The Adolescent Vaping Epidemic

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May 1, 2021

Disclosures
- None

Objectives
- Identify the scope of the adolescent vaping epidemic
- Recognize the clinical presentation of e-cigarette, or vaping, product-use-associated lung injury (EVALI)
- Discuss the treatment approach for adolescents with vaping related lung injury

Outline
- Case
- Vaping in Adolescents
- What are E-Cigarettes?
- Presenting Symptoms
- Associated Problems
- Workup and Treatment
- What can you do?
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Case

17-year-old boy presenting with productive cough, chest pain, dyspnea, fever, nausea, vomiting, diarrhea

- Chest pain: “knives are stabbing my lungs”
- Unintentional 10-pound weight loss

- Completed course of azithromycin (concern for atypical pneumonia) without improvement in symptoms

Vitals & Exam

- Vitals
  - T 102.6, HR 120, BP 114/60, RR 30, SpO2 86% in room air.
- Exam
  - General: pale, tired appearing
  - Eyes: right inferior conjunctival hemorrhage
  - HEENT: Dry and cracked lips
  - Lungs: Tachypneic, but non-labor. Crackles and decreased aeration at bases

Additional History

- PMH:
  - Depression, anxiety, prior inpatient hospitalizations x2

- Medications:
  - Sertraline and clonidine

- Social History:
  - Lives with adoptive parents (maternal grandfather and his fiancé).
  - History of physical abuse and neglect when previously living with biologic parents
  - Attends farming vocational school
Case

Additional Social History

CXR

Case

Labs

CRP 25.4

Absolute neutrophil count 8.01
Absolute lymphocyte count 0.26
Absolute eosinophil count 0.11
Absolute basophil count 0.03
Absolute monocyte count 0.14
Hospital Course

- Admitted to the Step-Down Unit
- Switched from vancomycin/zosyn to ceftriaxone and ultimately levofloxacin
- Persistent fevers and hypoxia
  - Maximal respiratory support: HFNC 25L, FIO2 40%

Additional Infectious Workup

- Respiratory culture and gram stain with normal upper respiratory flora
- Blood culture negative
- Influenza A/B negative
- Aspergillus galactomannan negative
- 1, 3-B-D-glucan negative
- Fungus culture negative
- KOH Fungal stain negative
- Cryptococcus antigen negative
- Pneumocystis carinii stain negative
- HIV non-reactive
- T-SPOT TB test negative

PFTs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Predicted</th>
<th>Actual</th>
<th>Scoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>4.42</td>
<td>2.85</td>
<td>56</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>79.7</td>
<td>63</td>
<td>95</td>
</tr>
<tr>
<td>FEV1</td>
<td>2.72</td>
<td>1.96</td>
<td>57</td>
</tr>
<tr>
<td>FEF25-75</td>
<td>4.31</td>
<td>2.90</td>
<td>06</td>
</tr>
<tr>
<td>FEF25</td>
<td>1.11</td>
<td>0.90</td>
<td>09</td>
</tr>
<tr>
<td>FEF75-85</td>
<td>3.94</td>
<td>3.03</td>
<td>49</td>
</tr>
<tr>
<td>FEF85</td>
<td>0.84</td>
<td>0.69</td>
<td>05</td>
</tr>
<tr>
<td>RV</td>
<td>4.49</td>
<td>3.94</td>
<td>06</td>
</tr>
<tr>
<td>RV/TLC</td>
<td>0.61</td>
<td>0.51</td>
<td>09</td>
</tr>
</tbody>
</table>

Chest CT

![Chest CT Image]
Bronchoscopy

- Notable for airway hyperemia
- Cytology with 56-60% neutrophils, 15-19% eosinophils, 15% macrophages, 10% respiratory epithelial cells. Abundant mucus. Moderate increase in fat-laden macrophages. No iron-laden macrophages.
- BAL negative for adenovirus, chlamydia pneumonia, enterovirus, human bocavirus, human coronavirus, human metapneumovirus, influenza, mycoplasma, parainfluenza, respiratory syncytial virus, AFB culture, aspergillus, fungus, legionella, nocardia

Overall, case thought to be consistent with eosinophilic pneumonia
- The patient was treated with steroids and followed closely as an outpatient with normalization of PFTs
- Started on nicotine replacement therapy (NRT)
- He resumed vaping while still on steroids

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  - Presenting Symptoms
  - Associated Problems
  - Workup and Treatment
  - What can you do?

Marketing is Influencing Adolescents

[Graph showing e-cigarette use among youth rising as e-cigarette advertising grows]

Marketing Toward Adolescents

Why Adolescents?

The adolescent brain is more susceptible to the effects of addiction

Majority of adult smokers are already addicted to nicotine by the age of 18

Why Adolescents are Using E-Cigarettes

<table>
<thead>
<tr>
<th>Reason</th>
<th>Use e-cigarettes only*</th>
<th>Use e-cigarettes and other tobacco products*</th>
</tr>
</thead>
<tbody>
<tr>
<td>They are cheaper than regular cigarettes</td>
<td>36.6 (34-38.1)</td>
<td>38.2 (34.5-41.3)</td>
</tr>
<tr>
<td>They are easier to get than other tobacco products, such as cigarettes</td>
<td>22.2 (19.5-25.1)</td>
<td>22.2 (19.5-25.1)</td>
</tr>
<tr>
<td>They are available in flavors, such as mint, vanilla, fruit, or chocolate</td>
<td>22.2 (19.5-25.1)</td>
<td>22.2 (19.5-25.1)</td>
</tr>
<tr>
<td>I used them because of friends</td>
<td>22.2 (19.5-25.1)</td>
<td>22.2 (19.5-25.1)</td>
</tr>
<tr>
<td>I was peer pressured into using them</td>
<td>17.2 (13.9-20.9)</td>
<td>19.1 (15.7-22.6)</td>
</tr>
<tr>
<td>I was under stress from school</td>
<td>14.5 (10.2-18.8)</td>
<td>22.2 (19.5-25.1)</td>
</tr>
<tr>
<td>I was under stress from home</td>
<td>14.5 (10.2-18.8)</td>
<td>22.2 (19.5-25.1)</td>
</tr>
<tr>
<td>They are less harmful than other forms of tobacco, such as cigarettes</td>
<td>6.9 (5.7-8.3)</td>
<td>7.5 (5.5-9.5)</td>
</tr>
<tr>
<td>They impressed me in terms of style or status</td>
<td>5.7 (4.3-7.4)</td>
<td>6.3 (5.1-7.6)</td>
</tr>
<tr>
<td>I was told I could get them on the internet</td>
<td>3.9 (3.0-5.0)</td>
<td>5.7 (3.7-9.5)</td>
</tr>
<tr>
<td>I saw people on TV, online, or in movies using them</td>
<td>3.9 (3.0-5.0)</td>
<td>5.7 (3.7-9.5)</td>
</tr>
<tr>
<td>To try to quit using other tobacco products, such as cigarettes</td>
<td>3.9 (3.0-5.0)</td>
<td>5.7 (3.7-9.5)</td>
</tr>
<tr>
<td>They cost less than other tobacco products, such as cigarettes</td>
<td>3.9 (3.0-5.0)</td>
<td>5.7 (3.7-9.5)</td>
</tr>
<tr>
<td>I used them for some other reason**</td>
<td>15.0 (11.4-18.6)</td>
<td>48.0 (34.5-62.4)</td>
</tr>
</tbody>
</table>


Scope of the Youth Vaping Epidemic


Outline

- Case
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- What are E-Cigarettes?
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- What can you do?

Timeline

- 2003: First commercially available e-cigarette is created in China
- 2006: First successful e-cigarette is created in China
- 2010: E-Cigarettes are introduced in Europe
- 2015: Juul Emerges and launches the vaporized campaign
- 2016: FDA rules to regulate e-cigarettes under the Family Smoking Prevention and Tobacco Control Act
- 2017: Surgeon General declares youth vaping an epidemic
- 2018: FDA gives E-Cigarette manufacturers until 2022 to provide information
- 2019: American Academy of Pediatrics wins case against FDA over failure to protect youth
- 2020: Federal ban on flavored vaping products

E-Cigarettes Today
E-Cigarettes Today

Devices that use HEAT to aerosolize e-liquids, flavoring, and nicotine or THC

- **Components:**
  - Power source
  - Electronic heating element
  - Liquid cartridge
    - Stabilizing agent
      - e.g. propylene glycol
    - Nicotine or THC
    - Flavoring additives

Nicotine Content in E-Cigarettes

- Significant variation in nicotine concentration depending on device, e-liquid, and user characteristics
  - A study of 16 different e-cigarettes showed nicotine level in 300 puffs of vapor varied from 0.5mg to 15.4mg (vs. 1.54mg to 2.6mg in one conventional cigarette)

- One Juul 5% pod = 1 pack of conventional cigarettes

- Many of cartridges labeled as “no nicotine” still delivered some nicotine
- Teens often unaware of this

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Vaping Marijuana

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Nicotine Salt
**Flavoring**

- FDA “generally recognized as safe” (GRAS) - for ingestion
  - Inhalant safety not tested and not known
- Thermal decomposition of propylene glycol, glycerol & flavorings produce toxic aldehydes with flavorings at levels that exceed occupational safety standards in most popular brands

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**When to Consider E-Cigarette Use**

**Symptoms**

- Respiratory
  - Cough in absence of cold or allergy symptoms
  - SOB, wheezing, worsening asthma
  - Decreased exercise tolerance
  - Hemoptysis
- Gastroenterological
  - Abdominal pain
  - Nausea
  - Vomiting
  - Diarrhea
- Constitutional
  - Weight loss
  - Fever
  - Night sweats

**Nicotine toxicity**

- Stomach pain
- Headache
- Dizziness
- Difficulty Concentrating
EVALI Presenting Symptoms

From Initial Wisconsin & Illinois Cases – 53 cases (median age 19 years)


EVALI - Definition

Using an e-cigarette in 90 days prior to symptom onset

AND

Pulmonary infiltrate, such as opacities, on plain film chest radiograph or ground-glass opacities on chest CT

Probable Case: Infection identified BUT clinical team believes it is not sole cause of underlying lung injury

OR minimum criteria to rule out pulmonary infection is not met and clinical team believes infection is not sole cause of underlying lung injury

AND

All other clinically-indicated respiratory infectious disease testing are negative

AND

No evidence of alternative plausible diagnosis (e.g. cardiac, rheumatologic)

Confirmed Case

Probable Case:

Infection identified BUT clinical team believes it is not sole cause of underlying lung injury

OR minimum criteria to rule out pulmonary infection is not met and clinical team believes infection is not sole cause of underlying lung injury

AND

All other clinically-indicated respiratory infectious disease testing are negative

AND

No evidence of alternative plausible diagnosis (e.g. cardiac, rheumatologic)

Emergence of EVALI

As of February 18, 2020:

- 2,807 cases of patients hospitalized with EVALI in USA
- 68 deaths confirmed


EVALI by Age

- Among the 2,668 hospitalized EVALI cases or deaths (as of 1/14/20):
  - Median age: 24 years
  - Age range: 13-85 years

EVALI – Products Used

- Among those with information on substances used in the 3 months prior to symptom onset (as of 1/14/20):
  - 82% reported using THC-containing products; 33% reported exclusive use, 16% from commercial sources
  - About half report nicotine-containing products; 14% reported exclusive use
  - Some reporting CBD use or just vapor use


EVALI Pathology: What is the Cause?

- Thermal burn injury
- Allergic reaction/eosinophilic pneumonia
- Hypersensitivity pneumonia
- Organizing pneumonia
- Toxic lung injury

Patterns are non-specific & there is likely more than one component contributing.

EVALI – Vitamin E Acetate

Blount BC, et al. NEJM. 2020;382:697-705
Vaping and Asthma

- Vaping is more popular among asthmatic teenagers vs. non-asthmatic peers
- EVALI cases occur at a higher than expected rate in asthmatics
- 33% of 11-17 year old with asthma had secondhand e-cigarette exposure which was associated with increased risk of exacerbation (Florida Youth Tobacco Survey)
- Case report of two adolescent asthmatics with history of e-cigarette use who presented with life threatening status asthmaticus requiring V-V ECMO

Vaping Leads to Chronic Respiratory Symptoms

- 45,000 adolescents in Hong Kong, vaping in the previous month was associated with increased odds of reporting chronic cough or phlegm
- 2000 HS students in Southern California, past and current vaping was associated with a nearly twofold increase in the risk of chronic bronchitis symptoms
- Vaping was found to be an independent risk factor for respiratory illnesses in adults, and dual use of combustible cigarettes and e-cigarettes is riskier

Vaping and COVID-19

- Important to still consider vaping related lung injury in COVID-19 era
- Compared to non-users, adolescents & young adults who use e-cigarettes:
  - Have more symptoms of COVID-19
  - Get tested more frequently for COVID-19
  - More commonly test positive for COVID-19
- COVID-19 diagnosis 5 times more likely among ever-users of e-cigarettes
  - Even more common in dual users

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E-Cigarettes are NOT approved NRT

- Marketed as safer alternative to cigarettes
- May perpetuate nicotine dependence
- Inconsistent labeling & poor regulation
- Major tobacco companies now own e-cigarette companies

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**E-Cigarettes vs. NRT in Smoking Cessation**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>E-Cigarettes (N=438)</th>
<th>Nicotine Replacement (N=466)</th>
<th>Primary Analysis: Relative Risk (95% CI)</th>
<th>Sensitivity Analysis: Adjusted Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome: abstinence at 52 wk — no. (%)</td>
<td>79 (18.0)</td>
<td>44 (9.9)</td>
<td>1.83 (1.36–2.38)</td>
<td>1.75 (1.24–2.46)</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abstinence between wk 26 and wk 52 — no. (%)</td>
<td>93 (21.2)</td>
<td>53 (11.9)</td>
<td>1.79 (1.32–2.44)</td>
<td>1.82 (1.34–2.47)</td>
</tr>
<tr>
<td>Abstinence at 4 wk after target quit date — no. (%)</td>
<td>192 (43.8)</td>
<td>134 (30.0)</td>
<td>1.45 (1.22–1.74)</td>
<td>1.43 (1.20–1.71)</td>
</tr>
<tr>
<td>Abstinence at 26 wk after target quit date — no. (%)</td>
<td>155 (35.4)</td>
<td>112 (25.1)</td>
<td>1.40 (1.14–1.72)</td>
<td>1.36 (1.15–1.67)</td>
</tr>
<tr>
<td>Carbon monoxide-validated reduction in smoking of ≥50% in participants without abstinence between wk 26 and wk 52 — no./total no. (%)</td>
<td>44/345 (12.8)</td>
<td>29/393 (7.4)</td>
<td>1.75 (1.12–2.72)</td>
<td>1.73 (1.11–2.69)</td>
</tr>
</tbody>
</table>

- At one year, 18% of those in the e-cigarette group & 9% of the NRT group were abstinent from smoking cigarettes
- In those abstinent, 80% of those in the e-cigarette group were still using e-cigarettes & only 9% of those in the NRT group were still using NRT
Increased Risk of Substance Use in Teens Who Vape

5.8X
6.5X
3.0X


Health and Wellness Vapes

Sleep on demand™

Melatonin is a hormone that helps regulate sleep timing. Take control of your circadian rhythm with a nighttime routine conditioned for good sleep.
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Recommended Evaluation

<table>
<thead>
<tr>
<th>Imaging</th>
<th>Diagnostic Testing</th>
<th>Infectious w/u</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest X-ray (PA and Lateral)</td>
<td>Spirometry (pre &amp; post)</td>
<td>Influenza PCR or rapid test</td>
</tr>
<tr>
<td></td>
<td>FEV1</td>
<td>SARS-CoV-2 PCR</td>
</tr>
<tr>
<td></td>
<td>FVC</td>
<td>Viral Panel</td>
</tr>
<tr>
<td></td>
<td>TLC</td>
<td>Sputum sample if productive cough</td>
</tr>
<tr>
<td></td>
<td>DLCO</td>
<td>Send for gram stain/culture, AFB, fungal</td>
</tr>
<tr>
<td></td>
<td>6 Minute Walk Test</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mycoplasma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PJP if risk factors</td>
</tr>
<tr>
<td>Chest CT (If symptoms persist and persistent abnormal PFTs and/or CXR)</td>
<td>LABS: CBC, CRP, ESR and liver function tests</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Urine Cotinine/Drug Screen</td>
</tr>
</tbody>
</table>

Recommended Evaluation

- Chest X-ray (PA and Lateral)
- Spirometry (pre & post)
- FVC
- TLC
- DLCO
- 6 Minute Walk Test
- Chest CT (If symptoms persist and persistent abnormal PFTs and/or CXR)
- LABS: CBC, CRP, ESR and liver function tests
- Urine Cotinine/Drug Screen

Admission and Follow-Up Criteria

- "Strongly consider admitting patients with potential lung injury, especially if respiratory distress present, have comorbidities that compromise pulmonary reserve, or decreased (<95%) oxygen saturation"
- Post-discharge follow-up ideally within 48 hours
- Patient not admitted to hospital
- Recommended follow-up within 24-48 hours

Prevention

- Flu Shot
- Consider PPSV23

Management and Follow-Up

<table>
<thead>
<tr>
<th>Indication</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic steroids/Severe Presentation</td>
<td>Vaping Cessation/Referral to Pulmonary &amp; Addiction Medicine</td>
</tr>
<tr>
<td>Mildly hypoxia 6mwt or decreased DLCO</td>
<td>Consider steroids</td>
</tr>
<tr>
<td>New ICS or ICS/LABA and vaping</td>
<td>Consider antimicrobial treatment</td>
</tr>
<tr>
<td>Still vaping, mildly abnormal or normal studies</td>
<td>Nicotine Replacement Therapy (NRT)</td>
</tr>
<tr>
<td>Quit vaping, mildly abnormal</td>
<td>Recommend Follow Up</td>
</tr>
<tr>
<td>6 months</td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td></td>
</tr>
<tr>
<td>2-3 months</td>
<td></td>
</tr>
<tr>
<td>1-2 weeks</td>
<td></td>
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</tbody>
</table>
Vaping Clinic at BCH

- Comprehensive pulmonary evaluation for patients who are vaping with concerning symptoms
  - Over 130 referrals, 103 patients seen to date
  - 39% distant asthma history & 66% mental health history
  - Half of referred patients met criteria for confirmed EVALI or probable EVALI with signs of infection
  - Many have obstructive spirometry, Low DLCO, and/or hypoxia on 6 min walk
  - Referred 70% patients to the Adolescent Substance Abuse Program (ASAP)

Vaping Clinic Goals

- Improve identification of youths & young adults who are vaping and have pulmonary symptoms
- Update tobacco screening to include vaping specific language to uncover patients at risk for EVALI
- Develop a vaping product use questionnaire
- Establish a comprehensive pulmonary evaluation
- Expand treatment resources in partnership with the Adolescent Substance Abuse Program (ASAP)
- Create a Pulmonary Vaping Program Biobank
- Provide advocacy and education

Vaping Clinic Demographics

<table>
<thead>
<tr>
<th>Vaping Clinic Evaluation</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine &amp; Marijuana</td>
<td>85%</td>
</tr>
<tr>
<td>Nicotine Only</td>
<td>7%</td>
</tr>
<tr>
<td>Marijuana Only</td>
<td>8%</td>
</tr>
</tbody>
</table>

Vaping Product Use Reported

- 26% Normal
- 25% Abnormal

PFTs

- 74% Abnormal

Abnormal PFT Findings

- 64% Decreased FVC
- 27% Decreased FEV1
- 24% Obstructive
Vaping Clinic Demographics

Comprehensive Diagnostic Evaluation and Diagnosis

- 64% Not EVALI
- 2% Probable EVALI
- 24% EVALI
- 54% Not EVALI

Resources for Quitting

- AAP Toolkit
- Truth Initiative
- Ditch JUUL
- Family Education Sheet
- SmokeFree.gov
- Smokefree Teen
- How to Quit Smoking
  This CDC web page provides free resources, including the quitSTART app and how to build a quit plan.

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Is Vaping Worse than Cigarettes?

“For years we’ve known that tobacco cigarettes were dangerous, but short-term use does not send people to the hospital. Now, there is increasing evidence that short-term use of e-cigarettes can send children to the emergency room. The public must be alerted to the dangers of vaping e-cigarette products, and healthcare professionals educated on what to look for in patients suffering from vaping-related respiratory distress.”

- Frank Leone, MD, member of the ATS Tobacco Action Committee
Lack of Federal Regulation in Vaping

- None of these products are regulated by the FDA
- In 2016, the FDA expanded its authority to regulate tobacco products to include e-cigarettes and cigars
  - FDA later announced manufacturers do not have to provide information about e-cigarettes until 2022
- In May 2019, federal judge rules in favor of the American Academy of Pediatrics and others in lawsuit against the FDA for allowing manufacturers to keep products on the market
- At end of 2019, Federal officials said they would forbid the sale of most flavored e-cigarette cartridges, but would exempt menthol and tobacco flavors, as well as flavored liquid nicotine sold in open tank systems at vape shops
  - 4/28/21: Biden administration planning to propose a ban on menthol cigarettes
  - 4/29/21: FDA announces that it will ban menthol cigarettes and all flavored cigars by 2022

Advocacy by the AAP

- Advocacy priorities:
  - Prohibit all flavored tobacco products, including menthol and mint
  - Regulate all tobacco products in the interest of public health
- AAP wins a lawsuit that was filed against the FDA for failure to protect children from the dangers of e-cigarettes in 2019.
- Vaping, JUUL and E-Cigarette Presentation Toolkit

Importance of Science & Public Policy in Reducing Cigarette Use

- Sale/distribution of e-cigarette is prohibited under age 21 including mail-order & internet sales
- Use of e-cigarettes prohibited in the same spaces where smoking prohibited
- In September 2019, due to EVALI, sale of all vaping products prohibited for 4 months
- November 2019, ban on the sale of flavored vaping and tobacco products including mint and menthol cigarettes
- AG Maura Healey files suit against Juul in February 2020

State Advocacy Results in Change
What Can you do to Limit the Scope of the Vaping Epidemic?

- **Ask** patients and families about vaping
- **Educate** patients and families
- **Don’t tolerate** vaping in our communities
- **Report cases** of pulmonary complications of vaping
- **Report violations** of state and federal laws
- **Participate** in anti vaping efforts/advocacy
- **Support legislation** to limit youth access to e-cigarette devices

**Take Home Points**

- E-cigarettes contain a power source, an electronic heating element, and liquid cartridge
  - Liquid cartridge contains stabilizing agent, psychoactive compound, and flavoring additives
- EVALI is diagnosed with e-cigarette use with respiratory/GI/constitutional symptoms, changes on imaging, no infectious etiology, and no evidence of alternative diagnosis
  - The most important treatment is e-cigarette cessation
  - Steroids and antibiotics can be considered
- Adolescents comprise a significant portion of EVALI cases
- Much is still unknown about EVALI, including underlying cause and best treatment
  - Referral to Pulmonary and Addiction Medicine is important
- Advocacy efforts by AAP and ATS, among others, are underway
  - We must continue these efforts to prevent widespread pulmonary complications

**Thank You**

- Alicia Casey, MD
- Vaping Team
  - Laura Chiel, MD
  - Eleanor Muise, MD
  - Jacky Steeding, RN
  - Jillian King, NP
  - Keri Sullivan, NP
  - Edward Boyer, MD
  - Daniel Overbeek, MD
- AAP