Juul, Suorin, Vaping-the new nicotine

Asha N. Chesnutt, MD

EVALI
E-cigarette or Vaping Associated Lung Injury
Disclosures

• I have no disclosures

New Yorker

• The Promise of Vaping and the Rise of Juul

Teens have taken a technology that was supposed to help grownups stop smoking and invented a new kind of bad habit, molded in their own image

New Yorker  May 14,2018

• “you’re expected to Juul , but you’re expected to not depend on it. If you’re cool then you Juul with other people, and you post about it , so everyone will see that you are social and ironic and funny. But if you are addicted, you go off by yourself and Juul because you need it, and everyone knows.”
Outline

• Terminology of e-cigarette devices
• Chemistry behind the flavorings
• VAPI/EVALI
• Vaping cannabis
• TIMELINE – how did we get here?
• The rise of Juul
• Adolescent vaping

E-cigarettes

• The term “electronic cigarettes” covers a wide variety of products like cigarettes, pens or USB drives
• Battery powered devices which heat a solution to create a vapor.
• Heating element is activated electronically which vaporizes the liquid and the vapor condenses to form an aerosol
• NO combustion
• ENDS (electronic nicotine delivery system) contain flavors +/- nicotine
## Comparison

<table>
<thead>
<tr>
<th>Cigarettes</th>
<th>E-cigarettes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon monoxide</td>
<td>Propylene glycol</td>
</tr>
<tr>
<td>Cyanide</td>
<td>Glycerin</td>
</tr>
<tr>
<td>Nicotine</td>
<td>Nicotine</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>Water</td>
</tr>
<tr>
<td>Arsenic</td>
<td>Flavorings</td>
</tr>
<tr>
<td>Nitrosamines</td>
<td>OTHER</td>
</tr>
<tr>
<td>Cadmium</td>
<td>OTHER (Hoffman list)</td>
</tr>
</tbody>
</table>

## Nicotiana tabacum

- Dates back to 1000BC
- Major industry in Europe by 1700
- Harvested then cured
Nicotine

• Not carcinogenic
• Highly addictive
• Reaches brain within 15 secs of inhalation
• This rapid increase in nicotine levels in the brain, faster than with intravenous administration, leads to activation of the dopaminergic reward system and produces rapid behavioral reinforcement (craving)
• Withdrawal causes anxiety and stress
Combustible cigarettes

- 7000 chemicals in the smoke by lighting tobacco leaves on fire
- >70 known carcinogens
- Average smoker inhales 1-2 mg nicotine/cig
- 10 puffs over the 5 min cigarette is lit
- 1 pack (20 cigs) is 200 hits of nicotine (20-40 mg nicotine)
- Rush followed by feelings of withdrawal (positive feedback)
Terminology

E-Cigarettes & Vape Pens Components

- **Battery**: The battery is the energy source of the device and powers the atomizer.
- **Atomizer**: The atomizer is the heating element that heats the e-liquid and is often coil shaped.
- **E-Liquid**: Sometimes called e-juice, this is put into the device and often contains flavors and nicotine.
- **Cartridge**: The cartridge (tank) holds the e-liquid and may also hold the atomizer.
- **Aerosol**: Heating e-liquid inside the device creates an aerosol that is inhaled into the body and out into the air.

Anatomy of a Pod-Based System

- **Cartridges/Pods**: These cartridges/pods do contain NICOTINE!
- **Devices with Rechargeable Battery**: rechargeable “closed systems” with pod or cartridge refills
Humectants

Nicotine in E-Liquids

- 27 clinical studies
- Product, nicotine content (16-48mg/ml), puffing protocol, biomarkers
- E Cig Naïve users – ecigs deliver lower levels of nicotine c/w combustible tobacco
- Experienced e-cigarette users - ecigs can deliver nicotine in range of combustible cigarettes
Flavorings

- Banana: isoamyl acetate
- Cinnamon: cinnamaldehyde
- Almond or cherry: benzaldehyde
- Vanilla: vanillin
- Butter flavor: diacetyl

- Meant to be eaten not INHALED

Diacetyl
Vape clouds

Vaping topography

- Puff duration
- Interpuff interval
- # puffs in a vaping session
- Longer puff duration is associated with higher nicotine yield
- User experience (throat hit)
- 3rd generation products (pods) have more watts
T3 website (UK lifestyle)

• Vegetable glycerin is a thick, sticky, sweet liquid that produces maximum vapour at the expense of throat grip and flavour.
• higher VG to PG ratios are preferred by ardent cloud chasers
• PG liquid, on the other hand, provides a much better throat hit similar to that of a tobacco cigarette.
• VG50/PG50 mix is best for those who like an intense flavour as well as a throat hit,
• PG20/VG80 provides a much smoother inhale with bigger clouds and a mild flavour.
• Nicotine is the final ingredient (3-18 mg e-liquid)

EVALI

VAPI

Ecig or Vaping Associated Lung Injury
Vaping Associated Pulmonary Illness
Timeline

• April  IL and WI state health departments
• Aug 23  first death in IL.  200 cases in 22 states
• OR - first death due to a store bought product (marijuana oil)
• Oct 14  first teenage death  17 yr old in Bronx
• Oct 11 MMWR -  1299 VAPI and 26 deaths
• Oct 22 CDC  1604 EVALI cases, 34 deaths (2.1%)
EVALI

- Clinical: fever, cough, vomiting, diarrhea, HA, dizziness, chest pain following use of a vaping device
- Subacute: days to weeks before seeking healthcare
- Labs: nonspecific, elevated WBC, ESR, CRP
- CXR/CT scan: bilateral pulmonary infiltrates (alveolar)
- BAL: neutrophilia, no infection,
Clinical MMWR 10.11.19

• 95% resp sx (cough, sob, chest pain)
• 77% GI sx (abd pain, N/V/D)
• 85% constitutional sx (fever, chills, wt loss)
• Demographics
  • Median age 23 yrs
  • 80% < 35 yrs
  • 15% < 18 yrs
• DX of EXCLUSION
  • In IL and WI 72% had outpatient or ED visit before the hospitalization

Clinical (MMWR)

• Tachycardia in 55% (169/310)
• Tachypnea in 45% (77/172)
• Pulse oximetry O2sat <95% at rest on RA in 57% (m(143/253)
• Mean first recorded saturation of
  • Pts requiring intubation 87%
  • Pts not requiring intubation 92%
• 47% admitted to ICU (159/342)
• 22% were intubated (74/338)
Vaping history

- Among 865 pts with available data (MMWR 11/1/19)
- 86% used THC
- 64% nicotine containing products
- 52% both
VAPI : Differential Diagnosis

- Community acquired pneumonia
- Acute eosinophilic pneumonia
- ARDS /Lung Injury
- Hypersensitivity pneumonitis
- Organizing pneumonia
- Respiratory bronchiolitis-associated pneumonia
- Lipoid pneumonia
Table 1. Berlin Definition of the Acute Respiratory Distress Syndrome (ARDS).\textsuperscript{a}

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset within 7 days after a known clinical insult or new or worsening respiratory symptoms</td>
<td>Observational data suggest that ARDS will develop within 72 hr in the majority of patients at risk for the syndrome and within 1 wk in nearly all patients at risk</td>
</tr>
<tr>
<td>Bilateral opacities that are “consistent with pulmonary edema” on chest radiographs or chest CT</td>
<td>There is poor interobserver reliability in interpreting the chest radiograph for the presence of edema. To address this issue, the Berlin definition offers more explicit criteria (e.g., opacities should be fully explained by effusions, lobes or lung atelectasis, or nodules or masses), with illustrative radiographs provided</td>
</tr>
<tr>
<td>Categorization of ARDS severity</td>
<td>A patient-level meta-analysis validated three thresholds for hypoxemia, all consisting of a PaO\textsubscript{2}/FiO\textsubscript{2} ratio ≤300 mm Hg</td>
</tr>
<tr>
<td>Mild</td>
<td>PaO\textsubscript{2}/FiO\textsubscript{2} ≥301 to 300 mm Hg; mortality, 27% (95% CI, 24–30)</td>
</tr>
<tr>
<td>Moderate</td>
<td>PaO\textsubscript{2}/FiO\textsubscript{2} ≥201 to 200 mm Hg; mortality, 32% (95% CI, 29–34)</td>
</tr>
<tr>
<td>Severe</td>
<td>PaO\textsubscript{2}/FiO\textsubscript{2} ≤100 mm Hg; mortality, 45% (95% CI, 42–48)</td>
</tr>
<tr>
<td>Minimum PEEP setting or CPAP, 5 cm of water; PaO\textsubscript{2}/FiO\textsubscript{2} assessed on invasive mechanical ventilation (CPAP criterion used for the diagnosis of mild ARDS)</td>
<td>Estimates of FiO\textsubscript{2} are not accurate with oxygen-delivery systems other than invasive or noninvasive ventilation (with a tight-fitting mask), with the exception of nasal high-flow oxygen delivery systems (at flow rates ≥45 liters per minute); requiring higher PEEP settings does not increase predictive validity of the Berlin severity strata and adds complexity</td>
</tr>
</tbody>
</table>

\textsuperscript{a} The definition and the quotation about opacities are from Ferguson et al.\textsuperscript{1} CI denotes confidence interval, CPAP continuous positive airway pressure, PaO\textsubscript{2}/FiO\textsubscript{2} ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen, and PEEP positive end-expiratory pressure.
Treatment

- Natural progression is not known
- Treat patients for CAP initially
- 92% of 50 pts in IL and WI got steroids
- Some pts have relapsed during taper so followup 1-2 weeks after discharge is recommended
- Influenza will complicate the picture if infected simultaneously
Histopathology

- Mayo Clinic  NEJM (Oct 2 correspondence)
- 17 lung biopsies; h/o vaping (71% cannabis oils)
- 11/17 confirmed diagnosis of VAPI
- All cases with patterns of acute lung injury
  - Diffuse alveolar damage
  - Organizing pneumonia
  - Acute fibrinous pneumonitis
- No case had lipid laden macrophages (lipoid pna)
Histopathology

Lipoid Pneumonia

Classic is inhalation of mineral oil in a elderly patient
Cause of Acute lung injury
CHEST 2012 Legacy Good Sam: case report of a pt developing lipoid pneumonia from recurrent exposure to glycerin based oils in ecigs
5 patients North Carolina with BAL with lipid laden macrophages

FIGURE 2. Microscopy of a bronchoalveolar lavage sample (Papanicolaou stain [A] and oil red O stain [B])
Lung injury associated with vaping. — North Carolina, July–August 2019

*Papanicolaou stain demonstrating alveolar macrophages laden with vacuoles.
*Oil red O stain showing lipid deposits staining red (400x magnification).
CDC

• Clinical evaluation for patients with recent history of use of e-cigarette, or vaping, products and suspected lung injury
  • Ask about respiratory, gastrointestinal, and constitutional symptoms (e.g., cough, chest pain, shortness of breath, abdominal pain, nausea, vomiting, diarrhea, and fever) for patients who report a history of use of e-cigarette, or vaping, products.
  • Ask all patients about recent use of e-cigarette, or vaping, products.
    • Types of substances used (e.g., tetrahydrocannabinol [THC], cannabis [oil, dabs], nicotine, modified products or the addition of substances not intended by the manufacturer); product source, specific product brand and name; duration and frequency of use, time of last use; product delivery system, and method of use (aerosolization, dabbing, or dripping).

EVALI

• Type of e-device
• Specific type of liquid (nicotine, flavor, THC)
• Were devices, liquids, shared with others?
• Were old cartridges or pods reused with homemade or other online items?
• Were devices used to inhale drugs that were concentrated by heating prior to vaping? (called dabbing, dripping
• Details of vaping behavior (cloud volume, puff frequency, zero or stealth vaping)
Current hypothesis

• Aerosolization of flavoring compounds of e-cigarette liquids
• Adulteration of devices with THC
• Black market THC with oils, contaminants
• Lipid emulsion
• Vitamin E used to extract THC
• None of above are mutually exclusive

For Immediate Release: October 04, 2019
Statement From: Acting Commissioner of Food and Drugs - Food and Drug Administration
Norman E. "Ned" Sharpless MD
VAPING THC

• In Colorado, 78% increase in number of marijuana concentrates (inc vape products) sold from 2017 to 2018
• THC is suspended in a oil solution which also includes chemicals
• FDA does not regulate THC vaping products (regulatory vacuum)
• Products containing <0.3% THC do not fall under DEA
• Black market (Wisconsin brothers NYT 9/16/2019)
• 14% of US adults report marijuana use in previous year; 1/3 report vaping it
Cannabis

- Cannabis oil vs plant
- Can vaporize the flower bud
- Contaminated by solvent residuals (70%) such as isopentane and propane and pesticides (30%)
- Vitamin E acetate
DANK VAPES

Empty Dank Vapes packaging.

FIGURE 1: Frequency reported and counts of state-physician-collected (THC)- and nicotine-containing electronic cigarettes (vapes) (unregulated), vaping products (THC reported by patients with lung injury) - Illinois and Wisconsin, 2019.
Vaping Lung Injury

• CDC Warns People Not To Use Vaping Supplies Bought On The Street And To Stop Modifying E-Cigarettes

• The New York Times (8/30, Kaplan) reported that in response to “more than 200 cases of respiratory illnesses possibly related to vaping,” the CDC “warned people not to use vaping ingredients bought on the street and to stop modifying either nicotine or cannabis e-cigarette device in an effort to curb the vaping-related lung sicknesses that have alarmed health officials in more than two dozen states this summer.”
How did we get here?

A 17-year-old boy presented to the emergency department with pain and swelling in his jaw 2 hours after an e-cigarette exploded during use. The patient was in a hemodynamically stable condition and had no respiratory distress. He had a circular puncture to the chin, extensive lacerations in his mouth, multiple disrupted lower incisors, and bony incongruity of the left mandible. Reconstructed computed tomography of the head revealed a comminuted and displaced mandibular fracture with disruption of the left central and lateral incisors (Panel A). The patient underwent open reduction and internal fixation of the fracture, dental extraction, and debridement of devitalized tissue. The increasing prevalence of vaping among adolescents is a public health concern. At the 6-week follow-up assessment, the patient had recovered well, and the mandibular–maxillary fixation was removed (Panel B).
Global View

• EU no THC tighter regulations; restrict marketing to children, lower limit nicotine content; UK cannot target teens, cannot depict users who are <25
• UJ 3.6 million regular e-cigarette users
• India banned all e-cigarette products
• China Juul went live in September for 2 weeks then Alibaba took it off its online market
E-Cigarettes Went Unchecked in 10 Years of Federal Inaction

A decade after Congress gave the F.D.A. the power to regulate tobacco products like e-cigarettes, the federal government has repeatedly delayed or weakened efforts that could have protected teenagers.

2007  Earliest forms of ecigs arrive in US
2009  FDA declared ecigs illegal drug-device combination and halted imported Companies sued
2010  FDA lost suit
2010-  slowly developed regulations; market became flooded
          FDA struggled
2015  FDA sent proposed rule for oversight of all ecigs and tobacco products 468 pages to OMB; White House deleted flavor ban
2017  Gottlieb handed ecig industry a 4 yr extension to comply with new rules
2018  FDA investigated Juul
One girl on his dorm hall sold Juul pods from stock she had bought from a guy who ordered armloads on the internet. Unlike back home in high school, college students vaped in public everywhere — in lecture halls, at hockey games, in the dorm common rooms.

Juul

- Monsees and Bowen 2007
- Came to market it had 5% nicotine c/w 1-3% in competition
- In US-Juul now has 75% market share
- Now most vape pen cartridges have 5-7% nicotine
- Salt based nicotine (protonated form, less acidic, less harsh)
**Juul**

**JUULPOD BASICS**
Our disposable, snap-in pods make it easy to customize your experience while you find what works for you. No messy refill, just snap the pod into the top of your device and puff.

We offer a variety of JUULpod flavors, with some flavors available in both 5% and 1% nicotine strengths.

---

**JUUL**

**PROPYLENE GLYCOL AND GLYCERINE (30/60MIX)**
(LIF TO 95%)
Propylene glycol and glycerine are clear liquids that are used to create a visible vapor, and are commonly used by the medical, beauty and food industries. A majority, if not all e-liquids, contain propylene glycol (PG).

**NICOTINE**
Nicotine is a stimulant that comes from the tobacco plant. We use highly purified/USP grade/pharmaceutical grade nicotine.

**BENZOIC ACID**
Benzoic acid is a naturally occurring ingredient, found in tobacco and other substances. When combined with nicotine as part of our nicotine salts formulation, it helps provide cigarette-like satisfaction.

**FLAVOR**
JUUL flavors consist of both naturally occurring and artificial flavor ingredients which provide the specific taste profile for each flavor.
**JUUL pod**

**Strength of a Pack**

<table>
<thead>
<tr>
<th></th>
<th>Mint</th>
<th>Mango</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 pack cigarettes</td>
<td>15 cigarettes</td>
<td>15 cigarettes</td>
</tr>
<tr>
<td>5 pack pod</td>
<td>No button</td>
<td>No button</td>
</tr>
<tr>
<td>5 pack pod</td>
<td>No button</td>
<td>No button</td>
</tr>
<tr>
<td>5 pack pod</td>
<td>No button</td>
<td>No button</td>
</tr>
</tbody>
</table>

*NOTE: ALL SALT-BASED E-JUICE/FLUID CONTAINS NICKEL/NI*.

**JUUL website**

**OUR MISSION**

**IMPROVE THE LIVES OF THE WORLD'S ONE BILLION ADULT SMOKERS BY ELIMINATING CIGARETTES.**
JUUL social MEDIA

You tube

Why is the JUUL so popular? - YouTube
https://www.youtube.com/watch?v=veA2asx0Ek

Helpful Tips & Tricks for the JUUL - YouTube
https://www.youtube.com/watch?v=LHIN-nv0Q0Q

JUUL by PAX Review - YouTube
https://www.youtube.com/watch?v=9UKygpDnM1I

Juuling: What It is and How It Works - YouTube
https://www.youtube.com/watch?v=BYQM8R5Ys4s
Twitter #JUUL

JUUL is cool
Vaping websites

Best vape 2019: vape pens and e cigarettes for the discerning vapour

Is vaping bad for you? Well, it’s not as bad as smoking. So enjoy the biggest clouds of fruity or herb-flavoured vapour possible with the best vape pens

69

Altria 12.8 billion for 35%

New Altria Deal Makes Juul Cofounders Billionaires

Kathleen Chaykowski Forbes Staff

70
The industry

- Vuse owned by RJ Reynolds
- Markten owned by Altria (parent company of Phillip Morris)
- Blu owned by Imperial brands
- Juul by Altria

Big Smoke
While tobacco alternatives have huge potential, cigarettes are still the main driver of the industry

$713.7\text{ billion}$
Global cigarette market 2018

$40.7\text{ billion}$
Tobacco alternatives

Source: Euromonitor International
Note: Tobacco alternatives include smokeless tobacco, electronic cigarettes and devices that heat, rather than burn tobacco.
Teen Vaping

E-cigarettes are the most commonly used tobacco product among youth.

In 2018, more than 3.6 million U.S. middle and high school students used e-cigarettes in the past 30 days, including:

- 4.9% Middle School Students
- 20.8% High School Students

Teen vaping


TO THE EDITOR: A rapid increase in the prevalence of nicotine use with any nicotine product, for all age groups, adolescents has emerged among users and nonusers alike, use the adolescent and teen health community by surprise. In 2011, less than 2% of U.S. high school students reported having used e-cigarettes in the previous month. By 2015, a popular pod mod brand, high, the percentage had jumped to 30%. Many anecdotal reports from times in which stronger nicotine concentrations can cause adverse user experiences. Pod and stick pod systems use pressurized nicotine formulations derived from the nicotine salts in loose-leaf tobacco. According to their advertisements, nicotine salt solutions contain nic-
Adolescent Vaping stats

Prevalence Of Nicotine Vaping

<table>
<thead>
<tr>
<th>Grade</th>
<th>2018</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>12th</td>
<td>20.9%</td>
<td>11%</td>
</tr>
<tr>
<td>10th</td>
<td>16.1%</td>
<td>8.2%</td>
</tr>
<tr>
<td>8th</td>
<td>6.1%</td>
<td>3.5%</td>
</tr>
</tbody>
</table>

CDC 2019 data

More high school students vape than smoke cigarettes

The rate of high school students using e-cigarettes eclipsed the rate of those smoking cigarettes in 2014, according to the CDC's National Youth Tobacco Survey.
Our mission

• "I will not allow a generation of children to become addicted to nicotine through e-cigarettes," Scott Gottlieb, commissioner of the Food and Drug Administration, said in a statement.

ATS Advocacy

• ATS involvement in the larger cigarette/tobacco issue has been extensive and is ongoing. During both the Obama and Trump administrations, the ATS called upon the FDA to strictly regulate all tobacco products, including e-cigarettes, in the following ways:
  • Ban the use of menthol as a characterizing flavor agent in all tobacco products
  • Ban the use of sweet, fruity and other child-luring flavors in all tobacco products
  • Require disclosure of all ingredients in e-cigarette products
  • Require the testing of flavoring agents with known or suspected respiratory toxicity
  • Require graphic warning labels on all tobacco products including e-cigarettes
  • Urge stricter regulation of online sales of e-cigarette products
  • Ban advertising and other marketing techniques intended to appeal to youth
TAKE HOME POINTS

• EVALI nonspecific resp/gi/const symptoms
• Ask detailed questions about vaping history
• Dx of exclusion
• Influenza season challenges (can have 2 diseases)
• Remember that a O2 sat of 95% is a PaO2 of 80
• Talk to patients about the dangers of vaping