Electronic Cigarette: The Knowns, Known Unknowns, and Unknown Unknowns

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A 7th person has died from vaping-related causes. The CDC is stepping up its probe of e-cigarette illnesses

(CNN) A California man has become the seventh person to die from a vaping-related illness in the United States as the nation's leading health...

Lung Damage From Vaping Resembles Chemical Burns, Report Says

The New York Times

The lung damage in some people who have become ill after vaping nicotine or marijuana products resembles a chemical burn, doctors from...

The recent vaping deaths are bad. The long term toll will be ...

Los Angeles Times

The Centers for Disease Control and Prevention has linked vaping to 1,479 cases of ... At least 33 people have died since the outbreak began.

4 days ago
The CDC and state agencies have reported 1,604 lung injury cases and 34 deaths linked to vaping.
What are E-cigs?

- Battery-powered nicotine delivery systems
- Unlike tobacco cigarette, e-cig emissions are generated by the vaporization of e-liquid

**E-liquid Main Ingredients:**
Propylene Glycol (PG)
Vegetable Glycerin (VG)
Nicotine
Flavorings
What comes out of E-cigs?

- **UFP**
  - Ultrafine particulates
  - 0.1 μm (microns) in diameter or 100 nanometers and less

- **PM2.5**
  - Combustion particles, organic compounds, metals, etc.
  - < 2.5 μm (microns) in diameter

- **PM10**
  - Dust, pollen, mold, etc.
  - < 10 μm (microns) in diameter

- **Human Hair**
  - 50-70 μm (microns) in diameter

- **Fine Beach Sand**
  - 90 μm (microns) in diameter
From E-cig emissions, to secondhand exposures, to potential health effects

Mainstream Emission
- E-cigarette Device
  - E-cigarette Type
  - Power Voltage
  - Heating Coil Temperature
- E-liquid
  - Propylene Glycol
  - Vegetable Glycerin
  - Nicotine
  - Flavorings

Exhaled Aerosol
- Puffing Topography
  - Puff Duration
  - Flow Rate
  - Inter-puff Interval
- Inhalation and Exhalation
  - Lung Environment (e.g., Humidity and Temperature)
  - Physiological Factor

Indoor Air Quality
- Aerosol Dynamics
  - Evaporation
  - Coagulation
  - Deposition
  - Gravitational Settling
- Room Environment
  - Dilution
  - Air Exchange Rate
  - Relative Humidity
  - Temperature

Health Effects
- Short-term Exposure
  - Respiratory
  - Cardiovascular
- Long-term Exposure

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E-cig Devices
E-cig Devices

• Peak temperature of heating coil ranged from 160 °C to 240 °C.

• Heating coil temperature increases with a longer puff duration and lower puff flow rate.
E-liquids

<table>
<thead>
<tr>
<th>Nicotine</th>
<th>No Nicotine</th>
<th>High</th>
<th>Super High</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 mg</td>
<td>16 mg</td>
<td>36 mg</td>
</tr>
</tbody>
</table>

Flavorings

- **PG** (Propylene Glycol) vs. **VG** (Vegetable Glycerine)

- **FLAVOR**
- **VAPOR**
- **THROAT HIT**
- **DEHYDRATION**
- **VISCOSITY**

For equal nicotine ratio, perceived throat hit, and difficulty of wicking.
E-liquids

- Particle loss rate varies at different PG/VG ratios and nicotine levels

- E-cig aerosol particles are more volatile than nonvolatile di-ethyl-hexyl sebacate (DEHS)

Li et al. 2019. submitted to Aerosol Science and Technology
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Effects of puff duration on the mainstream e-cig particles

Effects of puff flow rate on the mainstream e-cig particles

**Graph a.**
- Equation: $y = 7.68e8x + 1.77e8$
- $R^2 = 0.94$

**Graph b.**
- 15 nm (2 L/min)
- 17 nm (1.5 L/min)
- 20 nm (1 L/min)
- 27 nm (0.5 L/min)

Effects of the Lungs - Humidity & Temperature

- E-cig particles tend to grow in human lungs under high humidity due to the hygroscopic effect (Pichelstorfer et al. 2016; Sosnowski et al. 2016)

- Increasing temperature or decreasing relative humidity may enhance evaporation and reduce particle size (Wright et al. 2016, Schripp et al. 2013)

- Other physiological factors in the respiratory system might also affect e-cig aerosol dynamics

Schripp et al. 2013. Indoor Air 23: 25-31
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**PM$_{2.5}$ at 0.8 and 1.5 m away from e-cig users**

- **Background:** 8 µg/m$^3$
- **Mean peak PM$_{2.5}$ during puffing:** 1900 µg/m$^3$
- **Mean PM$_{2.5}$ during puffing at 1.5 m away:** 206 µg/m$^3$
- **1.5 m away:** Mean PM$_{2.5}$ during puffing: 13 µg/m$^3$

Effects of distances to e-cig users

E-cig particles transport from a vaping room to a nearby non-vaping room

Zhang et al. 2019. submitted to Indoor Air
What’s going on in Vape Shops
Vape Shop - PM$_{2.5}$

![Box plot showing PM$_{2.5}$ mass concentration for different ventilation settings and day types.]

- **Smoking Bar** (Waring & Siegel, 2006)
- **Hookah Lounge** (Zhou et al., 2015)
- **NAAQS**

Nguyen et al. 2019. Atmospheric Environment 211: 159-69
Vape Shop – Effects of Proximity from Vaping

- Personal space (0.45 to <1.2 m)
- Social space (1.2 to <3.6 m)
- Public space (≥ 3.6 m)

Nguyen et al. 2019. Atmospheric Environment 211: 159-69
E-cigs vs. T-cigs – Impacts on Indoor Air Quality

E-cigs vs. T-cigs – Chemical Composition

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?
In Vitro Studies (Cell Studies)

- Cytotoxicity (Farsalinos et al. 2013, Romagna et al. 2013)
- Inflammatory response, oxidative stress, cytokine release (Rubenstein et al. 2015)
- Decreased cell viability (Cervellati et al. 2014, Scheffler et al. 2015)
- Dose-dependent epithelial-cell death, reduced antimicrobial activity of macrophages (Hwang et al. 2016)
- Loss of endothelial barrier function (Schweitzer et al. 2015)

In Vivo Studies (Animal Studies)

- Impair lung functions in animals, with inflammation and immune abnormalities as the likely underlying mechanisms (Dinakar and O’Connor. 2016)
- Perturb the cardiovascular system (Olfert et al. 2018, Qasim et al. 2018)
- Respiratory and cardiovascular effects (Crotty Alexander et al. 2018, Nguyen et al. 2018)
- Carcinogenicity and neurological toxicity (Lee et al. 2018, Nguyen et al. 2018)
**In Vitro Case Study - Cytotoxicity**

### A. MTS

![Graph A: MTS Cell Viability](image)

- **20 puffs (10 min)**
- **120 puffs (1 h)**
- **960 puffs (8 h)**

### B. ATP

![Graph B: ATP Cell Viability](image)

- **20 puffs (10 min)**
- **120 puffs (1 h)**
- **960 puffs (8 h)**

### C. GSH

![Graph C: GSH Level](image)

- **20 puffs (10 min)**
- **120 puffs (1 h)**
- **960 puffs (8 h)**

### D. Color Representation

- **MTS**: % Cell Viability
- **ATP**: % Cell Viability
- **GSH**: % GSH Level

*Note: The color scale indicates the percentage of nicotine and the number of puffs.*

![Color Scale](image)
In Vivo Case Study

- E-cig aerosols can activate inflammatory pathway and induce stress responses in the lungs of animals [A]
- Results showed clear dose-dependent acute pulmonary effects in mice with high puff e-cig aerosols inducing more IL-1β production [B] and neutrophil infiltration [C]
Effects on Human Health

- **Respiratory Effects**
  - Increase airway resistance (Vardavas et al. 2012, Tzortzi et al. 2018)
  - Alter respiratory proteomic profiles among e-cig users indicative of impending airway obstruction (Dang et al. 2018)
  - Inconsistent results on lung function measures (Ferrari et al. 2015, Flouris et al. 2013, Vardavas et al. 2012)

- **Cardiovascular Effects**
  - Cardiac-autonomic imbalance (i.e., heart rate variability) (Moheimani et al. 2017)
Summary

- **The Knowns**
  - E-cig device, e-liquid parameters, and puffing topography substantially affect the e-cig aerosol emissions
  - E-cigs degrade indoor air quality
    - Indoor particle levels from e-cigs are similar to t-cigs
    - Because e-cig particles are highly dynamic, they decay rapidly over distances (>1.5 m) from vaping at relatively ventilated condition; However, exhaled e-cig particles persisted in the high-vaping density, low-ventilation environment (i.e., vape shops)
  - E-cigs produce substantial amounts of PG, VG, and nicotine, as well as some toxic compounds such as formaldehyde and heavy metals
  - Respiratory and cardiovascular effects have been reported in animal and cell studies
Summary

- **Known Unknowns**
  - The only commonality among all lung injury and death cases is that patients report the use of vaping products - the causes are largely unknown
  - Contributing factors to the results observed *in vitro* and *in vivo* are unclear
  - Current human studies focus on short-term acute effects but results sometimes are inconsistent
  - Dosimetry of e-cig aerosols is poorly understood
  - Limited studies on long-term human health effects

- **Unknown Unknowns**
  - We don’t know what the next generation of e-cig would look like
  - We don’t know what people will DIY to vape with in the future
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References


• Kim SY, Sim S, Choi HG. 2017. Active, passive, and electronic cigarette smoking is associated with asthma in adolescents. Scientific Reports 7: 1-8


