



# Outbreak of Lung Injury Associated with E-cigarette Product Use or Vaping

## Information for Clinicians

**CDC 2019 Lung Injury Response**

Updated as of September 16, 2019

# Overview

- **Background**
- **E-cigarette or vaping products**
- **Clinical Features**  
Frequent Clinical, Laboratory, Radiographic, and Pathologic Findings and Outcomes
- **CDC Recommendations for Clinicians**  
History, Diagnosis, Clinical Management, Evaluation of Pathologic Specimens at CDC, Autopsy, What to Tell Patients, Case Reporting to Public Health Authorities, Additional Resources
- **Limitations and Knowledge Gaps**

# Background

- As of September 17, 2019, 530 cases of lung injury associated with the use of e-cigarette products or vaping have been reported to CDC
  - data updated weekly at [CDC's outbreak website](#)
  - 38 states, 1 U.S. territory; 7 deaths have been confirmed
- No specific etiology has been identified, but all patients have reported using e-cigarette products, or vaping
  - Most have reported using products containing THC
  - Many have reported using THC and nicotine; some only nicotine
- CDC issued recommendations for clinicians, public health officials, and the public through its [health advisory network \(HAN\)](#) on August 30, 2019
- Initial clinical experience summarized in recent publications in [Morbidity & Mortality Weekly Report \(MMWR\)](#) and [New England Journal of Medicine \(NEJM\)](#)

# Patient Exposures in the Lung Injury Outbreak

- All have reported use of e-cigarette products, or vaping, within 90 days of illness
  - Most have reported using cannabinoids such as  $\Delta$ -9-tetrahydrocannabinol (THC) or cannabidiol (CBD)
  - Some have reported nicotine use alone
- No single device type has been reported consistently (though device types have not yet been well-characterized)
- No single e-cigarette product or substance (including cannabis products) has been reported consistently

# CDC Confirmed Case Definition (September 18, 2019)

- Using an e-cigarette ("vaping") or dabbing\* 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
- AND
- Absence of pulmonary infection on initial work-up. **Minimum criteria** are
  - A negative respiratory viral panel **and**
  - A negative influenza PCR or rapid test, if local epidemiology supports influenza testing; **and**
  - All other clinically-indicated respiratory ID testing (e.g., urine Antigen for *Streptococcus pneumoniae* and *Legionella*, sputum culture if productive cough, bronchoalveolar lavage (BAL) culture if done, blood culture, HIV-related opportunistic respiratory infections if appropriate) are negative
- AND
- No evidence in medical record of alternative plausible diagnoses (e.g., cardiac, rheumatologic, or neoplastic process)

# CDC Probable Case Definition (September 18, 2019)

- Using an e-cigarette ("vaping") or dabbing\* 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  
**AND**
- Infection identified via culture or PCR, but clinical team\*\* believes this infection is not the sole cause of the underlying lung injury **OR Minimum criteria** to rule out pulmonary infection not met (testing not performed) and clinical team\*\* believes this infection is not the sole cause of the underlying lung injury  
**AND**
- No evidence in medical record of alternative plausible diagnoses (e.g., cardiac, rheumatologic, or neoplastic process)

\*\*Clinical team caring for the patient.

# Patient Exposures in the Lung Injury Outbreak

- Series of 53 cases from Illinois and Wisconsin\*
  - All had history of e-cigarette use and related products
  - 41 extensively interviewed
    - 61% reported nicotine use; 80% reported THC use; 7% reported CBD use
    - 37% reported THC use alone; 17% reported nicotine use alone
    - 44% reporting both nicotine and THC product use
    - Various brands and flavors
  - Among patients with additional data, 94% used within week before symptom onset; 88% reported daily use

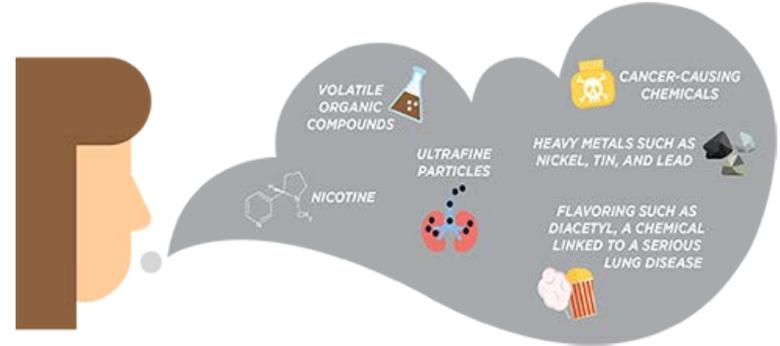
\* Layden J, et al. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin—preliminary report. *NEJM* 2019

# E-cigarette or Vaping Products



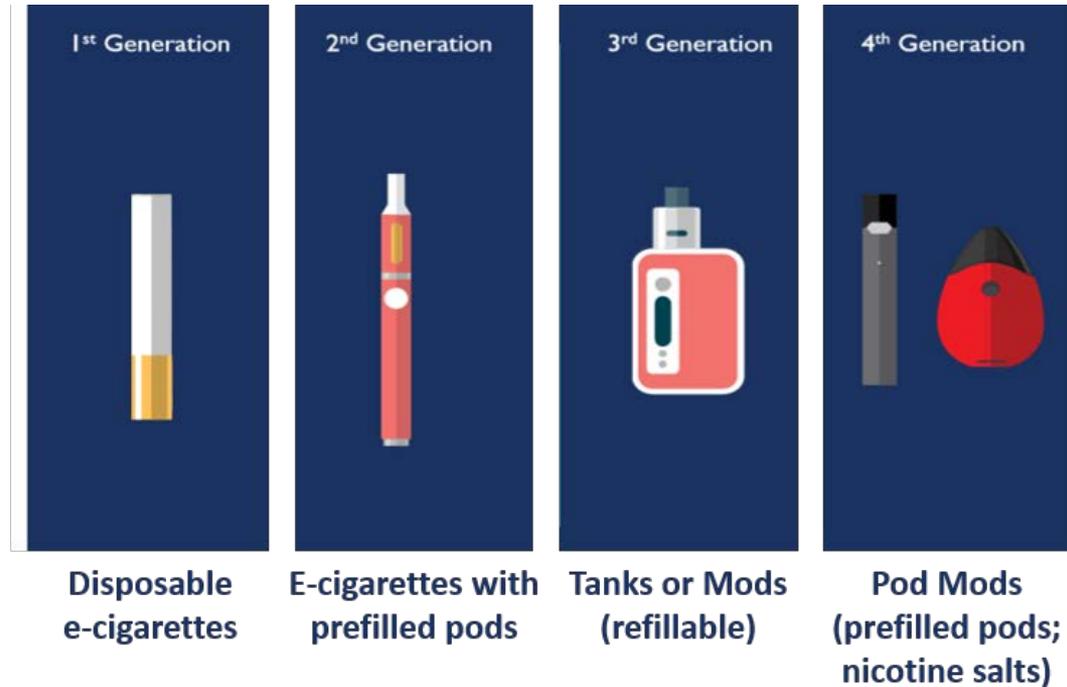
# E-cigarette or Vaping Products: The Basics

- E-cigarette products include devices, liquids, flavorings, refill pods, and cartridges
- Devices heat liquid to produce an aerosol that is inhaled by the user
- E-cigarette **aerosol** can contain harmful or potentially harmful substances
  - Nicotine
  - Heavy metals (e.g., lead, nickel, tin)
  - Volatile organic compounds
  - Ultrafine particles
  - Cancer-causing chemicals
  - Flavoring (e.g., diacetyl)



# E-cigarette Products: Devices

- Devices vary in shape, size, type, and manufacturer
- Common names
  - E-cigs
  - Vapes
  - E-hookahs
  - Vape pens
  - Mods
  - Tanks
  - Electronic nicotine delivery systems



# E-cigarette Products: Liquids, Cartridges, and Pods

- E-cigarette **liquid** can contain
  - Nicotine
  - Flavorings
  - Propylene glycol and vegetable glycerin used in varying proportions as carriers
  - Other chemicals also present
  - Cannabinoids:  $\Delta$ -9-tetrahydrocannabinol (THC), cannabidiol (CBD), butane hash oil (BHO)
  - Other substances
- E-cigarette liquid types
  - Commercial refillable e-liquid
  - Commercial non-refillable e-liquid
  - Homemade or street sources

# E-cigarette Products: Behaviors

- Hacking: modifying device in a way not intended by the manufacturer
  - Refilling single-use cartridges (e.g., with homemade or illicit substances)
  - Dripping: dropping liquid directly onto device heating coil to attain higher compound concentrations in the aerosol
- Dabbing: superheating substances containing high concentrations of THC or other cannabinoids (e.g., budder, BHO, 710, CBD)

## **Clinical Features:**

Frequent Clinical, Laboratory, Radiographic,  
and Pathologic Findings and Outcomes

# Information Sources on Clinical Features

- Anecdotal and verified reports from health departments
- Formal and informal discussions between CDC, clinicians, and medical professional societies
- Recent publications in *Morbidity and Mortality Weekly Report* and *New England Journal of Medicine* (published September 6, 2019)
  - [Schier JG, et al. Severe Pulmonary Disease Associated with Electronic-Cigarette–Product Use — Interim Guidance. \*MMWR\* 2019;68\(36\).](#)
  - [Layden J, et al. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin—preliminary report. \*NEJM\* 2019.](#)
  - [Davidson K, et al. Outbreak of e-cigarette-associated acute lipid pneumonia—North Carolina, July–August 2019. \*MMWR\* 2019;68\(36\).](#)
  - [Maddock S, et al. Pulmonary lipid-laden macrophages and vaping. \*NEJM\* 2019.](#)
  - [Henry TS, et al. Imaging of vaping-associated lung disease. \*NEJM\* 2019](#)

# Frequent Clinical Symptoms

- Most patients have been young and otherwise healthy
- Report gradual onset of various symptoms over days to weeks
  - Respiratory (cough, chest pain, shortness of breath)
  - Gastrointestinal (GI) (abdominal pain, nausea, vomiting, diarrhea)
  - Systemic symptoms (fatigue, fever, weight loss)
- GI symptoms sometimes precede respiratory symptoms
  - Tend to resolve quickly after admission
  - Evaluation for GI-related illness unrevealing
- Almost all published cases have been hospitalized
  - Many with  $\geq 1$  antecedent evaluation in ambulatory settings

# Frequent Presenting Signs upon Hospital Admission

- Fever
- Tachycardia
- Tachypnea
- Hypoxemia (even in patients without respiratory symptoms upon presentation)
  - One of 53 patients in the recently published 53-case series in *New England Journal of Medicine*\* did not report respiratory symptoms, but had oxygen saturation of 91% on room air on admission

\* Layden J, et al. Pulmonary illness related to cigarette use in Illinois and Wisconsin—preliminary report. *NEJM* 2019

# Frequent Laboratory and Radiographic Findings

- Laboratory
  - Serum leukocytosis with neutrophil predominance
  - Elevated serum markers of inflammation (e.g., ESR, CRP)
  - Transient, mild elevation in serum transaminases
- Chest imaging
  - Abnormal findings may or may not be present on initial imaging, but develop eventually
  - Bilateral opacities on plain radiograph or ground-glass opacities on chest computed tomography (CT), often with sub-pleural sparing
- Imaging of abdomen/pelvis usually unremarkable except for bilateral opacities in cuts of lower lung fields included on CT

# Clinical Course

- Initial therapies focused on presumed infectious etiologies
  - Empiric antibiotics with or without steroids
  - Observation with supportive therapy other than antibiotics or steroids
- Many patients have experienced sub-acute or acute hypoxemic respiratory failure requiring supplemental oxygenation and at times ventilatory support, including with intubation and mechanical ventilation or extracorporeal membrane oxygenation
- Patients who did not respond to antibiotics alone have tended to respond to systemic corticosteroids (either alone or concurrent with antibiotics)

# Frequently Performed Diagnostic Evaluations

- Appropriate extensive evaluations for infectious etiologies often completed without an identified cause
- Use of pulmonary function testing has been highly variable, mostly depending upon institutional practices
- Some patients evaluated for lung injury with bronchoscopy with bronchoalveolar lavage or lung biopsy (either transbronchial or surgical via video-assisted thoracoscopic surgery [VATS] or thoracotomy)
  - Additional patients considered for these procedures but were too ill
  - Roles and frequencies of biopsy methods remain unknown

# Evaluation of Pathologic Specimens

- Both routine histopathologic and special evaluations of specimens have been performed
- Routine processing of tissues includes the application of alcohol, which removes lipids
- Therefore, as a special evaluation, lipid-staining (e.g., Oil Red O, Sudan Black) has been performed on fresh tissues and bronchoalveolar lavage fluid

# Spectrum of Clinical and Pathologic Diagnoses

- Acute lung injury and adult respiratory distress syndrome (ARDS)
- Diffuse alveolar damage
- Lipoid pneumonia
- Acute necrotizing pneumonitis
- Organizing pneumonia with lipid-laden macrophages
- Non-specific inflammation
- Hypersensitivity pneumonitis
- Eosinophilic pneumonia

# Outcomes

- Specialists in pulmonary medicine, critical care, infectious diseases, pathology, or toxicology frequently involved in patients' care
- Despite illness severity, most patients have survived to hospital discharge
  - Most patients have been young and healthy pre-illness
  - Some patients who have not recovered to pre-illness pulmonary function at time of discharge, demonstrated improvement during post-hospitalization evaluation
  - Other patients still had reduced pulmonary function during post-hospitalization evaluation
  - 7 patients died in the hospital (as of September 17, 2019)

# Recommendations for Clinicians

# Recommendations for Clinicians: Overview

- History
- Diagnosis
- Clinical Management
- Evaluation of Pathologic Specimens at CDC
- Autopsy
- What to Tell Patients
- Case Reporting to Public Health Authorities
  
- **CDC will provide updates as more information becomes available**

## Recommendations for Clinicians: History

- Ask patients who report e-cigarette product use, or vaping, within the last 90 days about signs and symptoms of respiratory illness
- Ask patients who present with signs and symptoms of respiratory illness about e-cigarette use, or vaping, within the last 90 days
- If e-cigarette product use is suspected as a possible etiology of a patient's respiratory illness, obtain a detailed history about e-cigarette product use, or vaping

# Recommendations for Clinicians: History (Cont'd)— e-cigarette product use

- Substances used: nicotine, cannabinoids (e.g., marijuana, THC, THC concentrates, CBD, CBD oil, synthetic cannabinoids [e.g., K2 or spice], hash oil, Dank vapes), flavors, or other substances
- Substance sources: commercially refillable e-liquids (e.g., bottles, cartridges, or pods), commercial non-refillable e-liquids, homemade or street sources

## Recommendations for Clinicians: History (Cont'd)— e-cigarette product use

- Devices used: manufacturer; brand name; product name; model; serial number of the product, device, or e-liquid; if the device can be customized by the user; and any product modifications by the user (e.g., exposure of the atomizer or heating coil)
  - Where the devices were purchased
  - Method of use: aerosolization, dabbing, dripping, or re-use of old cartridges or pods with homemade or commercially bought e-liquids
  - Sharing e-cigarette products (devices, liquids, refill pods, or cartridges) with others (to identify other cases)

# Recommendations for Clinicians: Diagnosis

- Consider all possible causes of illness (e.g., infectious, rheumatologic, neoplastic) in patients reporting respiratory with or without GI symptoms and e-cigarette product use
- Consider consultation with specialists (pulmonary, infectious disease, critical care, medical toxicology, pathology) as clinically indicated
- Lipoid pneumonia associated with inhalation of lipids in aerosols generated by e-cigarettes, or vaping, has been reported based on the detection of lipid-laden alveolar macrophages obtained by bronchoalveolar lavage and lipid staining (e.g., Oil Red O, Sudan Black)
  - The decision about whether to perform bronchoalveolar lavage, with or without transbronchial biopsy, should be based on the overall clinical picture

## Recommendations for Clinicians: Diagnosis (Cont'd)

- Lung biopsies have been performed on some patients
  - The decision about whether to perform biopsy (whether transbronchial or surgical) should be based on the overall clinical picture.
  - If a lung biopsy is obtained, consider lipid-staining during pathologic examination.\* Because routine tissue processing involves the application of alcohols, which remove lipids, lipid-staining is best performed on fresh tissue.
  - Before the procedure consider consultation with pulmonary, critical care, pathology, or other specialties to inform any evaluation plan
  - However, conducting routine tissue processing and histopathologic evaluation is still important.

\* Additional information on lipid-staining is available at: [https://www.cdc.gov/tobacco/basic\\_information/e-cigarettes/severe-lung-disease/healthcare-providers/index.html](https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease/healthcare-providers/index.html).

## Recommendations for Clinicians: Diagnosis (Cont'd)

- Contact public health officials as needed for technical assistance with laboratory testing, including for guidance regarding whether to retain specimens, storage instructions in the event of long-term storage, and collection of specimens for indications other than clinical care
- If retaining of specimens is anticipated, contact your facility's laboratory since routine practice might result in discarding of specimens before desired

# Recommendations for Clinicians: Clinical Management

- Decisions regarding outpatient versus inpatient management should be based on individual clinical circumstances
- Evaluate and treat as appropriate for other possible causes of illness (e.g., infectious, rheumatologic, neoplastic)
- Consider consultation with specialists (pulmonary, infectious disease, critical care, medical toxicology)

# Recommendations for Clinicians: Clinical Management (Cont'd)

- Clinical improvement of patients with lung injury associated with e-cigarette use, or vaping, has been reported with the use of corticosteroids
  - Dosing, route of administration, duration, and timing have varied
  - The decision to use corticosteroids should be made on a case-by-case basis based on risks and benefits and the likelihood of other etiologies
- Patients who have received treatment for lung injury related to e-cigarette product use, or vaping, should undergo follow-up evaluation as clinically indicated to monitor pulmonary function

# Recommendations for Clinicians: Evaluation of Pathologic Specimens at CDC\*

- If feasible, submission of formalin-fixed (wet) lung tissues is encouraged
- CDC's Infectious Disease Pathology Branch can perform lipid-staining on formalin-fixed (wet) lung tissues using osmium tetroxide before routine tissue processing and paraffin embedding
  - However, lipid staining cannot be performed on formalin-fixed, paraffin-embedded lung tissue blocks, because they have undergone processing that removes lipids
- CDC's Infectious Disease Pathology Branch will also review tissue histopathology and perform additional testing, including testing for possible infectious etiologies

\* Additional information on lipid-staining is available at: [https://www.cdc.gov/tobacco/basic\\_information/e-cigarettes/severe-lung-disease/healthcare-providers/index.html](https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease/healthcare-providers/index.html).

# Recommendations for Clinicians: Evaluation of Pathologic Specimens at CDC\* (Cont'd)

- Please first report any possible cases of lung injury associated with e-cigarette product use, or vaping, to your state, territorial, tribal, or local health department
- Pre-approval is required prior to submission of any tissue specimens. For pre-approval, health departments should contact [pathology@cdc.gov](mailto:pathology@cdc.gov) and [VapingAssocIllness@cdc.gov](mailto:VapingAssocIllness@cdc.gov).

\* Additional information on lipid-staining is available at: [https://www.cdc.gov/tobacco/basic\\_information/e-cigarettes/severe-lung-disease/healthcare-providers/index.html](https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease/healthcare-providers/index.html).

# Recommendations for Clinicians: Autopsy

- In the event of a fatal outcome, autopsies can be considered
  - Collection of fresh lung tissue for staining of lipids, formalin-fixed (wet) lung tissue, and submission of lung and other tissues for routine tissue processing, paraffin-embedding, and evaluation of histopathology should be considered
  - Infectious disease testing, including postmortem microbiology and molecular testing, should also be considered if indicated by patient history or autopsy findings
- Contact public health officials as needed for technical assistance with laboratory testing

# Recommendations for Clinicians: What to Tell Patients

- Regardless of the ongoing investigation, e-cigarette products should not be used by
  - Youth and young adults
  - Pregnant women
  - Adults who do not currently use tobacco products
- Regardless of the ongoing investigation, anyone who uses e-cigarette products should
  - Not buy these products off the street (e.g., e-cigarette products with THC, other cannabinoids)
  - Not modify e-cigarette products or add any substances to these products that are not intended by the manufacturer
  - Monitor yourself for symptoms (e.g., abdominal pain, nausea, vomiting, diarrhea, cough, shortness of breath, chest pain)
  - Promptly seek medical attention if you have concerns about your health

# Recommendations for Clinicians: What to Tell Patients

- For adults trying to quit tobacco product use, including e-cigarettes
  - Use evidence-based treatments, including counseling from a healthcare provider and FDA-approved medications
- During the current investigation of lung injury associated with e-cigarettes, or vaping, if you are concerned about these specific health risks
  - Consider refraining from using e-cigarette or vaping products
  - If you are an adult who uses e-cigarettes because you have quit cigarette smoking, do not return to smoking cigarettes
  - If you continue to use e-cigarettes, carefully monitor yourself for symptoms and see a healthcare provider right away if you have symptoms like those reported in this outbreak

# Recommendations for Clinicians: What to Tell Patients (Cont'd)

- If you are concerned about harmful effects from e-cigarette products, call your local poison control center at: 1-800-222-1222
- Submit detailed reports of any unexpected tobacco or e-cigarette-related health or product issues to the FDA via the online Safety Reporting Portal: <https://www.safetyreporting.hhs.govexternal icon>

# Recommendations for Clinicians: Case Reporting to Public Health Authorities

- Report cases of lung injury of unclear etiology and a history of e-cigarette product use, or vaping, within the past 90 days to your state or local health department
  - Reporting of cases may help CDC and state health departments determine the cause or causes of these pulmonary illnesses
- Determine if any remaining product, including devices and liquids, are available for testing
  - Coordinate testing with the local or state health departments

# Recommendations for Clinicians: Additional Resources

- CDC will provide updates as more information becomes available
- CDC website with updates for the ongoing investigation of lung injury associated with e-cigarette products use, or vaping:  
[https://www.cdc.gov/tobacco/basic\\_information/e-cigarettes/severe-lung-disease.html](https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html)

# Limitations and Knowledge Gaps

# Limitations and Knowledge Gaps

- Information sources have included both confirmed and unconfirmed reports and small case series
  - Anecdotal data can generate hypotheses but alone are insufficient; clinical information to support range of diagnoses has been lacking
  - As of September 17, 2019, of 530 reported cases, <20% have been described in published literature; representativeness of published cases is unknown
- Outbreak surveillance case definitions are intended for public health data collection purposes and not intended for use as a clinical diagnostic tool or replacement for individual clinical judgment
  - No diagnostic criteria exist

## Limitations and Knowledge Gaps (Cont'd)

- Most cases have been severe illness resulting in hospitalization, but true spectrum of illnesses (including less severe illness) could be unrecognized
- Investigations in affected states have been ongoing, but national efforts to coordinate, centralize, and standardize data collection efforts have been underway since August 16, 2019
- No systematic data yet for exposure (including products, quantities, sources) or clinical information

## Limitations and Knowledge Gaps (Cont'd)

- Available data point away from a purely infectious etiology, but this does not exclude the possibility of concurrent processes
  - No decision-making tools to distinguish infection versus non-infection at presentation, so important to rule out and empirically treat infectious etiologies as appropriate, even in patients with exposure history
  - Patterns of illness could change with the approaching respiratory virus season
- Remains unclear whether this is a new syndrome or a newly recognized one previously thought to be pneumonia or pneumonitis of unclear etiology

## Limitations and Knowledge Gaps (Cont'd)

- Although most patients have survived to hospital discharge, whether there are post-illness sequelae (e.g., reduced pulmonary function) after hospital discharge is not yet known for most patients
- Age-related differences in illness have not been assessed
  - Outbreak predominantly has affected younger, healthy patients, possibly reflecting different use patterns conferring increased risk compared with older patients
  - Alternatively, diagnosis could be more complicated in adults who are more likely to have chronic lung disease or other medical comorbidities, leading to under-recognition of illness in adults
  - Unclear whether adults have more severe illness more likely to result in death

## Limitations and Knowledge Gaps (Cont'd)

- Lipoid pneumonia has been reported in historical and recent case reports and series, but important caveats remain
  - Clinical significance of lipid-laden macrophages remains undetermined— are these markers of disease or markers of exposure?
  - Bronchoalveolar lavage has not been obtained universally on bronchoscope evaluation, and in turn nor has lipid-staining (a non-routine procedure), so frequency of finding is uncertain
  - Characteristics of cellularity of bronchoalveolar lavage fluid are uncertain because they could be altered by antibiotics or steroids and influenced by timing of therapies and interventions
- Autopsy has not been performed for all cases resulting in death, and results have not been reported for all cases when performed

# Summary

- CDC's investigation has not yet identified any specific substance or e-cigarette product linked to all cases
  - Most patients have reported using cannabinoids such as THC or CBD
  - Some have reported nicotine use alone
- Most patients have been hospitalized with respiratory illness and received treatment for presumed infectious etiologies; some have responded to steroids with or without antibiotics
- Report possible cases to and coordinate product testing with your health department
- CDC will provide updates as information becomes available

[https://www.cdc.gov/tobacco/basic\\_information/e-cigarettes/severe-lung-disease/healthcare-providers/index.html](https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease/healthcare-providers/index.html)

For more information, contact CDC  
1-800-CDC-INFO (232-4636)  
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



# Appendix

Review of Recent and Historical Literature

**Recent Publications on Pulmonary Disease  
Associated with E-cigarette Product Use,  
Or Vaping**

# Recent Publications with Case Findings

Reference	Number of patients	Brief Description
<a href="#">Layden J, et al. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin—preliminary report. <i>NEJM</i> 2019</a>	53	Summary of clinical characteristics and use of e-cigarette products reported among initial reported cases in Wisconsin and Illinois
<a href="#">Davidson K, et al. Outbreak of e-cigarette-associated acute lipoid pneumonia—North Carolina, July–August 2019. <i>MMWR</i> 2019;68(36).</a>	5	Description of patients with lipoid pneumonia diagnosed at 2 hospitals in North Carolina
<a href="#">Maddock S, et al. Pulmonary lipid-laden macrophages and vaping. <i>NEJM</i> 2019.</a>	6	Summary of clinical characteristics and bronchoalveolar lavage findings for patients in Utah
<a href="#">Henry TS, et al. Imaging of vaping-associated lung disease. <i>NEJM</i> 2019</a>	19 (+15 in literature)	Review of imaging findings

# Comparison of Patients in North Carolina and Illinois/Wisconsin

# Patient Characteristics in North Carolina, Illinois, and Wisconsin

Characteristic	NC (n=5)	IL/WI (n=53)
Ages (years)	18–35	16–53 (median:19)
Male	Not reported	44/53 (83%)
Hospitalized	5/5	50/53 (94%)

# Reported Symptoms in North Carolina, Illinois, and Wisconsin

Symptom	NC (n=5)	IL/WI (n=53)
Shortness of breath	5/5	46/53 (87%)
Nausea or vomiting	5/5	37/53 (70%)
Abdominal pain or discomfort	5/5	23/53 (43%)
Diarrhea	Not reported	23/53 (43%)
Subjective fever	5/5	43/53 (81%)
Any systemic symptoms*	Not reported	53/53 (100%)

\*Subjective fever, chills, weight loss, fatigue or malaise

# Presentation Findings in North Carolina, Illinois, and Wisconsin

Finding	NC (n=5)	IL/WI (n=53)
Fever	Not reported	15/51 (29%)
Hypoxemia	5/5 with sat <90% on room air (RA)	20/52 (38%) with sat <95% on RA; 16/52 (31%) with sat <89% on RA
CXR with bilateral infiltrates	5/5 on initial	48/53 (91%) on initial
CT chest with bilateral opacities	5/5 (timing not specified)	48/48 (100%) on initial
Elevated white-cell count	5/5, all with neutrophil predominance; none with eosinophils	45/52 (87%); 34/36 (94%) with neutrophil predominance; none with eosinophils

# Clinical Course in North Carolina, Illinois, and Wisconsin

Finding	NC (n=5)	IL/WI (n=53)
Received empiric antibiotics	5/5	45/50 (90%)
Worsened on antibiotics	5/5	Not reported
Received steroids	5/5	46/50 (92%)
Improved on steroids (with or without antibiotics)	5/5	30/46 (65%)
Negative workup for infectious etiologies	5/5	“Nearly all”

# Clinical Course in North Carolina, Illinois, and Wisconsin

Finding	NC (n=5)	IL/WI (n=53)
Required ICU care	3/5	31/53 (58% overall, 62% of hospitalized)
Diagnosed with ARDS	3/5	15/53 (28%)
Required intubation and mechanical ventilation	1/5	17/53 (32% overall, 35% of hospitalized)
Received extracorporeal membrane oxygenation	0/5	2 (1 died)
Survived to discharge	5/5	52/53 (98%)

# Comparison of Bronchoalveolar Lavage Findings for Patients in North Carolina, Illinois/Wisconsin, and Utah

# Bronchoscopy Alveolar Lavage Findings in North Carolina, Illinois, Wisconsin, and Utah

Characteristic	NC (n=3)	IL/WI (n=24)	UT (n=6)
Lipid staining performed	3/3	Not specified	6/6
Lipid-laden macrophages identified	3/3	7/14 with cell counts reported	6/6
>5% eosinophils*	0/3	0/3	1/6

\* Timing of steroids or other interventions not specified.

# Review of Imaging Studies for 19 Patients and Review of Literature

Henry TS, et al. Imaging of vaping-associated lung disease. *NEJM* 2019

## Review of Imaging Studies ([correspondence from Henry, et al.](#))

- Based on review of imaging for 19 patients and 15 patients reported in literature
- No information provided regarding exposure other than “*all met the case definition of vaping-associated lung injury*”
- Most imaging patterns have basilar-predominant consolidation and ground-glass opacity, often with areas of lobular or subpleural sparing
- Authors noted that fat attenuation (highly suggestive of lipoid pneumonia) has not been frequently observed on CT

# Additional Data from Wisconsin and Illinois

Layden J, et al. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin—preliminary report. *NEJM* 2019

# Experience in Illinois and Wisconsin (n=53 patients)



- Patient demographics
  - Median age 19 years (range: 16–53 years)
  - 83% male
  - 30% with asthma; otherwise no underlying chronic lung disease
- Clinical presentations
  - Median symptom duration before admission 6 days (range: 0–61 days)
  - 94% of patients hospitalized; 72% evaluated as outpatient before admission
  - 45% of those evaluated as outpatients received outpatient antibiotic treatment, however all reported progression of symptoms

# Illinois and Wisconsin: Clinical Presentation

- Respiratory symptoms (98% of cases)
  - Shortness of breath (87%)
  - No report of upper respiratory symptoms (e.g., rhinorrhea, sneezing, congestion)
- GI symptoms (81% of cases)
  - Nausea (70%)
  - Vomiting (66%)
  - Diarrhea (43%)
- Systemic symptoms (100% of cases)
  - Subjective fever (81%)

# Illinois and Wisconsin: Clinical Presentation (Cont'd)

- Initial recorded vital signs
  - 64% with tachycardia (range 55–146 BPM)
  - 43% with tachypnea (range: 15–48 breaths/min)
  - 69% with SpO<sub>2</sub> <95% on room air
  - 31% with SpO<sub>2</sub> <89% on room air
  - 29% with fever
- Initial laboratory findings
  - 87% with leukocytosis (median: 15.9K/ml, range 12.3–18.1K/ml); 94% with neutrophil predominance; no eosinophilia >2%
  - 50% with mild transient transaminase elevations
  - Acute kidney injury reported in 1 patient who responded to intravenous fluid (IVF) hydration

# Illinois and Wisconsin: Imaging

- 91% with abnormal findings on chest radiograph at presentation
- All 48 patients who had CT chest had abnormal findings
  - Characteristic finding: bilateral ground-glass opacities with subpleural sparing
- All patients had bilateral lung opacities

# Illinois and Wisconsin: Biopsy Findings

- 3 patients underwent lung biopsy
  - 2 patients transbronchial only, 1 patient also had open lung biopsy
  - 2 on antibiotics/corticosteroids , 1 on neither before biopsy
  - Lipid staining not performed
  - Findings: mild and non-specific damage, acute diffuse alveolar damage and foamy macrophages suggesting inhalation toxin exposure, interstitial and peribronchiolar granulomatous pneumonitis

# Dosing of Corticosteroids in Recent Outbreak Reports

Publication	Dosages and medications
<p><u>Davidson K, et al. Outbreak of e-cigarette-associated acute lipid pneumonia—North Carolina, July–August 2019. <i>MMWR</i> 2019;68(36).</u></p>	<p>5/5 patients received intravenous methylprednisone (120 mg–500 mg daily); all discharged home on taper of oral prednisone (dose and duration not specified)</p>
<p><u>Maddock S, et al. Pulmonary lipid-laden macrophages and vaping. <i>NEJM</i> 2019.</u></p>	<p>2/6 patients received “high-dose glucocorticoids” (dose, duration, and discharge regimen not specified); 2 other patients received “short-course of prednisone” before hospitalization (dose and duration not specified)</p>
<p><u>Layden J, et al. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin—preliminary report. <i>NEJM</i> 2019</u></p>	<p>“majority of patients have received prolonged courses” of systemic glucocorticoid therapy</p>