Vaping Associated Pulmonary Injury

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E-cigarette, or Vaping, product use Associated Lung Injury
Disclosures

None
Objectives

- Recognize background and terminology of vaping
- Recognize the clinical and radiographic manifestations of EVALI
- Interpret and apply the CDC guidelines and recommendations
- Assess the risks and benefits of using E-cigarettes for smoking cessation
- Identify current and next steps in physician advocacy on vaping and regulation
Overview
A Young Man Nearly Lost His Life to Vaping

He thought vaping THC would be safer than smoking marijuana, but the fumes shut down his lungs.
What We Know So Far

As of December 3rd:

- 2291 cases of lung injury reported in 50 states and 2 territories
- 48 deaths confirmed
- CDC Data on 1378 patients
- 70% are male
- 79% < 35 years old
80% using THC-containing product (35% only THC)

54% nicotine-containing product (13% only nicotine)

12% CBD-containing products (1% only CBD)

5% NO nicotine, THC, or CBD

CDC Vaping Data
On 1782 Patients
CDC Data on THC-containing products

- 152 different THC-containing product brands reported by EVALI patients
  - Dank Vapes (Northeast and South)
  - TKO and Smart Cart (West)
  - Rove (Midwest)
Presenting Symptoms

**NEJM (n = 53)**
- Respiratory Symptoms – 98%
- GI Symptoms – 81%
- Constitutional Symptoms – 100%

**CDC (n = 393)**
- Respiratory Symptoms – 95%
- GI Symptoms – 77%
- Constitutional Symptoms – 85%
Evaluation and Management

**Highly Suggestive Case**
- Confirmed
- Probable

**Noninvasive Diagnostic Testing**
- Blood Cultures, Sputum Culture and Gram Stain, Legionella
  - RVP
  - HIV
  - ESR, CRP,
  - Procalcitonin, INR

**Empiric Therapy**
- Antibiotics
- Oxygen support
- Steroid therapy (no consensus dosing)

**Continued Treatment**
- Stop antibiotics
- Wean down steroids
- Wean down oxygen

**No Improvement**
- Bronchoscopy
- Intubation
- ECMO
Pathology

Lipoid Pneumonia
- Lipid laden macrophages

Organizing Pneumonia

Diffuse Alveolar Hemorrhage

Acute Eosinophilic Pneumonia
- BAL eos > 25%

Invasive testing not required
Background
The Basics

Vaping products include devices, liquids, flavorings, refill pods, and cartridges.

Devices heat liquids to produce an aerosol that is inhaled by the user.

Vaping aerosol can contain harmful or potentially harmful substances.
First Generation: Cig-alike
- Often disposable
- Single power setting

Second Generation: Pen Style
- Longer lasting battery
- Larger clearomizer capacity

Third Generation: Mods and Customizables
- User control over power and airflow settings
- Refillable clearomizers
- Highly customizable

Wick: cotton, silica, ceramic
Coil: NiChrome, kanthal, etc.

<table>
<thead>
<tr>
<th>Material</th>
<th>Known Risks</th>
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<tbody>
<tr>
<td>Silica</td>
<td>Silicosis</td>
</tr>
<tr>
<td>Nickel</td>
<td>Carcinogenesis, lung injury, immune suppression</td>
</tr>
<tr>
<td>Chromium</td>
<td>Carcinogenesis, lung injury, immune suppression, reproductive toxicity</td>
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Smoking Cessation
A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy


February 14, 2019
U.K. National Health Services Quit Smoking Services

Multisession Behavioral Support

Nicotine Replacement Group vs E-cigarette Group

Sustained 1 year abstinence 18.0% (EC) vs 9.9% (NRT)

NNT 12 patients – to have 1 sustained abstinence

EC provided greater satisfaction and were rated as more helpful to refrain than NRT

At 1 year – in those with abstinence – 80% were using EC and 9% were using NRT
What's the Harm?
Volatile organic compounds

Ultrafine particles

Nicotine

Cancer-causing chemicals

Heavy metals such as nickel, tin, and lead

Flavoring such as diacetyl, a chemical linked to a serious lung disease
**Overall Effects on the Lung:**
- Decreased exhaled nitric oxide (89, 127)
- Development of respiratory symptoms in adolescents (30, 93, 130)
- Cytotoxicity and increased lung weight (26, 61, 113)

**Effects on Airway Physiology:**
- Airway hyperreactivity (81)
- Increased airway resistance (49, 127)

**Effects on Host-Defense:**
- Downregulation of host-defense genes (91)
- Decreased antimicrobial activity (121, 137)
- Increased resistance of bacteria to host antimicrobial factors (62)

**Effects on Alveolar Compartment:**
- Decreased alveolar development (94)
- High levels of particle deposition (84)
- Increased levels of necrosis and cytotoxicity (26, 62, 97)
Heavy Metals

- Parts
  - Metallic coils
  - Joints
  - Wires
- Metals:
  - Chromium
  - Nickel
  - Lead
  - Tin

Hypothesis:
- Metals in the coil leach into the aerosol during the heating process.

- Major increases in metal concentrations in aerosol sample as compared to the unheated e-liquid
Nicotine

Effects of nicotine on the body

- Increased cancer risk in oral cavity, larynx and throat
- Dependence by increased dopamine release, Stroke risk increased
- Increased respiratory rate, Lung cancer, Chronic respiratory diseases
- Increased heart rate, Higher blood pressure, Atherosclerosis, myocardial infarction
- Diabetes, Pancreatic cancer
- Increased gastric juice production and Intestinal activity leads to faster Metabolism, weight loss
- Impotence, Erection problems, Infertility, Pregnancy complications
- Favors wrinkling, Increased sensitivity to cold
Humectants (Delivery Solvents)

Propylene Glycol and Glycerol
- 70:30 "throat hit"
- 50:50 "smoother hit"

FDA Approved – G.R.A.S
- Ingestion

Toxic Carbonyl Compounds on Thermal Decomposition
- Formaldehyde – Carcinogenic
- Acetaldehyde – Possibly carcinogenic
Flavorings

7500+

What is in a JUULPod?

- Nicotine
  Despite it's apparent differentiation from Cigarettes, Juul contain a comparable amount of nicotine, the same addictive substance.
- Glycerol & Propylene Glycol
  Common water retaining vaporization ingredients
- Benzoic Acid
  A 'naturally occurring acid found in the tobacco plant, which is a part of [their] proprietary formulation'
- Flavorants
  Juul Pods do not need to meet certain FDA regulations regarding marketing and public health disclosures until 2022. The exact formula their ingredients is also 'proprietary'.
Flavorants

- Cinnamaldehyde – damages cilia
- Vanillin – increased IL-6 and decreased NO
- Dimethylpyrazine (Strawberry) - cardiovascular cell death

Combinations – worse
• Butter flavor
• Bronchiolitis obliterans in popcorn manufacturing workers
<table>
<thead>
<tr>
<th>Vitamin E acetate</th>
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<tbody>
<tr>
<td>Oil derived from Vitamin E (tocopherol)</td>
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<tr>
<td>Routinely found in vegetable oils, nuts, seeds, green leafy vegetables</td>
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<tr>
<td>Available as Dietary supplement and skin treatment</td>
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<tr>
<td>FDA found Vitamin E acetate in many samples of THC oils but not in nicotine oils</td>
</tr>
<tr>
<td>THC oil cutting agent – 2018 (Honey Cutt)</td>
</tr>
<tr>
<td>Tocopherols bind to surfactant and impair gas exchange</td>
</tr>
<tr>
<td>Destabilizes lipo-hydrophilic balance of surfactant causing occlusion</td>
</tr>
</tbody>
</table>
Vitamin E Acetate

Chemical Compound: Vitamin E Acetate

- Safe as Supplement
- Safe on Skin

Harmful if Inhaled
• 29 Patients
• 10 states
• Isotope dilution mass spectrometry to analyze specific toxicants in BAL fluid
  • High Levels
    • Vitamin E acetate – all 29
  • Low Levels
    • Medium Chain Triglycerides
    • Plant Oils
    • Petroleum distillates (mineral oil)
• Cannabinoids
• Nicotine
• DPPC – phospholipid in surfactant – confirms adequate bronchial sampling
Explosions
Type of Injury

Mechanism

Direct Injury
- Type 1 – Hand Injury (7)
- Type 2 – Face Injury (8)
- Type 3 – Waist/Groin (11)
- Type 5A – Inhalation Injury from Device (2)

Indirect Injury
- Type 4 – House Fire (7)
- Type 5B – Inhalation Injury from Fire Started by Device (4)
Northwell Experience
• 40 cases
• M(32):F(8)
• Age: 24.5 (18-68)
• THC - 39
• HiFlow of BIPAP - 21
• Intubation - 2
• ECMO – 3
• Bronchoscopy - 14
• Death - 0
Cases
Case 1: 33-year-old female

- Fevers up to 102
- Nonproductive Cough
- Diarrhea
- No response to Z-pack
- Past Medical History: Anxiety
- Past Surgical History: D&C
- Recent Travel: None
- Pets: None
- Social History:
  - Vapes – THC oil weekly x 3 years
  - Tobacco – denied
  - EtOH - denied
- Employment: Cafeteria worker
Laboratory Analysis

- WBC 6.5
- Neutrophils – 72%
- ESR 111
- CRP – 26.60
- ANA – 1:320
- DsDNA - Negative
- ANCA – Negative
- BNP - 131
- Utox - THC

- RVP – Negative
- Urine Legionella – Negative
- Blood Cultures – Negative
- Sputum Culture – Negative
- Urinalysis – Negative
- HIV – Negative
- Fungitell - Negative
Diffuse Bilateral Ground Glass Opacities
Clinical Course

Day 1
• Admission

Day 2
• Pulmonary Consult

Day 3
• Bronchoscopy
• Nasal Canula – 6L
• Steroids 1mg/kg

Day 5
• Nasal Canula - 2L

Day 7
• Room Air
• Lipoid Pneumonia

Day 8
• Steroids 0.5 mg/kg
• Discharge Home
Case 2: 22-year-old male

- Fevers
- Chills
- Malaise
- Fatigue
- Cough
- Decrease PO intake
- Nausea
- Diarrhea
- Headaches

- Past Medical History: None
- Past Surgical History: None
- Recent Travels: None
- Pets: None
- Social History:
  - Vaping – THC oil
    Daily x 2 years
- Tobacco Use – None
- EtOH Use – None
- Employment: Waiter
Laboratory Analysis

- WBC 19.6
- Neutrophils – 85%
- ESR 113
- CRP – 29.40
- ANA - Negative
- ANCA - Negative
- Utox - THC
- RVP – Negative
- Legionella – Negative
- Blood Cultures – Negative
- Sputum Culture – Negative
- Urinalysis – Negative w/ no blood
- HIV – Negative
- GI PCR – Negative
- C. diff - Negative
IMPRESSION:

Diffuse curvilinear ground glass and consolidative opacities throughout the lungs bilaterally. Primary diagnostic consideration is multifocal infection versus inflammatory changes/interstitial lung disease.
Clinical Course

Day 1
- Admission
- Deferred Bronchoscopy

Day 3
- Bronchoscopy

Day 4
- Steroids 1mg/kg

Day 5
- Progressive Hypoxia – HiFlow 40L/60%

Day 7
- Nasal Canula - 2L

Day 9
- Room Air
- Diffuse Alveolar Damage
- Discharge Home

Day 9
- Diffuse Alveolar Damage
- Discharge Home
Vaping products
CDC Guidelines & Recommendations
**Table 1. Outbreak Surveillance Case Definitions of Severe Pulmonary Disease Associated with E-Cigarette Use — August 30, 2019.**

<table>
<thead>
<tr>
<th>Confirmed case</th>
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<tbody>
<tr>
<td>Use of an e-cigarette (vaping) or dabbing in 90 days before symptom onset; and</td>
</tr>
<tr>
<td>Pulmonary infiltrate, such as opacities on plain-film radiograph of the chest or ground-glass opacities on chest CT; and</td>
</tr>
<tr>
<td>Absence of pulmonary infection on initial workup: the minimum criteria include negative respiratory viral panel and influenza PCR or rapid test if local epidemiology supports testing. All other clinically indicated testing for respiratory infectious disease (e.g., urine antigen testing for <em>Streptococcus pneumoniae</em> and legionella, sputum culture if productive cough, bronchoalveolar-lavage culture if done, blood culture, and presence of HIV-related opportunistic respiratory infections if appropriate) must be negative; and</td>
</tr>
<tr>
<td>No evidence in medical record of alternative plausible diagnoses (e.g., cardiac, rheumatologic, or neoplastic process)</td>
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Probable case

Using an e-cigarette (vaping) or dabbing in 90 days before symptom onset; and

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

Infection identified by means of culture or PCR, but the clinical team caring for the patient believes that this is not the sole cause of the underlying respiratory disease process; or as the minimum criteria, to rule out pulmonary infection not met (testing not performed) and clinical team caring for the patient believes that this is not the sole cause of the underlying respiratory disease process; and

No evidence in medical record of alternative plausible diagnoses (e.g., cardiac, rheumatologic, or neoplastic process)

Current CDC case definition. Note that this diagnosis does not necessarily require bronchoscopy. This case definition may fail to capture mild or early cases (e.g. prior to development of pulmonary infiltrates).

Layden et al 2019 NEJM
CDC Recommendations

- **Ongoing Investigation – Refrain**
- **Symptoms – See a Physician**
- **Do Not Buy black market products**
- **Do Not Modify**
- **Youth should not vape**
- **Pregnant women should not vape**
- **Do Not Start**
- **If you have QUIT smoking by using E-cigarettes do NOT go back to smoking**
Social History

VAPING WITHIN PAST 90 DAYS

IDENTIFY SUBSTANCE USED

CALL POISON CONTROL/DOH
Knowledge Gaps
What We Don’t Know

The specific chemical exposures(s) causing lung injury

No single product or substance has been linked to all lung injury cases

Which vaping products, substances, or brands are responsible for this outbreak
Long Term Outcomes

- Nicotine addiction rates
- Pulmonary function
- Coagulopathy
- Cancer Risk
What We Don't Know

Why America?

Why Now?

Why Severity Varies?
Public Health, Policy, and Advocacy
Public Health and Policy
Timeline of Vaping and Policy

2003: first vape device is developed in Beijing, China, by Golden Dragon Holdings

2006: first vape device introduced in US

2008: “WHO does not consider it [vaping] to be a legitimate therapy for smokers trying to quit.”

July 2009: FDA follows WHO lead → cautions against vaping esp “increase nicotine addiction among young people”

June 2009: FDA now formally has regulatory power over the tobacco industry

May 2009: First FDA tests on vaping devices → “nicotine is present in both products,” inc. some products listed as containing no nicotine

August 2009: Suffolk County, NY – bans sale of vaping devices to < 19 years & restricts the use of the devices in public places

Sept 2009: Oregon DOJ bans sales of vaping devices at all Pilot Travel Centers & TA Operating (Travel stores)

December 2009: brand NJOY discontinues all flavors except traditional tobacco flavor & menthol in US, to curb teen vaping (only to backtrack in 2014)

Source: Vaping History. [https://www.beasleyallen.com/vaping-history/]
Timeline of Vaping and Policy

Aug 2010: Oregon acts against vaping device company - claims company (Smoking Everywhere) misled consumers about the safety of vaping devices & targeted marketing toward minors

2011: Department of Transportation proposed to ban use of vaping devices on planes

April 2013: U.S. Senators Durbin (D-IL), Lautenberg (D-NJ), Blumenthal (D-CT), Brown (D-OH), Reed (D-RI), call on FDA to issue regulation over vaping devices, to restrict sale, distribution & marketing of devices to children and young adults.

Sept 2013: AAFP, Cancer Action Network, AHA, APHA call on Obama to allow regulation of vaping device thru FDA

Oct 2015: US senators cont to push for ruling to allow FDA to regulate e-cigarette + products

Oct 2015: West Virginia Univ publishes first case report of suspected Vaping associated PNA in 31 yr old female

Nov 2014: NJOY announces a new line of flavored e-liquids

Oct 2014: U.S. Senators Boxer (D-CA), Durbin (D-IL), Blumenthal (D-CT), Reed (D-RI), Brown (D-OH), Markey (D-MA) reinforce the need for FDA to quickly finalize proposed regulations


Dec 2015: FTC urged to investigate vaping companies for “many cases of retailers advertising liquid nicotine as recognizable brand names of candy, breakfast cereal, and other foods and drinks.”

March 2016: Second case report of vaping associated nodules to lung + liver suspicious of widespread metastases but resolves after patient quite vaping


2017-2019: waiting...

2019 Timeline of Vaping and Policy

**March 2019**: FDA restricts sale of flavored vaping products at convenience stores, gas stations, pharmacies;

**March 2019**: FDA asks all manufacturers of vaping products submit applications showing products meet regulations by **August 9, 2021**;

**June 2019**: San Francisco becomes the **first city in the U.S. to ban the sale of vaping products.**

**July 2019**: JUUL CEO testifies to US House SubCommittee to explain the company's role in youth nicotine addiction;

**July 2019**: first suspected vaping-related death due to lung injury occurs;

**August 2019**: Alabama lawmakers enact law to improve oversight of manufacture, sale, marketing of alternative nicotine products including vaping devices;

**Sept 2019**: FDA sends warning letter to JUUL Labs, Inc. for illegally advertising nicotine pods as a safer alternative to cigarettes;

**Sept 2019**: NYS bans most flavors (except tobacco + menthol) for 90 days;

**Sept 2019**: Michigan bans sale of all flavored vaping products;

**Sept 2019**: FDA launches a criminal investigation epidemic of vape-related lung injuries;

**Sept 2019**: NYS raises tobacco purchasing age to 21;

**Nov 2019**: NYS raises tobacco purchasing age to 21.

Source: Vaping History. [https://www.beasleyallen.com/vaping-history/](https://www.beasleyallen.com/vaping-history/)
Timeline

2003 → 2019 = 16+ years of evolution in the technology / business of electronic cigarettes

Regulation / policy has yet to catch up

Evidence of benefits and harms are being identified
Main Issues

TARGETING OF YOUTH

VAPING OF ILLICIT SUBSTANCES

REGULATION OF E-CIGS
Main Issues: Targeting of Youth

- Multiple investigations nationally; multiple cases against companies such as JUUL
- At this time no clear conclusion on whether flavored products marketing will be held responsible for increase in teen vaping and subsequent nicotine dependence
- Also FDA not clear on its role/desire to ban all flavored e-cigarette products
- AMA, AAP, ACP calls to action:
  1. more e-cigarette regulation due to concerns about short- and long-term health consequences of vaping, especially for children.
  2. ban flavored vaping products, including mint and menthol flavors
  3. raise the national age to buy tobacco and e-cigarettes to 21

Main Issues: Vaping of Illicit substances

• Connection between banning e-cigarette products and increase in illicit substance use for vaping devices

• Several lawmakers have cited the concern about increase use of illicit substances or “at-home” creations for vaping devices
  • Industry backed advocacy groups are increasingly vocal against bans of e-cigarette products (ie American Vaping Association)

Main Issues: Regulation of E-Cigarettes

- 2009: FDA was granted control over regulation of tobacco products
- 2016: FDA finalized their regulatory process for tobacco products
- 2019: current Administration delayed start of regulation process to 2022
- E-cigarette companies filed case in U.S. Court of Appeals: whether the FDA has the authority to treat e-cigarettes as “tobacco products” and to subject the vaping products to the same set of rules and regulations as their conventional counterparts
  - Decision: unanimously YES → FDA has right to regulate and needs to implement the regulation expeditiously in 2020, not 2022
  - E-cigarette products are “indisputably highly addictive and pose health risks, especially to youth, that are not well understood.”

Next Steps

Connect with NYACP – Tobacco and e-cigarette products regulation are part of the legislative priorities for 2020

Create a bridge between organizations for advocacy

Continue to voice concern – it took us 16 years to reach here!

https://www.nyacp.org/i4a/pages/index.cfm?pageid=3747
Questions?