchoscopy was performed and then analyzed. Most samples were taken from patient's requiring ICU level of care. On the bronchoalveolar lavage cell count and differential a strong predominance white blood cells are noted. Of the leukocytes, almost all samples contained over 50% of neutrophils. A close second in predominance were macrophages. These macrophages contained lipids. This is potentially significant since the current theory of pathophysiology involves the inhalation fat-soluble vitamin E. Vitamin E is a common additive found within vaping solutions, most commonly those also containing THC, and could be a major pro inflammatory component.

What maybe considered a key in vaping induced lung injury is that bronchoalveolar lavage sample also contained no significant microbes on H+E. additionally blood cultures on these patients are often negative. Despite this, when a patient presents with suspected EVALI what is often provided in the therapy regimen includes daily corticosteroids, antibiotics, and respiratory therapies such as albuterol and/or ipratropium. This is an unsubstantiated regimen, but for now it's the temporary standard of care. To date, there is much about the pathophysiology, efficacy of treatment, sequela of lung injury that is unknown. Thus, CDC continues to recommend persons the refrain from using e-cigarette, or vaping, products, particularly those containing THC.

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