Electronic Cigarettes: Miracle or Menace

PEHSU Grand Rounds
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At the end of the presentation, the participant will be able to:

• Understand the biological role of nicotine in the brain and intent of the electronic cigarette
• Discuss the dangers of electronic cigarettes regarding unintentional exposures in toddlers and adolescent intentional use
• Describe the exposures of second-hand inhalation of vapors from electronic cigarettes
• Understand state and federal regulations as it pertains to prevention of exposures to minors and environmental contamination
Case Presentation

- 10 month old with vomiting, tachycardia, grunting respirations and truncal ataxia after ingesting “small” amount of e-liquid nicotine
- Vape shop states it contained 1.8% nicotine (18 mg per milliliter) and unknown concentrations of wintergreen (methyl salicylate), glycerin and propylene glycol

NEJM 2014, DOI: 10.1056/NEJMct1403843
OTC liquid nicotine products

NEJM 2014, DOI: 10.1056/NEJMc1403843
Electronic Cigarettes

- Introduced as alternative to smoking
- Considered part of tobacco harm reduction strategy
  - Psycho-behavioral (motor and sensory stimulation)
  - Chemical aspects of addiction
- Recent concerns by World Health Organization and Food and Drug Administration
How an electronic cigarette works

The electronic cigarette contains a battery that activates a heating device, atomizing liquid nicotine inside a cartridge and producing a vapor that is inhaled.

Liquid nicotine cartridge  Inhaler  Atomizer/heating device  Lithium battery  Tip lights up

Source: allhookah.net

Tim Summers / The Detroit News
Nicotine

Benowitz et al. Handb Ex Pharmacol. 2009; 192: 29-60
Nicotine absorption – electronic cigarette

Konstantinos et al. Scientific Reports 2014; 4: 4133
Nicotine absorption – other products

Benowitz et al.  Handb Ex Pharmacol. 2009; 192: 29-60
Nicotine distribution

Nicotine metabolism

Benowitz et al. Handb Ex Pharmacol. 2009; 192: 29-60
Nicotine pharmacodynamics

- Blood: Increased clotting tendency
- Lungs: Bronchospasm
- Muscular: Tremor, Pain
- Gastro-intestinal: Nausea, Dry mouth, Dyspepsia, Diarrhea, Heartburn
- Joints: Pain
- Heart: Increased or decreased heart rate, Increased blood pressure, Tachycardia, More (or less) arrhythmias, Coronary artery constriction
- Endocrine: Hyperinsulinemia, Insulin resistance
Nicotine Toxicity

- Low dose – stimulant effects (e.g., tachycardia)
- CNS toxicity – ataxia, seizures
- Increasing dose – muscarinic toxicity of extreme secretions and GI disturbance
- High dose – neuromuscular blockade, respiratory failure, and death.
- Lethal dose – 1-13 mg/kg of body weight (1 teaspoon (5 ml) of 1.8% could be lethal in 90 kg person.)
Nicotine Exposure

• Liquid nicotine products often express the concentration (mg/mL) as “mg”
• Products marked “0 mg/mL” nicotine may contain significant amounts of nicotine, up to 10 mg per cartridge
• Nicotine toxicity is strongly influenced by history of nicotine use/tolerance
<table>
<thead>
<tr>
<th>Sample ID</th>
<th>Brand*</th>
<th>Expected concentration level</th>
<th>Replicate analyses</th>
<th>Mean (±S.D.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Vapour liquid (high)</td>
<td>24 mg/ml (marked)</td>
<td>19.8</td>
<td>19.1 (±2.52)</td>
</tr>
<tr>
<td>B</td>
<td>No brand, hand-labelled liquid (high)</td>
<td>25–36 mg/ml (est.)</td>
<td>12.4</td>
<td>12.3 (±0.17)</td>
</tr>
<tr>
<td>C</td>
<td>Smart smoke liquid (high)</td>
<td>25–36 mg/ml (est.)</td>
<td>13.2</td>
<td>13.1 (±0.40)</td>
</tr>
<tr>
<td>D</td>
<td>Smart smoke liquid (medi)</td>
<td>10–18 mg/ml (est.)</td>
<td>12.7</td>
<td>11.9 (±0.75)</td>
</tr>
<tr>
<td>E</td>
<td>Smart smoke liquid (low)</td>
<td>6–14 mg/ml (est.)</td>
<td>8.3</td>
<td>8.5 (±0.16)</td>
</tr>
<tr>
<td>F</td>
<td>BE112 prefilled cartridge (super high)</td>
<td>25–36 mg/ml (est.)</td>
<td>19.8</td>
<td>19.9 (±0.46)</td>
</tr>
<tr>
<td>G</td>
<td>Vapour prefilled cartridge (high)</td>
<td>24 mg/ml (marked)</td>
<td>22.4</td>
<td>22.2 (±0.62)</td>
</tr>
</tbody>
</table>

Precision and accuracy of the LC-MS analyses for the quality control test solutions were as follows: Low: target concentration=20 ng/ml, measured nicotine mean (SD)=18.5 (±0.95); Medium: target concentration=300 ng/ml, measured nicotine mean=301.4 (±6.05); High: target concentration=1300 ng/ml, measured nicotine mean=1314 (±42.5).

*Nicotine solutions were obtained from local vendors in Spokane, Washington, USA. All labelled brands (Vapour, Smart Smoke, BE112) were also found available for purchase on the internet. Information on country of manufacture was only found for Vapour (USA).
### Adult Toxicity

#### Nicotine Concentration (mg/mL) in Common Products

<table>
<thead>
<tr>
<th>Exposure Quantity (mL)</th>
<th>0 mg/mL*</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>0</td>
<td>3</td>
<td>6</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>6</td>
<td>12</td>
<td>18</td>
<td>24</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>12</td>
<td>24</td>
<td>36</td>
<td>48</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>30</td>
<td>60</td>
<td>90</td>
<td>120</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>60</td>
<td>120</td>
<td>180</td>
<td>240</td>
</tr>
<tr>
<td>20</td>
<td>0</td>
<td>120</td>
<td>240</td>
<td>360</td>
<td>480</td>
</tr>
<tr>
<td>30</td>
<td>0</td>
<td>180</td>
<td>360</td>
<td>540</td>
<td>720</td>
</tr>
<tr>
<td>50</td>
<td>0</td>
<td>300</td>
<td>600</td>
<td>900</td>
<td>1200</td>
</tr>
<tr>
<td>100</td>
<td>0</td>
<td>600</td>
<td>1200</td>
<td>1800</td>
<td>2400</td>
</tr>
</tbody>
</table>

**For an adult**

- Unlikely to cause symptoms
- Low exposure: GI symptoms possible
- Potentially lethal exposure
- Multiple times potentially lethal dose

*Label may not accurately reflect nicotine quantity*

Prepared by: Rebecca Smith, B.S., PharmD, Connecticut Poison Control Center
## Child Toxicity

<table>
<thead>
<tr>
<th>Exposure Quantity (mL)</th>
<th>0 mg/mL*</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>0</td>
<td>0.6</td>
<td>1.2</td>
<td>1.8</td>
<td>2.4</td>
</tr>
<tr>
<td>0.25</td>
<td>0</td>
<td>1.5</td>
<td>3</td>
<td>4.5</td>
<td>6</td>
</tr>
<tr>
<td>0.4</td>
<td>0</td>
<td>2.4</td>
<td>4.8</td>
<td>7.2</td>
<td>9.6</td>
</tr>
<tr>
<td>0.5</td>
<td>0</td>
<td>3</td>
<td>6</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>6</td>
<td>12</td>
<td>18</td>
<td>24</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>12</td>
<td>24</td>
<td>36</td>
<td>48</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>30</td>
<td>60</td>
<td>90</td>
<td>120</td>
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<tr>
<td>10</td>
<td>0</td>
<td>60</td>
<td>120</td>
<td>180</td>
<td>240</td>
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<td>20</td>
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<td>360</td>
<td>480</td>
</tr>
</tbody>
</table>

Unlikely to cause symptoms
Low exposure: GI symptoms possible
Potentially lethal exposure
Multiple times potentially lethal dose

*Label may not accurately reflect nicotine quantity

For a 10 kg child
Are electronic cigarettes successful for smoking cessation?
Electronic Cigarettes

- Originally marketed as a tobacco reduction or smoking cessation product, recreational use of e-cigarettes in adolescents and adults has doubled from 2010 to 2012.
- Current use in Great Britain rose from 2.7% of adult smokers studied in 2010 to 6.7% in 2012.
- Alternatively, adolescent data reveals that 9.3% of ever cigarette users had reported never smoking conventional cigarettes.
Number of calls to poison centers for cigarette or e-cigarette exposures, by month — United States, September 2010–February 2014

MMWR 04/04/2014
Survey with 1 year follow-up

<table>
<thead>
<tr>
<th>Follow-up e-cigarette use</th>
<th>Baseline</th>
<th>Follow-up</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>13.3 (8.9)</td>
<td>13.5 (8.9)</td>
<td>0.2 (4.7)</td>
</tr>
<tr>
<td>Primary analysis, use initiated after baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-daily</td>
<td>13.5 (7.9)</td>
<td>13.9 (8.9)</td>
<td>0.4 (5.9)</td>
</tr>
<tr>
<td>Daily</td>
<td>14.3 (9.8)</td>
<td>13.0 (9.4)</td>
<td>−1.4 (6.8)</td>
</tr>
<tr>
<td>Secondary analysis, some use at baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-daily</td>
<td>14.9 (8.9)</td>
<td>15.0 (8.0)</td>
<td>0.09 (5.4)</td>
</tr>
<tr>
<td>Daily</td>
<td>14.1 (7.9)</td>
<td>11.5 (7.2)</td>
<td>−2.5 (6.1)</td>
</tr>
</tbody>
</table>

SD = standard deviation.

Brose et al. Addiction early online 23 April 2015
Adolescent Use

Figure. Electronic Cigarette Use and Conventional Cigarette Smoking in 2011 and 2012

Dutra et al. JAMA Pediatrics. 2014; 168: 610-617
Adolescent Use

FIGURE. Ever electronic cigarette use* among middle and high school students, by year — National Youth Tobacco Survey, United States, 2011–2012

* Ever electronic cigarette use defined as having ever used electronic cigarettes, even just one time.
† 95% confidence interval.
§ Statistically significant difference between 2011 and 2012 (chi-square, p<0.05).

MMWR. 2013; 35. September 6, 2013
Adolescent Use

IMAGES OF BRAIN DEVELOPMENT IN HEALTHY CHILDREN AND TEENS (AGES 5–20)

AGES

SIDE VIEW

TOP VIEW

Blue represents maturing of brain areas.


Prefrontal Cortex
Measured airborne markers of secondhand exposures (nicotine, PM2.5, CO, and VOCs)
Secondhand exposure to nicotine but not to combustion toxicants.
Nicotine exposure 10X in regular cigarettes compared to electronic cigarettes.

Czogala et al. Nic and Tob Res. 2013
Secondhand smoke

- Education on dangers from secondhand tobacco smoke have been largely successful in resulting in smoke-free homes and/or cars.
- Perception of “safer” smoking may result in increased use of e-cigs indoors.
- Increased exposure to nicotine, propylene glycol, glycerin and other toxicants.
- Studies on third-hand smoke from e-cigs deposits of nicotine on indoor surfaces and absorbed by adult non-users.

Goniewicz et al. Nicotine Tob Res. 2015; 17: 256-268
Legislation and FDA

- (April 2014) Proposed rule for comments on whether to regulate e-cigs and additional tobacco products including cigars, pipe tobacco, certain dissolvables that are not “smokeless”, gels and water pipe tobacco.
- Proposed rules would ban sales to minors, require health warnings, require registration with FDA, and allows health claims if scientific evidence supports claim.
The FDA Center for Tobacco Products will hold the third, and final, public workshop to obtain information on electronic cigarettes and the public health on June 1-2, 2015. Even if you cannot attend the public workshop, you are invited to submit comments, supported by research and data, regarding electronic cigarettes and the public health. FDA is accepting public comments on e-cigarettes and the public health through July 2, 2015.
Sales to Minors

FIGURE 1. States with and without laws prohibiting sales of electronic nicotine delivery systems (ENDS) to minors* — United States, November 30, 2014

* Minors are defined by statute as persons aged <18 years, except in four states where they are defined as persons aged <19 years (Alabama, Alaska, New Jersey, and Utah).

MMWR. 63: December 12, 2014
Indoor Smoking

FIGURE 2. States with and without laws prohibiting smoking and use of electronic nicotine delivery systems (ENDS) in indoor areas of private worksites, restaurants, and bars — United States, November 30, 2014

- Prohibits indoor smoking, and indoor ENDS use (n = 3)
- Prohibits indoor smoking only (n = 24)
- No comprehensive* smoke-free air law or prohibition on indoor ENDS use (n = 24)

* CDC defines a state smoke-free air law as comprehensive if it prohibits smoking in indoor areas of private worksites, restaurants, and bars.

MMWR. 63: December 12, 2014
Summary

• Electronic cigarettes are intended to promote cessation of conventional tobacco use, but has not been shown to be effective.

• Nicotine is highly toxic and may cause significant toxicity in young children due to overdoses and detrimental effects on adolescents.

• Environmental exposures from second- and third-hand smoke can occur, but is less than conventional smoking.

• Regulatory and public health policies are needed.
Questions?