Electronic Cigarettes

Jon O. Ebbert, M.D.
Professor of Medicine
Mayo Clinic
Email: ebbert.jon@mayo.edu
Ecigarette ad
Goals & Objectives

• Understand the mechanics of Ecigarettes

• Summarize the data regarding Ecigarette nicotine delivery

• Define the known health risks of Ecigarettes

• Identify how cigarette smokers use Ecigarettes

• Cite evidence regarding the efficacy of Ecigarettes for smoking cessation
The Major Ingredient in E-Cigarettes is:

1. Isopropyl alcohol
2. Propylene glycol
3. Nicotine
4. Glycerol
Which of the following is False:

1. Smokers generally like Ecigarettes
2. Ecigarettes help smokers reduce smoking
3. Ecigarettes help people quit smoking
4. Ecigarettes have potential health risks
Electronic cigarettes

- Patented & launched in 2003 by Ruyan (Beijing, China)
  - Ruyan translation = “to resemble smoking”
  - Designed by Chinese pharmacist Hon Lik
  - Earliest known description in 1963
    - Patent by Herbert A. Gilbert
- Battery-powered device that provides inhaled doses of vaporized nicotine solution
  - Heat
  - Ultrasonics
“Vaping”
Ecigarettes: In the Beginning…
“Mods” = Design Modifications
Ecigarettes
Basic Structure

- **Atomizer** (or "atty")
- **Microprocessor** controls heater and light
- **Sensor** detects when smoker takes a drag
- **Heater** vaporises liquid and nicotine
- **Cartridge** holds nicotine dissolved in propylene glycol
- **LED Lights** up when the smoker draws on the cigarette
- **Battery**
- **Steam aspiration**
Cartomizer Anatomy

- Batting Material
- Juice
- Heater Coil
- Air Tube
- Battery Connector
Cartomizer Sizes
Disposable: ~$7
Ecigarettes – Liquid Solution Composition

<table>
<thead>
<tr>
<th>Substance</th>
<th>Recipe 1</th>
<th>Recipe 2</th>
<th>Recipe 3</th>
<th>Recipe 4</th>
<th>Recipe 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propylene glycol</td>
<td>85%</td>
<td>80%</td>
<td>90%</td>
<td>80%</td>
<td>&lt;65%</td>
</tr>
<tr>
<td>Nicotine</td>
<td>6%</td>
<td>4%</td>
<td>2%</td>
<td>0.1%</td>
<td>&lt;3%</td>
</tr>
<tr>
<td>Glycerol</td>
<td>2%</td>
<td>5%</td>
<td>-</td>
<td>5%</td>
<td>&lt;20%</td>
</tr>
<tr>
<td>Tobacco essence</td>
<td>-</td>
<td>4%</td>
<td>4.5%</td>
<td>1%</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Essence</td>
<td>2%</td>
<td>-</td>
<td>1%</td>
<td>1%</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Organic acid</td>
<td>1%</td>
<td>-</td>
<td>-</td>
<td>2%</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

*Propylene glycol*: pharmaceutical solvent, food additive, moisturizer (cosmetics & toothpaste), hand sanitizer, non-toxic antifreeze, deodorants, aircraft de-icer, asthma inhalers & nebulizers.
Propylene glycol

Vegetable glycerin
“E-Juice”: Pre-Mixed or Mix Your Own

<table>
<thead>
<tr>
<th>Flavour Descriptions:</th>
<th>Aromatic</th>
<th>Carmel</th>
<th>Cherry Cheroot</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A relaxing pipe-style vape, with no niar required.</td>
<td>Our take on Camel, with a light turkish twist.</td>
<td>A flavoursome combination of sweet cherries and smokey Tobacco.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cuban Cigar</th>
<th>Gallois</th>
<th>Hylton</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rich and mellow with notes of leather, sandalwood and shadegrown leaf.</td>
<td>A french style blend of Turkish and oriental flavours.</td>
<td>Sweeter than the Real Tabs, with a touch of Caramel.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Flavour Descriptions:</th>
<th>Amaretto</th>
<th>Angelica</th>
<th>Apple</th>
<th>Apricot</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>An Italian liqueur which is normally strong, with a subtle flavour of almonds, with which you may get along. Amaretto is usually associated with the taste of almond paste (marzipan). <strong>Recommended concentration:</strong> 20-25% (4 to 5 drops per ml).</td>
<td>As in the sweet succulent leaves of old, you will find this flavour sweet and bold. Angelica is a candied peel, often seen on cake decorations. <strong>Recommended concentration:</strong> 10% (2 drops per ml)</td>
<td>Sweet and tangy as in the skin, savour the flavour of the apple within. <strong>Recommended concentration:</strong> 10% (2 drops per ml)</td>
<td>Sweeter than plum yet not like a peach, the rich golden flesh is a wonderful treat. <strong>Recommended concentration:</strong> 10% (2 drops per ml)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Flavour Descriptions:</th>
<th>Banana</th>
<th>Beer</th>
<th>Betel Nut</th>
<th>Black Tea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>If you want you can act the ape, but really this banana is a jolly good vape. <strong>Recommended concentration:</strong> 10% (2 drops per ml)</td>
<td>Hops and yeast you'll want cheer, pull up a seat and have a beer. <strong>Recommended concentration:</strong> 10% (2 drops per ml)</td>
<td>Pacific palms provide the fruit, a sweet syrup taste for you might suit. Betel Nut is not the nut from the palm trees grown in the South Pacific, with the taste of Palm Dates. <strong>Recommended concentration:</strong> 10% (2 drops per ml)</td>
<td>If you enjoy the flavour of tea, then this is the one it has to be, fragrant and perfumed with the tang of the leaf. I'm sure it's winner, a great spirit. <strong>Recommended concentration:</strong> 10% (2 drops per ml)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Flavour Descriptions:</th>
<th>Black Walnut</th>
<th>Blackcurrant</th>
<th>Blueberry</th>
<th>Brandy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dry and smoky with</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Ecigarettes & Nicotine Delivery
Comparing Ecigarettes to Conventional Cigarettes

Photo courtesy of P. Talbot

Trtchounian A. Nicotine Tob Res. 2010 Sep;12(9):905-12.
“Vacuum”: Conventional vs. Ecigarettes

Trtchounian A. Nicotine Tob Res. 2010 Sep;12(9):905-12.
Changes in Vacuum During Ecig “Smoke Out”

Trtchounian A. Nicotine Tob Res. 2010 Sep;12(9):905-12.
Ecig Properties

- E-cigarettes required stronger suction to smoke than conventional brands.
- Amount of aerosol produced by e-cigarettes decreased during smoking:
  - Necessitated increasing puff strength to produce aerosol.
- “Decreased efficiency of aerosol production during e-cigarette smoking makes dosing nonuniform over time and calls into question their usefulness as nicotine delivery devices.”

Trtchounian A. Nicotine Tob Res. 2010 Sep;12(9):905-12.
Do Ecigarettes Alleviate Craving?

- Smokers
- Aged 18 and 70 years
- Smoked ≥ 10 cigarettes
- Overnight abstinence

- 16 mg ENDD less desire to smoke than placebo
- No difference in desire to smoke between 16 mg ENDD & inhaler
- ENDDs more pleasant than inhaler

**Figure 2** Change in desire to smoke from baseline over the first hour after each product use.

*Bullen C et al. Tob Control 2010 19: 98-103.*
Pharmacokinetics of Cigarette, Ecigs, and Inhaler

<table>
<thead>
<tr>
<th>Product</th>
<th>Mean $t_{\text{max}}$ (min) (95% CI)</th>
<th>Mean $C_{\text{max}}$ (ng/mL) (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual cigarette (n=9)</td>
<td>14.3 (8.8 to 19.9)</td>
<td>13.4 (6.5 to 20.3)</td>
</tr>
<tr>
<td>16 mg ENDD (n=8)</td>
<td>19.6 (4.9 to 34.2)</td>
<td>1.3 (0.0 to 2.6)</td>
</tr>
<tr>
<td>Nicorette inhalator (n=10)</td>
<td>32.0 (18.7 to 45.3)</td>
<td>2.1 (1.0 to 3.1)</td>
</tr>
</tbody>
</table>

ENDD, electronic nicotine delivery device.
*Corrected for baseline nicotine levels.

Health Effects of Ecigarettes
In 2009, FDA's Center for Drug Evaluation, Division of Pharmaceutical Analysis (DPA) analyzed:

- 2 samples of electronic cigarettes & components from two leading brands
  - 18 of the flavored, nicotine, and no-nicotine cartridges
- Nicotine inhaler (control)
DPA's analysis
- Diethylene glycol in one cartridge @ 1%
  - Ingredient used in antifreeze & toxic to humans
- Tobacco-specific nitrosamines (TSNA’s) in half of samples
  - Human carcinogen
- Tobacco-specific impurities detected in a majority of the samples tested
- May be harmful to humans
  - Anabasine
  - Myosmine
  - β-nicotyrine
Ecigarettes & Cytotoxicity

• Embryonic and adult cells & refill fluids
  • Cytotoxicity varied among fluids and was correlated with the number and concentration of chemicals used to flavor fluids
  • Cytotoxicity was not due to nicotine

Peering through the mist: What does the chemistry of contaminants in electronic cigarettes tell us about health risks?

Igor Burstyn, PhD

Department of Environmental and Occupational Health
School of Public Health
Drexel University
1505 Race St., Mail Stop #1034
Philadelphia, PA 19102
USA
Tel: 215.762.2909  Fax: 215.762.8846
igor.burstyn@drexel.edu

http://publichealth.drexel.edu/~media/Files/publichealth/ms08.pdf
Burstyn, Technical Report

• Review of recent Ecigarettes peer reviewed and “grey” literature and made predictions about compliance with occupational exposure limits

• Conclusions
  • Individual and combined exposures to contaminants in Ecigarettes fall below thresholds for concern for compounds with known toxicity, including volatile organic chemicals (VOCs), tobacco specific nitrosamines (TSNA), polycyclic aromatic hydrocarbons (PAHs), metals.
  • Ongoing monitoring health effects related to propylene glycol and glycerin. Magnitude of the exposure is novel and at levels for concern given the lack of data on inhalation of these chemicals at levels found in EC aerosol.

• Does not consider inhalation of flavoring chemicals.
Ecigs: Health Effects

• 30 healthy smokers (Athens, Greece)
  • Minimum of 5 pack-years
  • Aged 19-56 years
  • 14 male

• Ecigarettes for 5 minutes

• Ecigarettes associated with a significant increase in airway resistance

Ecig & Lipoid Pneumonia

- Ecigarettes x 7 months
- SOB, fevers, cough
- Chest CT showed opacities consistent with lipoid pneumonia.
- Macrophages in bronchoalveolar lavage fluid were loaded with lipid.
- Patient stopped Ecigarettes
- Hypothesized condition may have been caused by inhaling Ecigarette aerosol.

Ecig & Acute Eosinophilic Pneumonitis (AEP)

- 20-year-old active-duty healthy male sailor
- Presented to the Emergency Department (ED) for the chief complaint of 3 days of persistent cough, shortness of breath, and facial flushing.
- Symptom cluster beginning 1 h after smoking an e-cigarette 3 days prior.
- BAL negative and c/w AEP
- 60 mg of prednisone on hospital day 5 with improvement in his symptoms.
What are the Use, Perceptions & Impact of Ecigs on Smokers?
Sales (Millions of Dollars) of E-cigarettes in the U.S., 2008-2013
(Source: UBS)

Etter, 2013.
Ecigarette Awareness & Use

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Awareness</td>
<td>38.5%</td>
<td>40.9%</td>
<td>57.9%</td>
</tr>
<tr>
<td>Ever use</td>
<td>2.1%</td>
<td>3.3%</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

- Ever use of Ecigarettes was significantly higher among current smokers compared to former and never smokers.

Percentage of current Ecigarette users who stated that they used Ecigarettes for various reasons: Ecigs, electronic nicotine delivery systems (US, UK, Canada, Australia)

U.S. Tobacco Quitline callers (n=2,758)

- 30.9% of respondents reported ever using or trying e-cigarettes
  - 61.7% for < 1 month

- Help quit other tobacco (51.3%)
- Replace other tobacco (15.2%).

- Ecigarette users were significantly **less likely** to be tobacco abstinent at the 7-month survey compared with participants who had never tried e-cigarettes
  - 30-day point prevalence quit rates: 21.7% and 16.6% vs. 31.3%, *p < .001*}

Are Ecigs Effective for Smoking Cessation?
# Randomized Trials of Ecigs

<table>
<thead>
<tr>
<th></th>
<th>Caponnetto, 2013 (PlosOne)</th>
<th>Bullen, 2013 (Lancet)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>Unmotivated to quit</td>
<td>Motivated to quit</td>
</tr>
<tr>
<td><strong>Inclusion criteria</strong></td>
<td>≥10cpd for at least 5 years</td>
<td>≥10cpd for last year</td>
</tr>
<tr>
<td></td>
<td>18-70 years</td>
<td>≥18 years</td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>300</td>
<td>657</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>7.2 mg E-cig</td>
<td>16 mg E-cig</td>
</tr>
<tr>
<td></td>
<td>7.2-5.4 mg E-cig</td>
<td>21 mg NRT patch</td>
</tr>
<tr>
<td></td>
<td>0 mg E-cig</td>
<td>0 mg E-cig</td>
</tr>
<tr>
<td></td>
<td>No behavioral support</td>
<td>Minimal behavioral</td>
</tr>
<tr>
<td></td>
<td></td>
<td>support</td>
</tr>
<tr>
<td><strong>Intervention period</strong></td>
<td>12 weeks</td>
<td>13 weeks (1 wk pre-quit)</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>6 months</td>
<td>6 months</td>
</tr>
</tbody>
</table>

- Reductions in cigarettes/day use and eCO levels were observed at each study visits in all three study groups
  - $P < 0.001$ vs baseline
  - No differences between groups

- Smoking reduction:
  - 22.3% at week 12
  - 10.3% at week 52

- Abstinence:
  - 10.7% at week 12
  - 8.7% at week 52

- Smoking abstinence (6 months)
  - Ecig 7.3%
  - Nicotine patches 5.8%
  - Placebo Ecig 4.1%
  - Not statistically different

- 16 mg Ecig increased time to first relapse compared to nicotine patch (35 days vs. 14 days, P < 0.0001)

- No significant differences in adverse events
## Change from Baseline, Cigarette/day

<table>
<thead>
<tr>
<th></th>
<th>Ecig</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SE</td>
<td>Mean</td>
<td>SE</td>
<td>SE</td>
<td>P-value</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>11.1</td>
<td>0.4</td>
<td>9.1</td>
<td>2.0</td>
<td>0.5</td>
<td>&lt;.0001</td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>12.9</td>
<td>0.4</td>
<td>10.5</td>
<td>2.4</td>
<td>0.6</td>
<td>&lt;.0001</td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>10.8</td>
<td>0.4</td>
<td>9.1</td>
<td>1.7</td>
<td>0.6</td>
<td>.006</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>9.7</td>
<td>0.4</td>
<td>7.7</td>
<td>1.9</td>
<td>0.6</td>
<td>.0017</td>
<td></td>
</tr>
</tbody>
</table>

Summary of Ecig RCTs

- In smokers who use Ecigarettes for 12-13 weeks with little to no behavioral support
  - Six month quit rates are low (5-12%)
  - Quit rates are similar for nicotine vs nicotine-free e-cigs
  - Cigarette consumption is reduced
  - Mild, self-limiting side effects are reported

- In those motivated to quit:
  - Ecigs are of similar effectiveness to nicotine patches
  - Nicotine Ecigs delay relapse back to regular smoking
The Major Ingredient in E-Cigarettes is:

1. Isopropyl alcohol
2. Propylene glycol
3. Nicotine
4. Glycerol
The Major Ingredient in E-Cigarettes is:

1. Isopropyl alcohol
2. Propylene glycol
3. Nicotine
4. Glycerol
Which of the following is **False**:

1. Smokers generally like Ecigarettes
2. Ecigarettes help smokers reduce smoking
3. Ecigarettes help people quit smoking
4. Ecigarettes have potential health risks
Which of the following is False:

1. Smokers generally like Ecigarettes
2. Ecigarettes help smokers reduce smoking
3. Ecigarettes help people quit smoking
4. Ecigarettes have potential health risks
Goals & Objectives

- Understand the mechanics of Ecigarettes
- Summarize the data regarding Ecigarette nicotine delivery
- Define the known health risks of Ecigarettes
- Identify how cigarette smokers use Ecigarettes
- Cite evidence regarding the efficacy of Ecigarettes for smoking cessation