Acute Lung Injury

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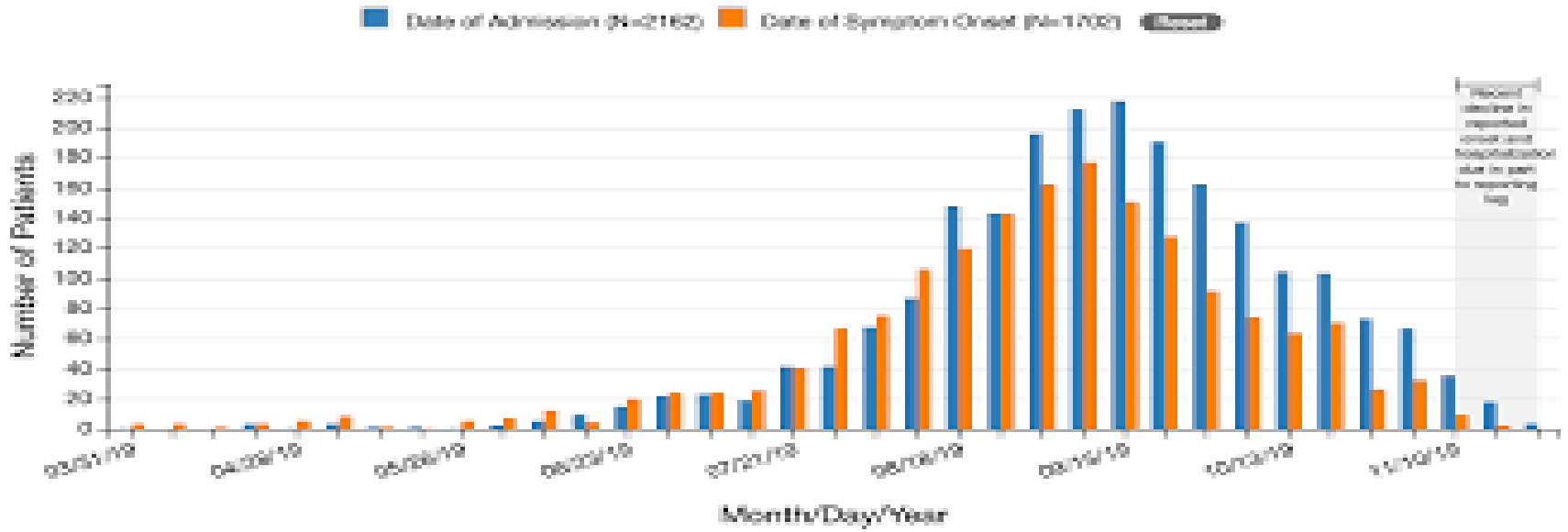
Outline

- Definition
- Etiologies
- Mechanism
- Pathology
- Symptoms
- EVALI or COVID-19
- Treatment
- Outcomes
- Other inhalants
- Prevention

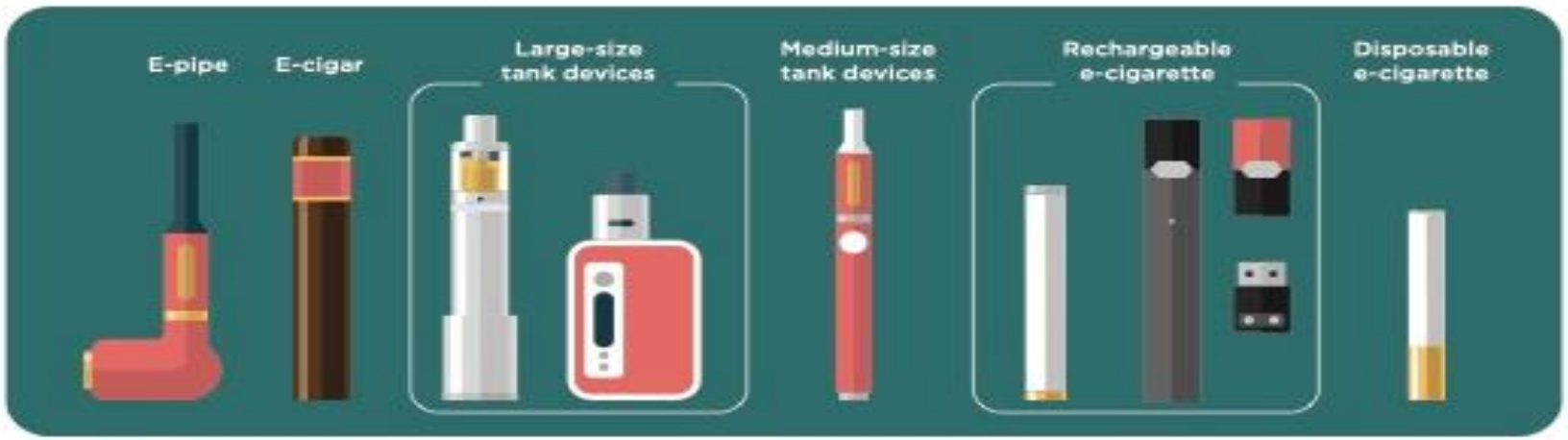
Definition

- EVALI—E-cigarette or vaping product related acute lung injury
- Officially recognized by the CDC in the summer of 2019
- Peaks in incidence June through September 2019 with a decrease since, likely due to information/surveillance



WHAT ARE E-CIGARETTES?

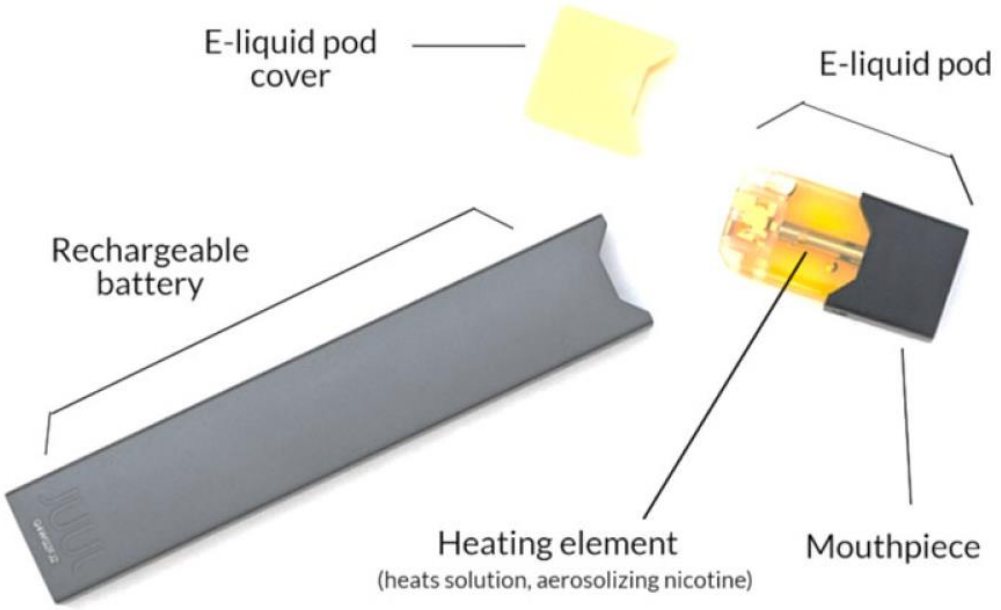
- E-cigarettes are known by many different names. They are sometimes called "e-cigs," "e-hookahs," "mods," "vape pens," "vapes," "tank systems," and "electronic nicotine delivery systems."
- Some e-cigarettes are made to look like regular cigarettes, cigars, or pipes. Some resemble pens, USB sticks, and other everyday items.
- E-cigarettes produce an aerosol by heating a liquid that usually contains nicotine—the addictive drug in regular cigarettes, cigars, and other tobacco products—flavorings, and other chemicals that help to make the aerosol. Users inhale this aerosol into their lungs. Bystanders can also breathe in this aerosol when the user exhales into the air.
- E-cigarettes can be used to deliver marijuana and other drugs.



CS284159-B

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

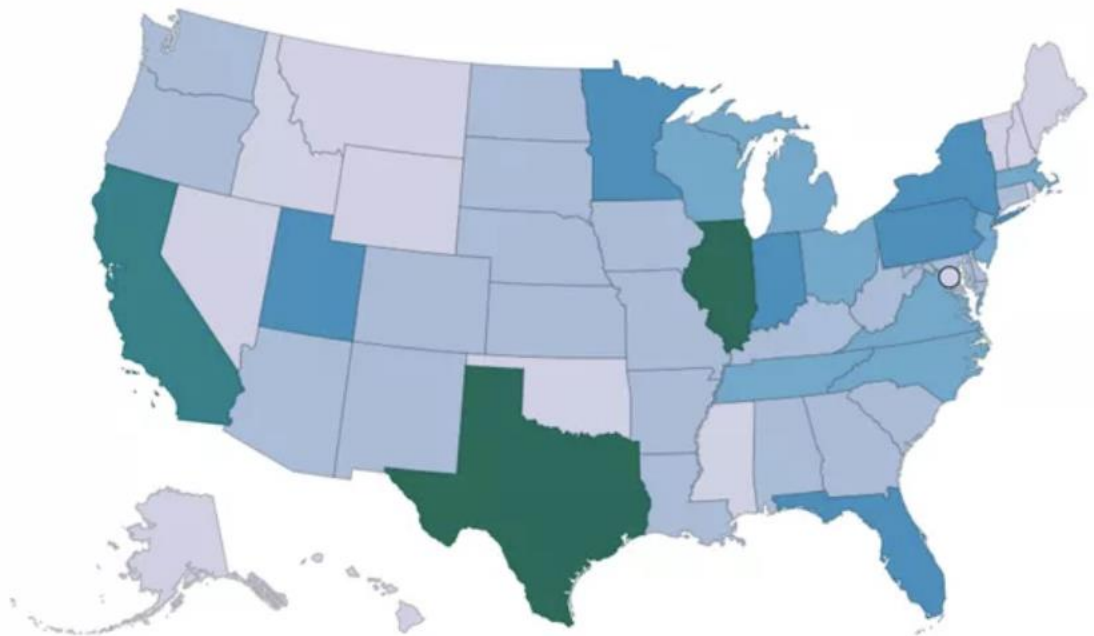

Mouth Piece
Tank (E-liquid is stored here)
Heating Coil
(Sits in center of the tank)
Firing Button
Charging Port
Mod/Battery


E-liquid pod cover
E-liquid pod
Rechargeable battery
Heating element
(heats solution, aerosolizing nicotine)
Mouthpiece

EVALI—National Statistics

- As of February 18, 2020
  - 2807 hospitalizations—all states
  - 68 deaths—29 states, not AZ, age range 15-75
- Hospitalizations: 66% male, median age 24, range 13-85 years, 15% under 18 y.o., 37% 18-24 y.o., 24% 25-34 y.o., 24% over 35 years
- As of January 14, 2020
  - 82% using THC products, 33% exclusively—78% getting “informally”
  - 57% using nicotine products, 14% exclusively—69% getting commercially
- Numbers are declining during COVID

Number of Hospitalized Lung Injury Cases Reported to CDC as of December 17, 2019



Territories AS GU MH FM PW PR VI

Legend

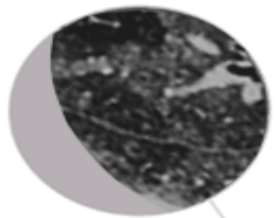
Number of lung injury cases per state

- 0 cases
- 1-9 cases
- 10-49 cases
- 50-99 cases
- 100-149 cases
- 150-199 cases
- 200-249 cases

Pathology

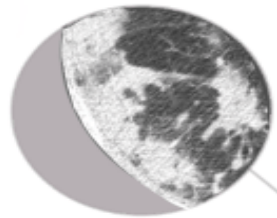
- Acute fibrinous pneumonitis, diffuse alveolar damage, organizing pneumonia
- Acute eosinophilic pneumonia
- Diffuse alveolar hemorrhage
- Lipoid pneumonia
- Bronchiolar interstitial lung disease
- All suggest more than one mechanism and a continuum of disease

THE MANY FLAVORS OF EVALI...



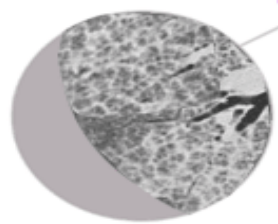
HYPERSENSITIVITY PNEUMONITIS

- OFTEN SYMMETRICAL
- MID-TO-UPPER LUNG GROUND-GLASS MOSAICISM
- ILL-DEFINED CENTRILOBULAR NODULES



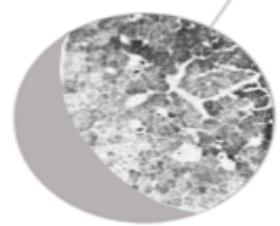
ORGANIZING PNEUMONIA

- OFTEN DENSE AND/OR GROUND GLASS CONSOLIDATIONS
- OFTEN PERIPHERAL OR PERI-LOBULAR DISTRIBUTION
- CLASSICALLY SUBPLEURAL SPARING



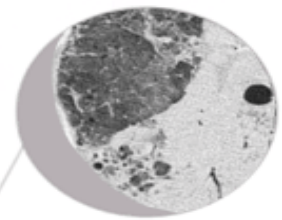
LIPOID PNEUMONIA

USUALLY DEPENDENT AREAS, MAY CONTAIN ANY OR ALL OF:
- CRAZY PAVING (ABOVE)
- GROUND GLASS
- CONSOLIDATIONS



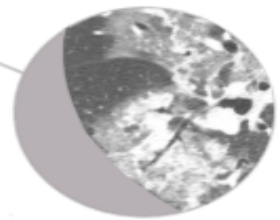
ACUTE EOSINOPHILIC PNEUMONIA

- SYMMETRICAL GROUND GLASS WITH SEPTAL THICKENING AND PLEURAL EFFUSIONS (NON-SPECIFIC)
- PERIPHERAL EOSINOPHILIA ABSENT ON PRESENTATION
- DIAGNOSIS CLINCHED BY BAL WITH 25% EOSINOPHILS



DIFFUSE ALVEOLAR DAMAGE

- HETEROGENOUS CONSOLIDATIONS (CRAZY PAVING, GROUND GLASS, ETC)
- GRAVITY DEPENDENT
- ORGANIZING PHASE WITH TRACTION BRONCHIECTASIS AND RETICULATIONS



DIFFUSE ALVEOLAR HEMORRHAGE

- MAY HAVE CENTRILOBULAR NODULES
- GROUND GLASS
- CONSOLIDATIONS
- COMBINATION OF ANY OF ABOVE

E-liquid component	Chemical or compound
Carrier solution	• Propylene glycol • Vegetable glycerin
Flavourants	• Diacetyl • 2,3-Pentanedione • Acetoin
Additives	• Nicotine • Tetrahydrocannabinol • Cannabidiol • Butane hash oil • Other oil-rich additives
Adulterants	• Vitamin E acetate (tetrahydrocannabinol adulterant)
Aerosol emissions	• Carbonyls from heating propylene glycol and vegetable glycerin • Particulates • Trace metal elements • Volatile organic compounds
Contaminants	• Bacterial endotoxins • Fungal glucans

Simon T. Landman et al. CMAJ 2019;191:E1321-E1331

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Risks

- THC—present in lung lavage samples from 75-80% of acute injury victims
- Vitamin E acetate—used as a thickener, usually with THC—present in lung lavage of over 90% of acute injury victims
- Nicotine—present in lung lavage of over 60% of acute injury victims. Also present in lavage of smokers without symptoms
- Other elements—CBD, plant oils, medium chain triglycerides, petroleum products, byproducts

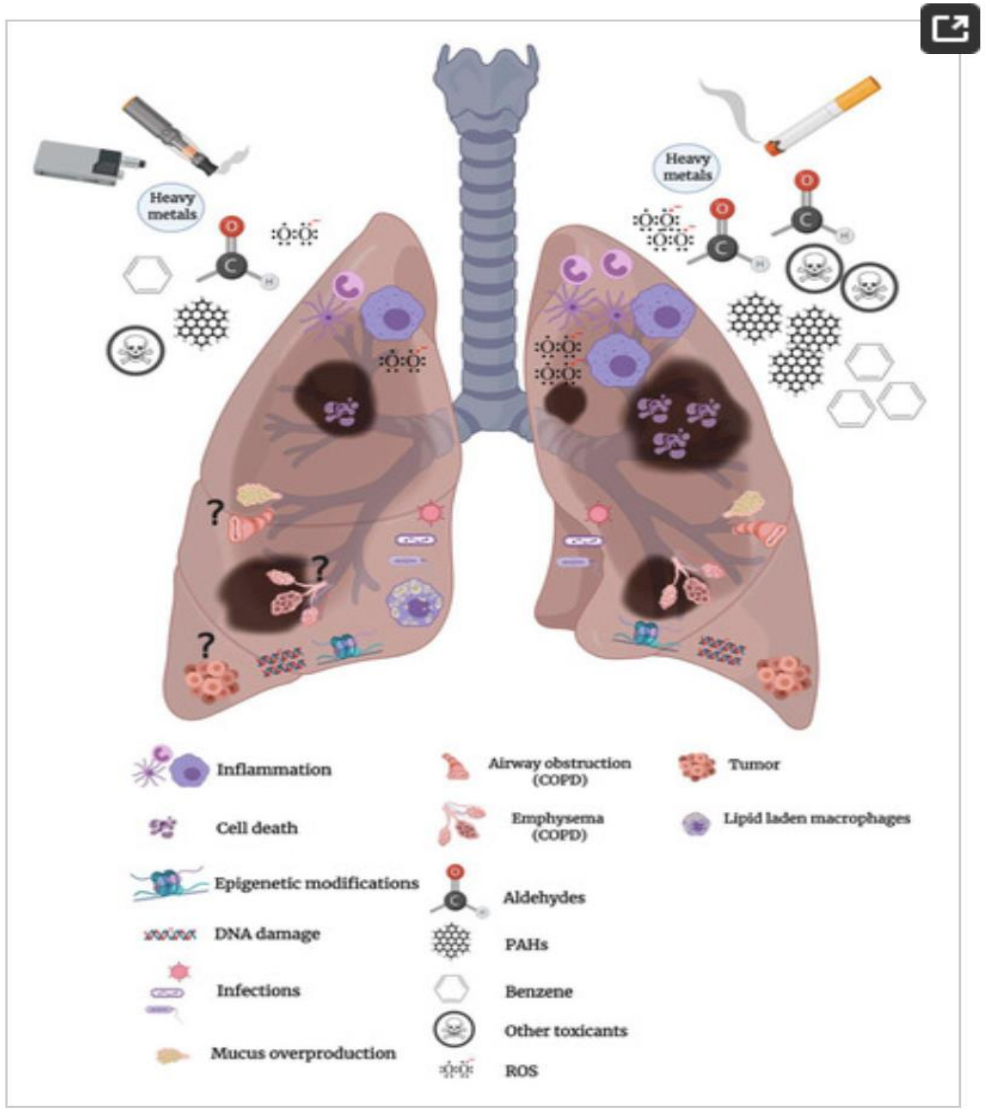

Figure 1. The known and unknown health effects of vaping in comparison to cigarette smoke. The major toxic effects of compounds found in cigarette smoke (Right lung) and in vaping aerosols (Left lung) are lunginflammation, oxidative stress, cell death, impaired immune response, DNA damage and epigeneticmodifications. The respiratory diseases caused by cigarette smoke (lung cancer, COPD [emphysema and/orobstruction of airways]) are not yet established to be caused by vaping (represented by question marks in theleft lung). The presence of lipid-laden macrophages is a feature predominantly associated with vaping products containing THC and has been a feature of EVALI.

Traboulsi H *J Int Mol Sci* 2020

Patterns of disease shown in case reports of vaping-associated pulmonary illnesses: an overview of the medical literature up to Oct. 30, 2019*.

Type of lung injury or predominant disease pattern	No. of cases	Age and sex	Associated imaging findings	Level of care required
Organizing pneumonia[10–13,26]	12	64M, 40F, 54M, 22M, 20M, 21M, 28M, 19M, 28M, 38M, 35M, 39M	1 patchy infiltrates, 11 diffuse GGO, 1 tree in bud, 1 pneumothorax with bilateral central opacities, bilateral reticulonodular opacities with subpleural sparing	7 hospital ward, 2 ICU, 3 unknown
Acute fibrinous pneumonitis with organization[26]	11‡	44M, 42M, 51M, 25M, 21M, 34F, 28M, 54F, 67M, 19M, 40M	5 diffuse GGO, 2 bilateral centrilobular GGO, 1 perihilar GGO, 1 tree in bud, 1 diffuse bronchocentric micronodular GGO, 1 diffuse bilateral opacities	11 unknown
Lipoid pneumonia[17–21]	10	42F, "young" F, 35F, 31F, 20§, 23§, 23§, 25§, 29§, 47§	8 diffuse GGO, 3 "crazy paving," 1 consolidation, 1 basilar GGO	6 hospital ward, 4 ICU
Acute alveolitis or diffuse alveolar damage[9,13,26–28]	8¶	46M, 33M, 35M, 61M, 47F, 21M, 34F, 28M	6 bilateral diffuse GGO, 1 traction bronchiectasis	1 hospital ward, 6 ICU, 1 unknown
Pneumomediastinum or pneumothorax[29–33]	6	17M, 16M, 21M, 15M, 16M, 18M	2 pneumomediastinum, 1 tension pneumothorax, 3 nontension pneumothorax	6 hospital ward
Hypersensitivity pneumonitis[5–8]	4	73F, 16F, 23M, 18F	2 diffuse GGO, 2 septal thickening, 1 traction bronchiectasis, 1 honeycombing, 1 diffuse nodules	2 hospital ward, 1 ICU with ECMO, 1 ICU without ECMO
Granulomatous disease[34,35]	2	43F, 34F	2 bilateral nodules	2 hospital ward
Eosinophilic pneumonia[15,16]	2	18F, 20M	2 diffuse GGO, 1 airspace disease, 1 coalescing nodules	1 ICU, 1 hospital ward
Status asthmaticus[36]	2	16M, 14F	2 pneumomediastinum	2 ICU with ECMO
Bronchitis[37,38]	2	43M, 56F	1 no acute abnormality, 1 diffuse GGO, 1 "crazy paving"	1 outpatient, 1 hospital ward
Inhalational injury[39,40]	2	35F, 60M	1 nodular infiltrates, 1 mediastinal adenopathy, 1 bilateral GGO	1 ICU with ECMO, 1 hospital ward
Respiratory bronchiolitis–associated interstitial lung disease[41]	1	33M	Tree in bud	Hospital ward
Diffuse alveolar hemorrhage[9]	1	33M	Diffuse GGO	ICU
Hypereosinophilia with eosinophilic asthma[42]	1	18F	NA	Outpatient
Transient nodules in lung and liver[43]	1	45F	Multiple pulmonary and hepatic nodules	Hospital ward
Pleural effusion[44]	1	63M	Left-sided pleural effusion	Hospital ward
Severe persistent airflow obstruction in a long-standing smoker†[45]	1	45M	Patchy GGO, mosaic attenuation	Outpatient
Upper airway damage[46]	1	30M	Moderate uvulitis and edema of the paratracheal musculature	ICU

Note: ECMO = extracorporeal membrane oxygenation, F = female, GGO = ground-glass opacities, ICU = intensive care unit, M = male, NA = not available.
*"Case reports" refers to individual cases reported with pathology and imaging findings. Table 1 does not include the 53-person case cohort published by Layden et al.[22] or 805 cases reported by Perrine et al.[47]
†Patient was a long-standing smoker. No baseline pulmonary function tests before illness.
‡One death.
§Sex not defined
¶Two deaths.

Simon T. Landman et al. CMAJ 2019;191:E1321-E1331

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Presentation, Characteristics, and Outcome of Six Patients in Utah with Pulmonary Illness Related to E-Cigarette

Table 1. Presentation, Characteristics, and Outcome of Six Patients in Utah with Pulmonary Illness Related to E-Cigarette Use.*

Variable	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (yr)	20	25	29	23	23	47
Approximate time from symptom onset to presentation†	9 days	9 days	2 wk	2 mo	5 days	6 wk
Initial laboratory studies†						
Blood white-cell count (per mm^3)	16,300	18,200	10,600	4800	12,300	13,800
Differential count (%)						
Granulocytes	92.0	93.7	92.2	84.5	90.2	89.2
Lymphocytes	1.5	3.8	6.0	8.9	5.7	7.0
Eosinophils	0.9	0.0	0.3	2.9	0.8	0.0
ESR (mm/hr)‡	NA	122	105	90	128	60
C-reactive protein (mg/dl)§	30.7	20.4¶	22.6	28.0	25.8	21.7
Bronchoalveolar lavage						
Lipid-laden macrophages (%)‖	>50	Approx. 50	30	25	>75	Approx. 60
Differential count (%)						
Macrophages	32	79	71	61	43	46
Bronchial lining cells	12	2	7	1	5	0
Lymphocytes	5	0	3	9	14	25
Neutrophils	49	18	19	26	38	27
Eosinophils	12	1	0	3	0	2
Management and outcomes						
Medical therapy	Antibiotics; high-dose glucocorticoids	Antibiotics; high-dose glucocorticoids	Glucocorticoids; antibiotics**	Glucocorticoids; antibiotics**	Antibiotics	None
Other interventions	Mechanical ventilation; venovenous ECMO	High-flow nasal cannula	None	Supplemental oxygen by nasal cannula	Supplemental oxygen by nasal cannula	Supplemental oxygen by nasal cannula
Outcome	Alive; hypoxemia resolved	Alive; oxygen at discharge	Alive; fevers resolved	Alive; hypoxemia resolved	Alive; hypoxemia resolved	Alive; hypoxemia resolved

* ECMO denotes extracorporeal membrane oxygenation, ESR erythrocyte sedimentation rate, and NA not available.
† Shown are data at admission to our facility.
‡ The reference range is 0 to 10 mm per hour.
§ The reference range is 0.0 to 0.8 mg per deciliter.
¶ Shown are data for high-sensitivity C-reactive protein; the reference range is less than 0.3 mg per deciliter.
‖ Lipid-laden macrophages were measured by means of oil red O staining.
** With respect to glucocorticoids, a short course of prednisone was prescribed by an outpatient provider before hospitalization.

SD Maddock et al. N Engl J Med 2019;381:1488-1489.

Table 2. Laboratory Studies on Initial Presentation

Laboratory study	Median (IQR)
White blood cell count, /μL	15 300 (12 300-17 900)
Differential, median (IQR), %	
Granulocytes	90.3 (88.0-92.4)
Lymphocytes	5.7 (4.2-7.9)
Monocytes	2.4 (2-3.2)
Basophils	0.2 (0.1-0.3)
Eosinophils	0.3 (0.1-0.9)
ESR, mm/h	75 (42-100)
CRP, mg/dL	25.8 (18.7-30.2)
Elevated, No./total No. (%)	
ESR[a]	25/26 (96)
CRP[b]	27/27 (100)
ESR or CRP	28/28 (100)
ESR >100 mm/h	7/26 (27)
Procalcitonin, ng/mL	0.3 (0.1-0.7)
Creatinine, mg/dL	0.85 (0.73-0.94)
Total bilirubin, mg/dL	1.0 (0.6-1.4)
AST, U/L	31 (25-37)
ALT, U/L	24 (18-39)
Elevated, No./total No. (%)	
AST[c]	6/30 (20)
ALT[d]	5/30 (17)
AST or ALT	7/30 (23)
Alkaline phosphatase, U/L	85 (72-114)
HIV 1, 2 antigen or antibody	
Negative, No./total No. (%)	19/19 (100)
BAL performed, No./total No. (%)	24/31 (77)
Cytologic differential, %	
Macrophages	53 (33-79)
Neutrophils	28 (12-48)
Lymphocytes	6 (2-12)
Eosinophils	0 (0-2)
Presence of LLMs, No./total No. (%)[e]	21/23 (91)
LLMs, median (IQR), %	52 (33-76)
Urine drug screen, No./total No. (%)	
Marijuana	11/11 (100)
Cocaine	0/11
Heroin	0/1
Methamphetamine	1/11 (9)
Narcotics	2/11 (18)
Benzodiazepine	0/11
Methadone	0/11
Buprenorphine	0/11

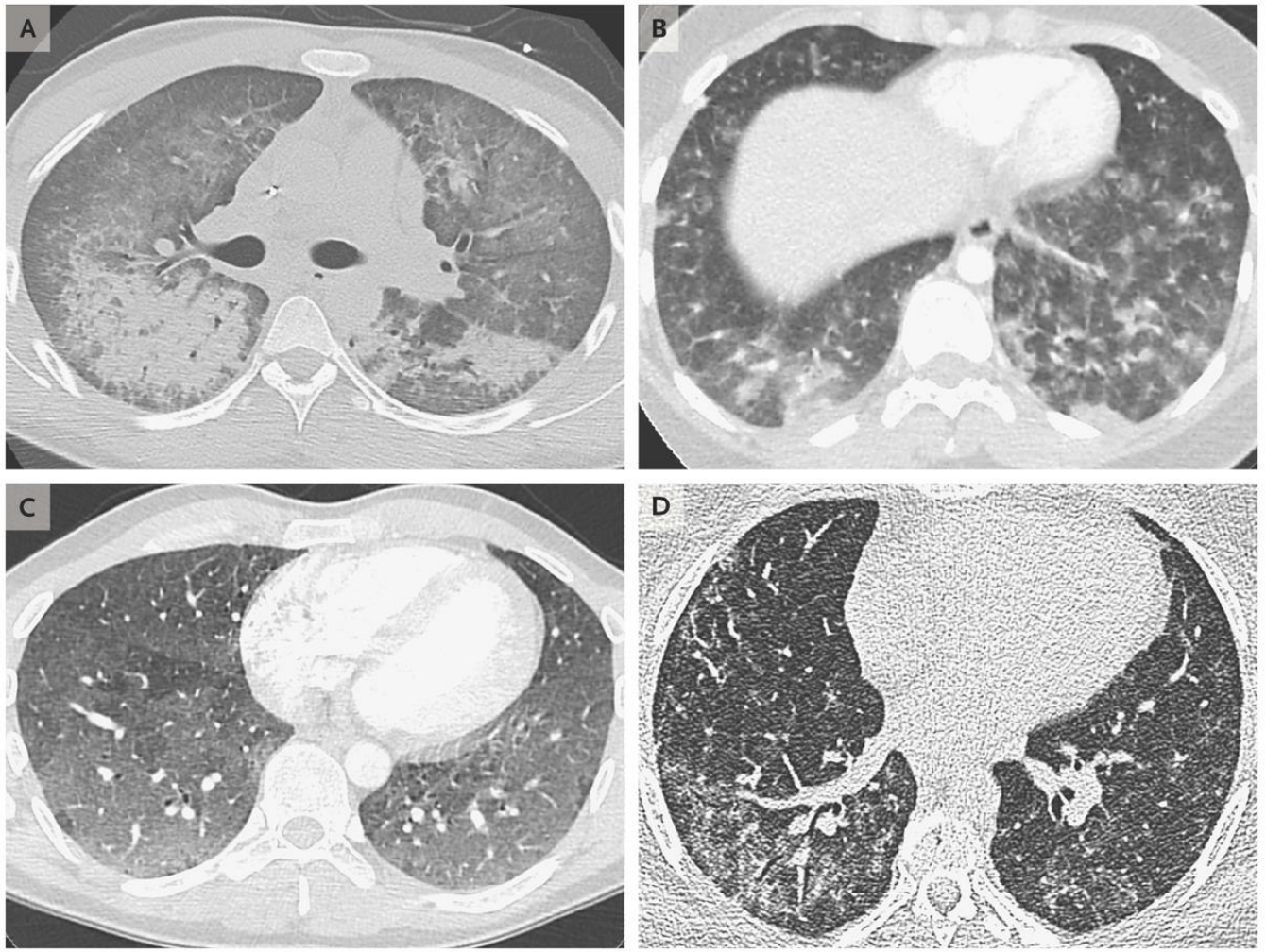
Newest Case Series

Table 3. Computed Tomography Findings

Pattern	Patients, No. (%) (n = 26)[a]
Organizing pneumonia[b]	26 (100)
Pneumonitis	
Hypersensitivity[c]	5 (19)
Acute	
Eosinophilic[d]	1 (4)
Lung injury[e]	1 (4)
Exogenous lipoid pneumonia[e]	1 (4)
Diffuse alveolar hemorrhage	0
Subpleural sparing	
Yes	10 (39)
Some	5 (19)
Any[f]	15 (58)
No	11 (42)
Airway wall thickening	
Yes	21 (81)
No	5 (19)

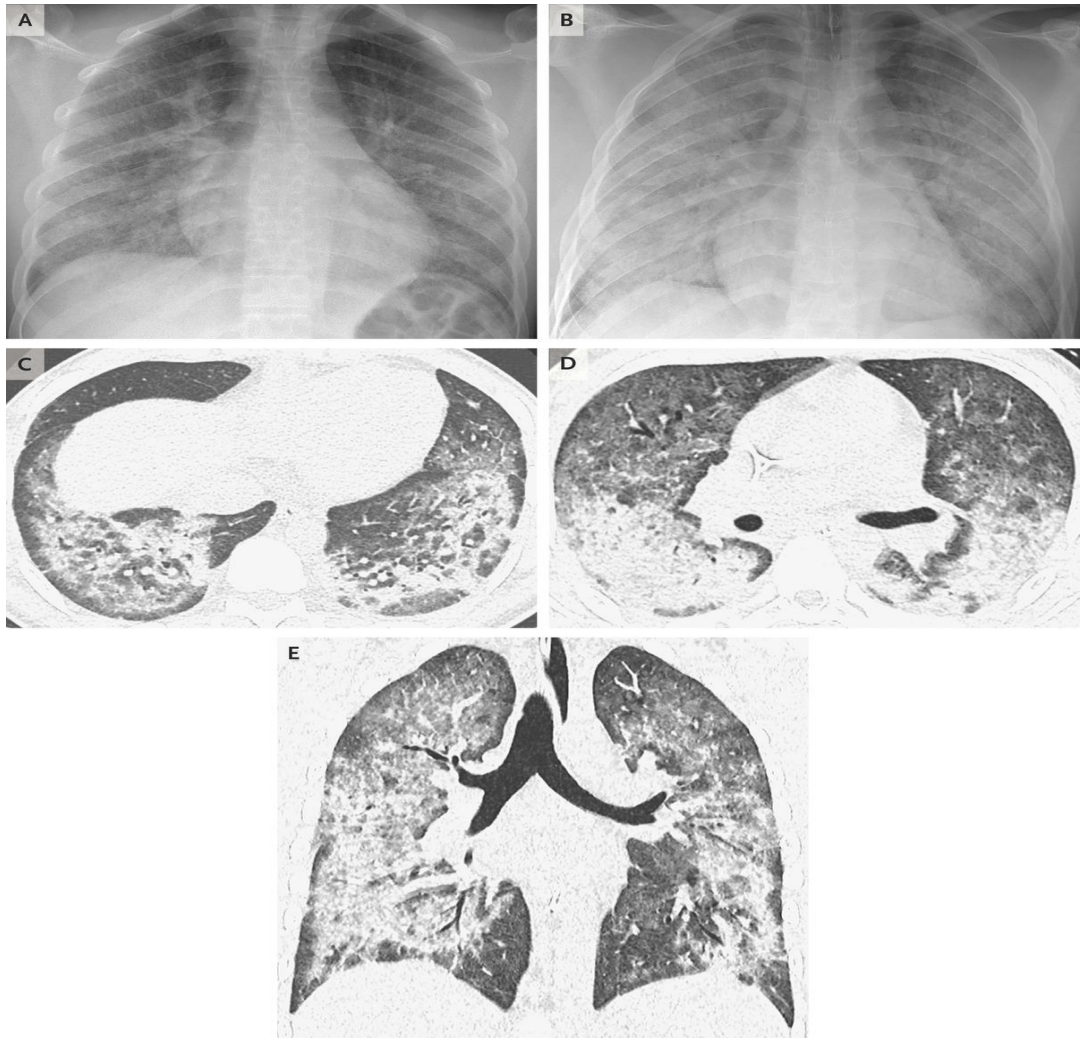
Aberegg SK et al, *JAMA Network Open* 2020

Computed Tomographic Scans of the Chest Obtained from Patients with Vaping-Associated Lung Injury.



TS Henry et al. N Engl J Med 2019;381:1486-1487.

Chest Radiographs and High-Resolution Computed Tomographic Imaging in a 17-Year-Old Male Patient with Diffuse Lung Disease.



JE Layden et al. N Engl J Med 2019. DOI: 10.1056/NEJMoa1911614

EVALI—Clinical Features

- Shortness of breath
- Cough
- Chest pain
- Pleuritic chest pain
- Hemoptysis
- Fever and chills
- Nausea, vomiting, diarrhea
- Abdominal pain
- Present days to months ahead of acute process

Clinical Characteristics of Nonhospitalized Patients

- **85%** (47/55) initially experienced respiratory symptoms
  - e.g., cough, chest pain, and shortness of breath

- **57%** (27/47) had gastrointestinal symptoms
  - e.g., abdominal pain, nausea, vomiting, and diarrhea

- **76%** (41/54) had symptoms accompanied by constitutional symptoms
  - e.g., fever, chills, and weight loss

Proposed criteria for EVALI

Confirmed case

- Use of an e-cigarette ("vaping") or "dabbing" in the previous 90 days*
- Lung opacities on chest radiograph or computed tomography
- Exclusion of lung infection based on:
  - Negative influenza PCR or rapid test (unless out of season)
  - Negative respiratory viral panel
  - Negative testing for clinically-indicated respiratory infections (eg, urine antigen test for *Legionella* and *Streptococcus pneumoniae*, blood cultures, sputum cultures if producing sputum, and bronchoalveolar lavage if performed)
  - Negative testing for HIV-related opportunistic respiratory infections (if appropriate)
- Absence of a plausible alternative diagnosis (eg, cardiac, neoplastic, rheumatologic)

Probable case

- Use of an e-cigarette ("vaping") or "dabbing" in the previous 90 days*
- Lung opacities on chest radiograph (diffuse hazy or consolidative opacities) or computed tomography (ground glass or consolidative opacities)
- 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 infection is not the sole cause of the underlying lung injury
- Absence of a plausible alternative diagnosis (eg, cardiac, neoplastic, rheumatologic)

EVALI or COVID-19

- Symptoms similar: cough, chest pain, shortness of breath, hypoxia
- Even fever, nausea, vomiting, diarrhea, fatigue
- Maybe different: nasal congestion, loss of taste/smell
- Lab findings of inflammation in both
- Imaging may be similar

Confounders—the ACE2 Receptor

- ACE2 is a receptor protein on epithelial cells
- Breaks down large protein angiotensin II which causes inflammation and bronchoconstriction
- In smokers and likely vapers, ACE2 is upregulated—more receptors
- ACE2 is also the target of the SARS-CoV-2 virus, so more ACE2 means more sites for virus to bind
- Rates of ICU hospitalization and ventilator need in COVID-19 are 2 times higher in smokers

	Ever-use of inhaled tobacco and…			Past 30-day use of inhaled tobacco and…		
	COVID-19–related symptoms (n = 4,043)	COVID-19 test (n = 4,048)	COVID-19–positive diagnosis (n = 4,048)	COVID-19–related symptoms (n = 4,043)	COVID-19 test (n = 4,048)	COVID-19–positive diagnosis (n = 4,048)
	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)
Inhaled tobacco products						
Cigarettes only	1.40 (.83, 2.38)	**3.94 (1.43, 10.86)**	2.32 (.34, 15.86)	1.15 (.58, 2.27)	1.16 (.64, 2.12)	1.53 (.29, 8.14)
E-cigarettes only	1.18 (.80, 1.73)	**3.25 (1.77, 5.94)**	**5.05 (1.82, 13.96)**	1.43 (.84, 2.43)	**2.55 (1.33, 4.87)**	1.91 (.77, 4.73)
Dual use	1.36 (.90, 2.04)	**3.58 (1.96, 6.54)**	**6.97 (1.98, 24.55)**	**4.69 (3.07, 7.16)**	**9.16 (5.43, 15.47)**	**6.84 (2.40, 19.55)**
Never used	Ref	Ref	Ref	Ref	Ref	Ref

Children and youth 13-24 yrs

More common symptoms if smoked and vaped – cough, fever, fatigue, difficulty breathing

And more likely to get a COVID-19 test

But even more likely to have a POSITIVE COVID-19 test

Giaha SM, et al *J Adol Health* 2020

And What About MIS-C?

- Multisystem inflammatory syndrome in children
- Usually post-COVID but symptoms are similar
- Fever
- Abdominal pain, vomiting, diarrhea
- Rash
- Bloodshot eyes
- Difficulty breathing

Treatment

- Hospitalization
- Include or exclude viral illnesses—Influenza, SARS-CoV-2
- Respiratory support—oxygen, ventilation, ECMO
- Antibiotics to cover community acquire pneumonia
- Consider steroids
- Prognosis – complete resolution to death—no clear associations

Management algorithm

Patient arrives with signs and symptoms such as:
fever, cough, sore throat, shortness of breath, muscle aches, headaches, fatigue, nausea, or vomiting

Ask if patient uses e-cigarette, or vaping, products

No

Evaluate and manage patient as clinically indicated

Yes

Initial clinical assessment
- Obtain pulse oximetry with vital signs
- Focused history and physical exam
- Evaluate for other possible etiologies

Is patient a candidate for outpatient management?
- ❑ Normal O_2 saturation (≥95%)
- ❑ No respiratory distress
- ❑ No comorbidities that may compromise pulmonary reserve
- ❑ Reliable access to care/ strong social support systems
- ❑ Able to follow-up within 24–48 hours

Yes

Outpatient clinical evaluation
- Consider CXR (chest pain, dyspnea, clinical exam findings)
- Consider influenza testing per established guidelines

Outpatient clinical management

Manage for possible EVALI
- Discontinue use of e-cigarette, or vaping, products
- Consider corticosteroids with caution

Manage other possible infections, if present
- Consider early initiation of antivirals for possible influenza or appropriate antibiotics for community acquired pneumonia

Ensure follow-up within 24-48 hours

Emphasize importance of routine influenza vaccination

Offer cessation services

No

Inpatient clinical evaluation
- Conduct laboratory and infectious disease testing guided by clinical findings
- Obtain a chest X-ray and consider CT if chest X-ray is normal
- Consider consultation with specialists
- Additional testing with bronchoalveolar lavage or lung biopsy as clinically indicated, in consultation with pulmonary specialists

Inpatient clinical management
- Discontinue use of e-cigarette, or vaping, products
- Consider empiric use of antibiotics, antivirals, or both
- Consider corticosteroids with timing, depending on severity
- Offer cessation services
- Ensure follow-up no later than 1-2 weeks after discharge
- Emphasize importance of routine influenza vaccination

COVID-19 Testing

Ask about Use

- **Ask about the use of e-cigarette, or vaping, products and types of substances used**
- Confidentiality is essential especially for young adults and adolescents
- Empathetic, nonjudgmental, and private questioning of patients*
- Continue to ask questions during follow-up encounters

*AAFP Article on Patient-Centered Communication and Interview Tool for Adolescents

Exposure History

- **Types of substances used**
  - THC/cannabis [oil, dabs], nicotine, modified products or the addition of substances not intended by the manufacturer
- **Where products were obtained**
  - THC containing products obtained through informal sources such as friends, family members, or in-person or online-dealers have been implicated
- **Clinicians might seek additional information to inform the ongoing investigation**

*AAFP Article on Patient-Centered Communication and Interview Tool for Adolescents

Physical Examination

- Should include vital signs and pulse-oximetry
  - Vital signs findings include tachycardia, tachypnea, O_2 saturation <95% at rest on room air
- Pulmonary findings on auscultation exam have been unremarkable, even among patients with severe lung injury

Considerations for Management Setting

- Some patients may be candidates for outpatient management
  - Normal oxygen saturation (≥95%)
  - No respiratory distress
  - No comorbidities that might compromise pulmonary reserve
  - Reliable access to care, strong social support systems
  - **Ensure follow-up within 24–48 hours**

Outpatient Clinical Evaluation

- Consider influenza testing
- Consider chest radiograph (CXR), if indicated by
  - Chest pain
  - Dyspnea
  - Clinical exam findings

*Consider modifying factors such as altitude to guide interpretation of measured O_2 saturation.

Consider COVID-19 Testing

Outpatient Management: Manage Possible EVALI

- Advise patient to discontinue use of e-cigarette, or vaping, products
  - Some patients have had recurrences with continue use
- Corticosteroids might worsen respiratory infections and should be considered with caution in the outpatient setting
  - Not well studied; consider with caution
  - Might worsen commonly seen respiratory infections
  - Most patients had rapid improvement with corticosteroids
  - Some patients who have not received corticosteroids had clinical improvement with e-cigarette cessation

Blagev DP, Harris D, Dunn AC, Guidry DW, Grissom CK, Lanspa MJ. Clinical presentation, treatment, and short-term outcomes of lung injury associated with e-cigarettes or vaping: a prospective observational cohort study. Lancet 2019;19:32679–0.

Outpatient Management: Manage Other Infections

- Manage other infections, if present, in accordance with established guidelines*
  - Early initiation of antivirals for possible influenza
  - Appropriate antibiotics for community acquired pneumonia

* CDC Summary of Influenza Antiviral Medications; IDSA Clinical Practice Guidelines for Seasonal Influenza; Pneumonia guidelines; Pneumonia guidelines for infants and children

Co-Management of COVID-19

- Supportive—oxygen, ventilation
- Prone positioning
- EVALI, COVID-19 and MIS-C should receive steroids
- Remdesivir
- Convalescent plasma

Outpatient Management: Cessation Counseling

- Offer or connect all patients to services to stop using e-cigarette, or vaping, products
- Adults tobacco smokers should be
  - advised not to return to smoking cigarettes, if using e-cigarette, or vaping, products to quit cigarette smoking
  - provided with evidence-based interventions: behavioral counseling, FDA-approved cessation medications
- Adolescents and young adults might benefit from specialized services like
  - addiction treatment services
  - providers who have experience with counseling and behavioral health

Outpatient Management: Follow-Up Instructions

- Ensure follow-up within 24-48 hours; additional follow-up might be indicated, based on clinical findings
- Patients should return immediately if they develop new or worse respiratory symptoms
- Emphasize importance of routine influenza vaccination

Follow-up

- Close follow up with primary MD
- May need repeat evaluations such as CXR or lung function testing
- Long term side effects are still unknown
  - Some resolve completely
  - Some relapse as steroids taper or vaping recurs
  - Some have long-term oxygen need and pulmonary follow up
  - Some develop adrenal insufficiency and need Endocrine follow up
- Long term side effects from COVID may be the same!

Table 5. Treatment and Outcomes

Treatment or outcome	Patients, No. (%) (N = 31)[a]
Admitted	
Hospital	28 (90)
ICU	8 (26)
Hospital length of stay, median (IQR), d	4 (3-7)
Highest respiratory support	
Room air	4 (13)
Nasal cannula	19 (61)
High flow nasal cannula	5 (16)
Noninvasive positive pressure ventilation	0
Mechanical ventilation	2 (7)
Extracorporeal membranous oxygenation[b]	1 (3)
Treatment	
Steroids	24 (77)
IV methylprednisolone	16 (52)
Starting daily dose, median (IQR), mg[c]	60 (60-156)
Planned duration, median (IQR), d	7 (1-15)
Antibiotics	26 (84)
Pulmonary function tests at follow-up, median (IQR)	
Predicted FEV_1, %	92 (83-104)
Predicted FVC, %	99 (93-107)
FEV_1/FVC	84 (75-86)
Predicted DLCO, %	76 (64-83)

Residual symptoms 65%
Persistent radiographic abnormalities 40%
Abnormal PFT's 44%

Aberegg SK et al, *JAMA Network Open* 2020

Risks to Our Children

WHAT ARE E-CIGARETTES?

Electronic cigarettes (e-cigarettes) are battery-powered devices that deliver nicotine, flavorings, and other ingredients to the user. Using e-cigarettes is sometimes called "vaping." E-cigarettes do not create harmless "water vapor" – they create an aerosol that can contain harmful chemicals.

HOW MANY YOUTH ARE USING E-CIGARETTES?

- E-cigarettes have been the most commonly used tobacco product among U.S. youth since 2014.
- In 2019, CDC and FDA data showed that more than 5 million U.S. youth, including over 1 in 4 high school students and about 1 in 10 middle school students, used e-cigarettes in the past 30 days.
- During 2017 and 2018, e-cigarette use skyrocketed among youth, leading the U.S. Surgeon General to call the use of these products among youth an epidemic in the United States.

WHAT ARE THE RISKS FOR YOUTH?

- Most e-cigarettes contain nicotine, which is highly addictive. Nicotine exposure during adolescence can:
  - Harm brain development, which continues until about age 25.
  - Impact learning, memory, and attention.
  - Increase risk for future addiction to other drugs.
- Young people who use e-cigarettes may be more likely to go on to use regular cigarettes.
- Many e-cigarettes come in kid-friendly flavors – including mango, fruit, and crème – which make e-cigarettes more appealing to young people.
- E-cigarette aerosol is not harmless. It can contain harmful substances, including:
  - Nicotine
  - Cancer-causing chemicals
  - Volatile organic compounds
  - Ultrafine particles
  - Flavorings that have been linked to lung disease
  - Heavy metals such as nickel, tin, and lead

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CDC.gov/e-cigarettes

E-CIGARETTES SHAPED LIKE USB FLASH DRIVES:

INFORMATION FOR PARENTS, EDUCATORS, AND HEALTH CARE PROVIDERS

Electronic cigarettes (e-cigarettes) are battery-powered devices that can deliver nicotine and flavorings to the user in the form of an aerosol. E-cigarettes come in many shapes and sizes.

WHAT'S THE BOTTOM LINE?

A new e-cigarette shaped like a *USB* flash drive is being used by students in schools.

Nicotine is highly addictive and can *harm brain development*, which continues until about age 25.

The use of any tobacco product — including e-cigarettes—is *unsafe* for young people.

Parents, educators, & health care providers can help prevent and reduce the use of all tobacco products, including e-cigarettes, by young people.

>> *Learn HOW* in this fact sheet.

CS292647-A

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

AN INCREASINGLY POPULAR E-CIGARETTE DEVICE, CALLED JUUL, IS SHAPED LIKE A USB FLASH DRIVE.

Use of JUUL is sometimes called "JUULing."

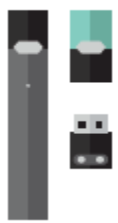
JUUL's nicotine liquid refills are called "pods." JUUL is available in several flavors such as Cool Cucumber, Fruit Medley, Mango, and Mint.

All JUUL e-cigarettes have a high level of nicotine. According to the manufacturer, a single JUUL pod contains as much nicotine as a pack of 20 regular cigarettes.

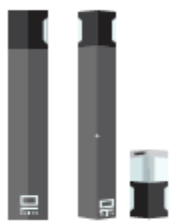
JUUL became available for sale in the United States in 2015. As of December 2017, JUUL is the top-selling e-cigarette brand in the United States.

News outlets and social media sites report widespread use of JUUL by students in schools, including in classrooms and bathrooms.

Other devices are becoming available that look like USB flash drives. Examples include the MarkTen Elite, a nicotine delivery device, and the PAX Era, a marijuana delivery device that looks like JUUL.



JUUL

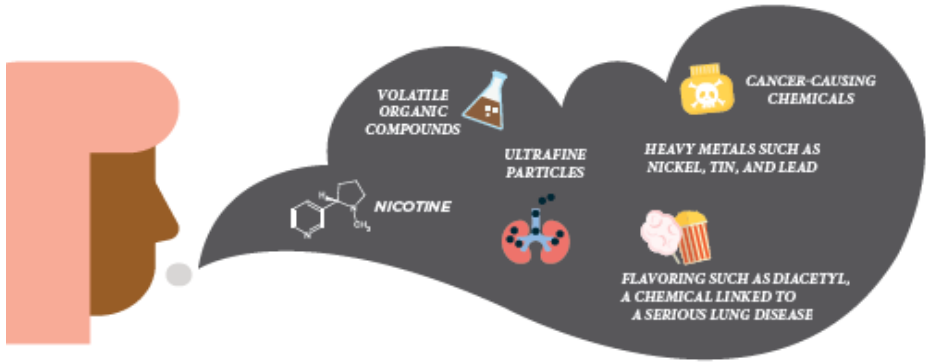


MarkTen Elite

PAX Era

E-CIGARETTE USE IS NOT SAFE FOR YOUNG PEOPLE.

E-cigarette aerosol is not harmless. It can contain harmful ingredients. However, e-cigarette aerosol generally contains fewer harmful chemicals than smoke from burned tobacco products, like regular cigarettes.



Most e-cigarettes contain *nicotine*, which is highly addictive and can *harm brain development*, which continues until about *age 25*.

YOUNG PEOPLE WHO USE E-CIGARETTES MAY BE MORE LIKELY TO GO ON TO USE REGULAR CIGARETTES.

PARENTS, EDUCATORS, AND HEALTH CARE PROVIDERS CAN HELP PREVENT AND REDUCE THE USE OF E-CIGARETTES BY YOUNG PEOPLE.

PARENTS CAN:

- Learn about the different shapes and types of e-cigarettes and the risks of all forms of e-cigarette use for young people.
- Talk to their children about the risks of e-cigarette use among young people. Express firm expectations that their children remain tobacco-free.
- Set a positive example by being tobacco-free.

EDUCATORS CAN:

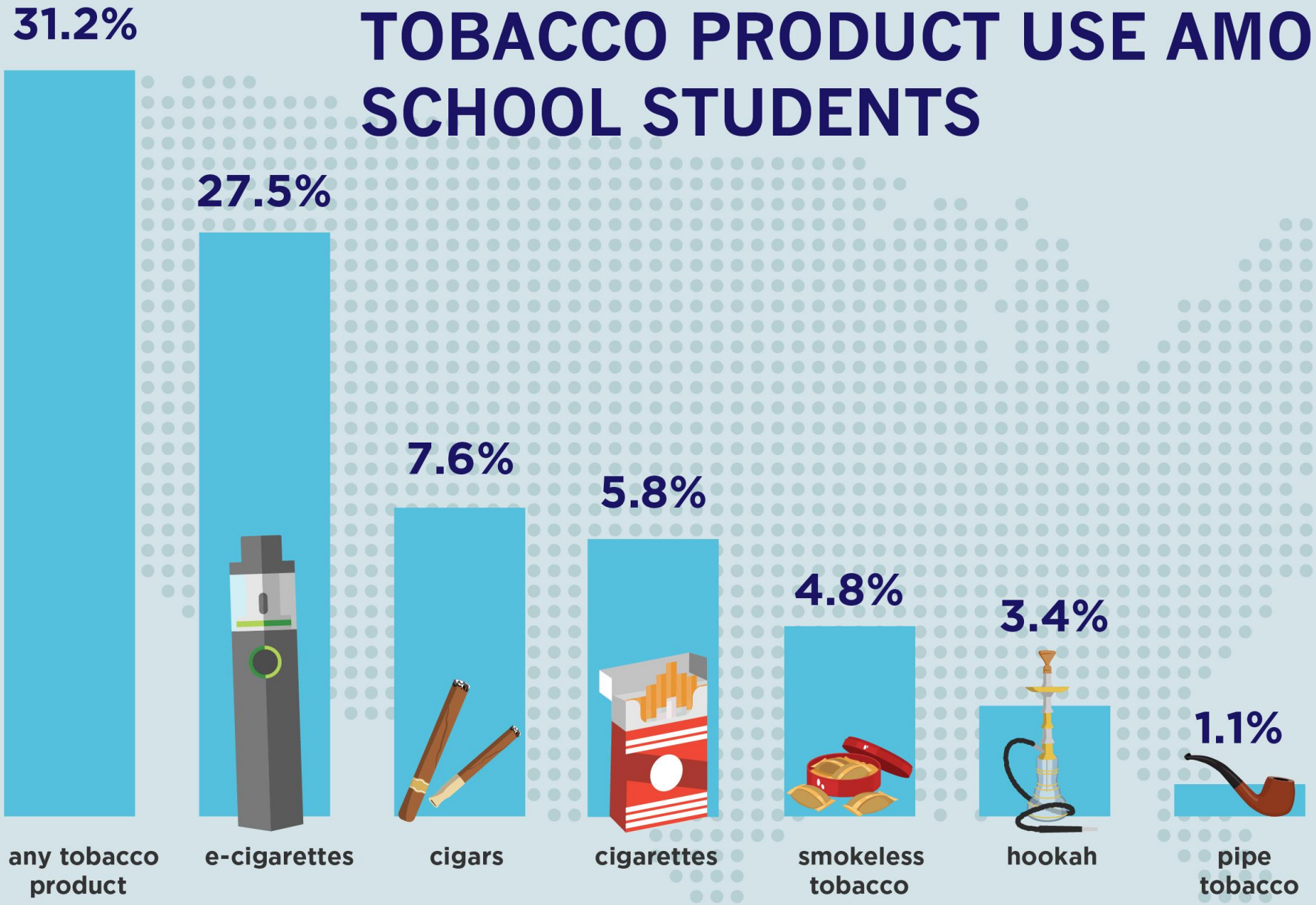
- Learn about the different shapes and types of e-cigarettes and the risks of all forms of e-cigarette use for young people.
- Develop, implement, and enforce tobacco-free school policies.
- Reject youth tobacco prevention programs sponsored by the tobacco industry. These programs have been found to be ineffective for preventing youth tobacco use.

PEDIATRIC HEALTH CARE PROVIDERS CAN:

- Ask about e-cigarettes, including devices shaped like USB flash drives, when screening patients for the use of any tobacco products.
- Warn patients about the risks of all forms of tobacco product use, including e-cigarettes, for young people.

NYTS

TOBACCO PRODUCT USE AMONG HIGH SCHOOL STUDENTS



Learn more at bit.ly/NYTS-2019

***Source**: National Youth Tobacco Survey, 2019*

Print Only

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA
CDC

7 out of 10 middle and high school students who currently use tobacco have used a **FLAVORED** product.

63%
of students who currently use e-cigarettes have used **flavored** e-cigarettes.
(1.6 million)

61%
of students who currently use hookah have used **flavored** hookah.
(1 million)

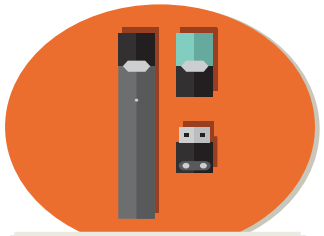
64%
of students who currently use cigars have used **flavored** cigars.
(910,000)

Source: Morbidity and Mortality Weekly Report (MMWR)

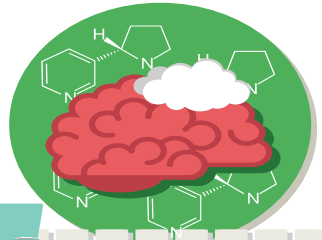
For Educators

E-cigarettes are the most commonly used tobacco product among U.S. middle and high school students.

Some e-cigarettes don't look like tobacco products, so some kids use them unnoticed in schools, including in classrooms and bathrooms.



An increasingly popular e-cigarette, called JUUL, is shaped like a USB flash drive.

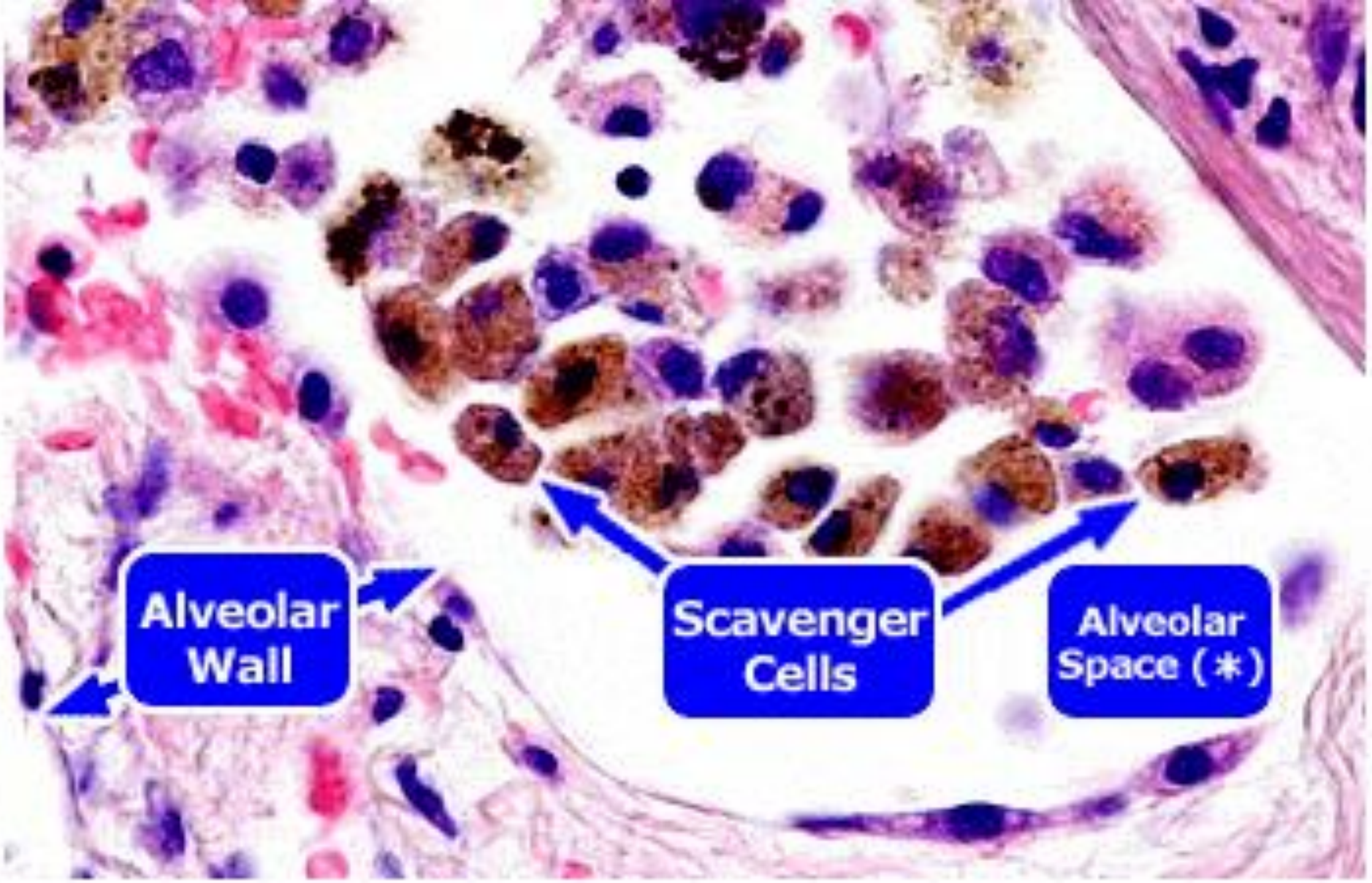


JUUL delivers a high dose of nicotine. Nicotine is highly addictive and can harm adolescent brain development.

TOBACCO PRODUCT USE IN ANY FORM, INCLUDING E-CIGARETTES, IS UNSAFE FOR YOUTH.

What Else—Cigarette Smoking

- Declining but still 12% of high school students actively smoking cigarettes
- Over 80% of adolescent smokers persist into adulthood
- Symptoms—chronic cough, exacerbations of asthma, pulmonary exacerbations, atherosclerosis
- Clear risk of development of lung cancer and many other cancers as well as heart disease and COPD
- Nicotine dependence—as little as 100 cigarettes
- 31% of adolescent cigarette smokers vaped previously


Alveolar Wall
Scavenger Cells
Alveolar Space (*)

And—Marijuana

- Current use of 12th graders 23%
- Prevalence of vaping marijuana at 14% in 2019
- Combustibles of tar and hydrocarbons
- Youth are using THC in vaping devices more and more

Cannabis Lung Manifestations

- Symptoms—cough, sputum productions, wheezing, dyspnea
- Acutely actually increased FEV1 and decreased EIB in asthma patients
- Chronic use associated with obstructive lung disease with decreased FEV1, decreased MMEF, decreased airway conductance and diffusing capacity
- Associated with lung cancer
- Much higher likelihood of EVALI if used via vaping vs nicotine products alone

Outpatient Management: Cannabis Use Disorder

- People with cannabis use disorder should receive evidence-based interventions, such as
  - Cognitive-behavioral therapy
  - Contingency management
  - Motivational enhancement therapy
  - Multidimensional family therapy
  - Addiction medicine services consultation
  - www.findtreatment.gov or 1–800–662-HELP (4357).

*Budney AJ, Moore BA, Rocha HL, Higgins ST. Clinical trial of abstinence-based vouchers and cognitive-behavioral therapy for cannabis dependence. J Consult Clin Psychol 2006;74:307–16. PubMed Link to article

Our Children at Risk

- Previous experimentation
- Previous vaping
- Smoking by parents and peers
- Attitudes and beliefs about the social implications and health consequences of smoking
- Depression
- Poor school performance
- Adverse experiences
- Substance use disorder

Our Children at Risk

- Children with underlying lung disease at increased risk
- Children and adolescents believe vaping to be “safer”
- Approximately 30% of children and adolescents who are actively vaping have asthma—may be more prone to EVALI
- Approximately 5-10% of adolescents with cystic fibrosis smoke cigarettes or vape

The 6 A’s

- Anticipate the risk of initiating
- Ask about smoking/vaping/exposure
- Advise risks and cessation
- Assess readiness to quit
- Assist those ready to quit—develop a plan
- Address nicotine withdrawl or other barriers

CDC Public Health Recommendations

- CDC recommends that people should **NOT**
  - Use e-cigarette, or vaping, products that contain THC
  - Buy any type of e-cigarette, or vaping, products, particularly those containing THC, from informal sources (such as family, friends, or in-person or online dealers)
  - Modify or add any substances to e-cigarette, or vaping, products that are not recommended by the manufacturer

CDC Public Health Recommendations

- Since the specific cause or causes of lung injury are not yet known, the only way to assure that people are not at risk while the investigation continues is to consider refraining from use of **all** e-cigarette, or vaping, products

CDC Public Health Recommendations

- E-cigarette, or vaping, products should never be used by used by youth, young adults, or women who are pregnant
- People who do not currently use tobacco products should not start using e-cigarette, or vaping, products
- Adults using e-cigarettes to quit smoking should not go back to smoking; they should weigh all risks and benefits and consider utilizing FDA-approved nicotine replacement therapies*
- If people continue to use e-cigarette, or vaping, products, they should:
  - Carefully monitor themselves for symptoms
  - See a health care provider immediately if symptoms develop

AAFP Pharmacologic Product Guide of FDA-Approved Medications for Smoking Cessation

References

cdc.gov

COCA presentations (many of the slides)

State health offices