Alcohol-based Hand Sanitizers

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Outline

Alcohol-based Hand Sanitizers (AbHS):

- Poison Center Statistics
- COVID-related issues
- Kinetics and Clinical Effects (ethanol and methanol)
American Association of Poison Control Centers Annual Data

National Poisoning Data System

Website: aapcc.org
Clinical Toxicology

2019 NPDS Report


David D. Gummin, James B. Mowry, Michael C. Beuhler, Daniel A. Spyker, Daniel E. Brooks, Katherine W. Dibert, Laura J. Rivers, Nathaniel P. T. Pham & Mark L. Ryan


To link to this article: https://doi.org/10.1080/15563650.2020.1834219
**NPDS 2019 Data**

“Alcohols” 3rd largest category associated with deaths

One of the fastest growing cause of serious outcomes

(~ 935 more cases/year)

<table>
<thead>
<tr>
<th>AGENT</th>
<th>DEATHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methanol</td>
<td>21*</td>
</tr>
</tbody>
</table>

* reporting bias/limitations
NPDS 2019 Ethanol Data

Ethanol involved in ~ 7% of all reported deaths

Ethanol results in ~ 75,000 calls to US PCCs

Hand sanitizers involved in ~ 22,000 calls
Alcohol-based Hand Sanitizers

AbHS:
- common disinfectant in hospitals / public spaces
- liquid, foam or gel
- typically contain 60-95% alcohol (ethanol or isopropanol)
- use greatly increased during COVID response
- increased need resulted in production/sales of illicit products, some of which contained methanol
Alcohol-based Hand Sanitizers

Methanol

\[
\begin{align*}
\text{Methanol} & \xrightarrow{\text{ADH Rate limiting}} \text{Formaldehyde} \\
\text{Formaldehyde} & \xrightarrow{\text{ALDH Rapid}} \text{Formic acid} \\
\text{Formic acid} & \xrightarrow{\text{Folate}} \text{CO}_2 + \text{H}_2\text{O}
\end{align*}
\]

Ethanol

Isopropanol

\[
\begin{align*}
\text{Isopropanol} & \xrightarrow{\text{alcohol dehydrogenase}} \text{Acetone}
\end{align*}
\]
Alcohol-based Hand Sanitizers

Purell® - AbHS and non-alcohol (benzalkonium chloride)

A 37-year-old man with a history of ethanol abuse, ethanol withdrawal seizures and bipolar disorder called into our PCC after ingesting Purell®

Serum ethanol concentration (SEC) was 323 mg/dL

Several months later: another ingestion resulted in a SEC of 295 mg/dL

Review of PCC records found 12 ED visits related to AbHS

The average SEC = 239 mg/dL (range: 58-418)
NPDS 2020 Emerging Data

2020 Preview – Methanol Containing Hand Sanitizers

The Food and Drug Administration’s Center for Drug Evaluation and Research (FDA CDER) initiated contact with the AAPCC, NPDS emergency codes were generated on June 23, 2020 and a Special Report (available under NPDS Enterprise Reports) was developed to provide case epidemiology (Figure 8). To provide the earliest and strongest signal, the epidemiology curve includes exposure and non-exposure contacts, open and closed cases, and single and multiple substance reports. Of the 2,467 cases received, beginning on May 7 (start date of first report) through September 6, 2020: 87.7% were exposures, 39.0% were chronic, 15.9% were unknown age ≥20 years, 49.8% were female, 74.7% were dermal exposures, 30.0% were not followed with minimal clinical effects possible 72% were managed on site (non-health care facility). The COVID-19 product code was reported along with the sanitizer in 10.0% of the cases. During this period, FDA released 25 Recalls, Market Withdrawals, & Safety Alerts (https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts) concerning methanol contaminated hand sanitizers.

Poison Centers in Arizona and New Mexico collaborated with the CDC and published a report of 15 severe poisonings including 4 deaths [13].

https://doi.org/10.1080/15563650.2020.1834219
Methanol-containing Hand Sanitizer

Calls to US PCCs

Figure 8. Exposures per Day – All methanol-containing hand sanitizer cases, June 1, 2020 through September 17, 2020. The figure shows the frequency of methanol-containing hand sanitizers human exposure cases by day.
CDC Warning about Methanol

Serious Adverse Health Events, Including Death, Associated with Ingesting Alcohol-Based Hand Sanitizers Containing Methanol — Arizona and New Mexico, May–June 2020

Luke Yip, MD1; Danae Bixler, MD1; Daniel E. Brooks, MD2; Kevin R. Clarke, MD1; S. Deblina Datta, MD1; Steven Dudley Jr., PharmD3; Kenneth K. Komatsu4; Jennifer N. Lind, PharmD1; Annaliese Mayette, PhD5; Michael Melgar, MD1; Talia Pindyck, MD1; Kristine M. Schmit, MD1; Steven A. Seifert, MD6; Farshad Mazda Shirazi, MD, PhD3; Susan C. Smolinske, PharmD7; Brandon J. Warrick, MD6; Arthur Chang, MD1
### CDC Warning about Methanol

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Chief complaint(s)*</th>
<th>Serum methanol concentration (mg/dL)</th>
<th>Anion gap† (mEq/L)</th>
<th>Serum bicarbonate§ concentration (mEq/L)</th>
<th>Blood pH§</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>M</td>
<td>Gastrointestinal</td>
<td>44</td>
<td>30</td>
<td>6</td>
<td>7.15</td>
<td>4MP</td>
<td>D/C, no sequelae</td>
</tr>
<tr>
<td>30</td>
<td>M</td>
<td>Visual disturbance</td>
<td>35</td>
<td>43</td>
<td>11</td>
<td>N/A</td>
<td>4MP</td>
<td>D/C, no sequelae</td>
</tr>
<tr>
<td>35</td>
<td>M</td>
<td>Unresponsive, seizures</td>
<td>198</td>
<td>49</td>
<td>&lt;5</td>
<td>6.87</td>
<td>4MP</td>
<td>Died</td>
</tr>
<tr>
<td>36</td>
<td>M</td>
<td>Decreased responsiveness</td>
<td>&gt;500</td>
<td>42</td>
<td>7</td>
<td>7.23</td>
<td>4MP, HD</td>
<td>Remains hospitalized**</td>
</tr>
<tr>
<td>38</td>
<td>M</td>
<td>Gastrointestinal</td>
<td>131</td>
<td>35</td>
<td>&lt;5</td>
<td>6.81</td>
<td>4MP, HD, CRRT</td>
<td>D/C, no sequelae</td>
</tr>
<tr>
<td>38</td>
<td>F</td>
<td>N/A</td>
<td>21**</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>4MP</td>
<td>Died</td>
</tr>
<tr>
<td>39</td>
<td>M</td>
<td>Seizures, unconscious</td>
<td></td>
<td>23</td>
<td>11</td>
<td>N/A</td>
<td>4MP, HD</td>
<td>Died</td>
</tr>
<tr>
<td>40</td>
<td>M</td>
<td>Dog bite</td>
<td>319</td>
<td>35</td>
<td>&lt;5</td>
<td>7.00</td>
<td>4MP, CRRT</td>
<td>Remains hospitalized**</td>
</tr>
<tr>
<td>44</td>
<td>M</td>
<td>Visual disturbance, seizures</td>
<td>97</td>
<td>32</td>
<td>&lt;6</td>
<td>7.09</td>
<td>4MP, HD</td>
<td>D/C with visual impairment</td>
</tr>
<tr>
<td>47</td>
<td>M</td>
<td>Headache, visual disturbance</td>
<td>43</td>
<td>34</td>
<td>8</td>
<td>7.25</td>
<td>4MP, HD</td>
<td>D/C with visual impairment</td>
</tr>
<tr>
<td>50</td>
<td>M</td>
<td>Visual disturbance</td>
<td>410</td>
<td>22</td>
<td>9</td>
<td>6.70</td>
<td>4MP, CRRT</td>
<td>Remains hospitalized**</td>
</tr>
<tr>
<td>51</td>
<td>F</td>
<td>Dyspnea</td>
<td>42</td>
<td>23</td>
<td>6.2</td>
<td>7.14</td>
<td>4MP</td>
<td>D/C with visual impairment</td>
</tr>
<tr>
<td>54</td>
<td>M</td>
<td>Media alert§§</td>
<td>56</td>
<td>17</td>
<td>13</td>
<td>N/A</td>
<td>4MP</td>
<td>D/C, no sequelae</td>
</tr>
<tr>
<td>63</td>
<td>M</td>
<td>Altered mental status</td>
<td>548</td>
<td>30</td>
<td>11</td>
<td>7.12</td>
<td>4MP, HD</td>
<td>Remains hospitalized**</td>
</tr>
<tr>
<td>65</td>
<td>M</td>
<td>Unresponsive, seizures, cardiac arrest</td>
<td>308</td>
<td>31</td>
<td>&lt;5</td>
<td>N/A</td>
<td>4MP, HD, CRRT</td>
<td>Died</td>
</tr>
</tbody>
</table>
National Poison Data System (NPDS) Bulletin
COVID-19 (Hand Sanitizer)

Case Counts
Hand Sanitizer Cases
(1/1/21 - 2/21/21)

<table>
<thead>
<tr>
<th>Month</th>
<th>2020</th>
<th>2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan.</td>
<td>2,031</td>
<td>3,074</td>
</tr>
<tr>
<td>Feb.</td>
<td>1,510</td>
<td>1,996</td>
</tr>
<tr>
<td>TOTAL</td>
<td>3,541</td>
<td>5,070</td>
</tr>
</tbody>
</table>

Age Distribution
Hand Sanitizer Cases
(1/1/21 - 2/21/21)

Medical Outcome
Hand Sanitizer Cases
(1/1/21 - 2/21/21)

- Death
- Major effect
- Moderate effect
- Minor effect
- No effect
- Not followed, judged as nontoxic exposure
- Not followed, minimal clinical effects possible
- Unable to follow, judged as a potentially toxic exposure

*Confirmed nonexposure and Unrelated effect cases are not included in this pie chart
*Single and multiple exposure cases included; additional NPDS data is required to correlate cases with outcomes

https://aapcc.org/data-system

<table>
<thead>
<tr>
<th>Gender Distribution Hand Sanitizer Cases (1/1/21 - 2/21/21)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Unknown</td>
</tr>
</tbody>
</table>
COVID-19 and AbHS

Age Distribution
Hand Sanitizer Cases
(1/1/21 - 2/21/21)

Gender Distribution Hand Sanitizer Cases (1/1/21 - 2/21/21)

<table>
<thead>
<tr>
<th>Gender</th>
<th>2021 Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>2,668</td>
<td>52.6%</td>
</tr>
<tr>
<td>Female</td>
<td>2,387</td>
<td>47.1%</td>
</tr>
<tr>
<td>Unknown</td>
<td>15</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

Hand Sanitizer Case Counts
2020 vs. 2021
(January 1 - February 21)

<table>
<thead>
<tr>
<th>Month</th>
<th>2020</th>
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https://aapcc.org/data-system
COVID-19 and AbHS

Prevention >> Treatment

Masks       Social Distancing

Quarantine  Hand Hygiene
2020 Calls = 98,555

Many calls about Treatment and Prevention
COVID-19 and AbHS

Man dies after ingesting chloroquine in an attempt to prevent coronavirus

The man and his wife thought the ingredient, used to treat sick fish, could prevent the disease.
COVID-19 and AbHS

Based on:

- Local Poison Center Calls
- Patients transferred to our service
- Regional Cases
- CDC Analysis (MMWR)

Intentional misuse of AbHS
Intentional misuse of AbHS

Ingestion
(not dermal absorption)

Trying to get inebriated
(alcohol substitute)

Attempting to prevent COVID
(rare events)
Pharmacokinetics and Clinical Effects

Ethanol and Methanol
Ethanol Intoxication

Each ‘drink’ contains about 14.4g of ethanol

- 12 oz beer (5%)
- 1.25 oz liquor (40%)
- 5 oz 12% wine

For an average person (70 kg) this results in a serum concentration of ~ 25 mg/dL
Ethanol Metabolism

Average Rate for EtOH Metabolism:

~ 20 mg/dL/hr  (9 - 29 mg/dL/hr; 95% CI)

Units: 100 mg/dL = 1g/L = 100 mg% = .100%

Medical units = mg/dL in plasma
Legal units = mg/dL (%) whole blood

Plasma Etoh : BAC (whole blood) = 1.16 to 1

Plasma [EtOH] 80 mg/dL ~ whole blood EtOH of 68mg/dL
**Acute Ethanol Intoxication**

*Intoxication* best described by clinical effects
(don't correlate well with alcohol concentration)

Inebriating at low doses
CNS and Respiratory depressant at higher doses

“Uncouples” cortex from integrated control
(dis-inhibition)

Underlying personality defects
Acute Ethanol Intoxication

- Poor decision-making
- Impaired motor skills
- Impaired perception (memory formation)
- Delayed reaction time

→ Risky Behaviors
Ethanol Abuse and Trauma

FIG. 2. Alcohol-associated injury. The incidence of associated alcohol intoxication varies for selected mechanisms of injuries. MCA, motorcycle accident; MVA, motor vehicle accident; GSW, gunshot wound.
Alcohol-Related Trauma Recidivism

Studies show approximately 15% of trauma patients have a previous hospital admission for alcohol-related injuries

246 pts with alcohol-related trauma injuries

44% readmitted within 5 years
20% of these pts died

Rivera FP et al: The Effect of alcohol abuse on readmission for trauma. JAMA 1993
Methanol

Clear, flammable liquid

AKA: Methyl alcohol, Wood alcohol, Carbinol

Sources:

- Bootleg whiskey adulterant
- Window washers
- Carburetor cleaners
- Embalming fluids

- Anti-knock agent
- Deicers
- Paint removers
- Model fuels
Methanol

Rapid absorption (oral, dermal, inhalational)

Lethal Dose < 1 mL/kg of 100% solution
Blindness reported after 4 mL ingestion

Peak blood concentration within 60 minutes

Metabolism:
Alcohol Dehydrogenase and Aldehyde Dehydrogenase
10% excreted unchanged, 5 % via ventilation
Methanol - Metabolism

Methanol \( \xrightarrow{\text{ADH}} \) Formaldehyde \( \xrightarrow{\text{ALDH}} \) Formic acid \( \xrightarrow{\text{Folate}} \) CO\(_2\) + H\(_2\)O

NAD \( \xrightarrow{\text{ADH}} \) NADH + H\(^+\)
Methanol - Clinical Effects

Inebriating
  (CNS depressant)

Metabolic Acidosis
  (Anion and Osmolal Gaps)

Ocular Toxicity
  (Formaldehyde formation)
Methanol - Clinical Effects

Toxicity greatest in organs with high metabolic demand (e.g. CNS, kidney, optic nerve)

Ocular Toxicity

Inhibition of energy (ATP) production

Causes axonal swelling / optic nerve demyelination

Hemorrhagic stroke also possible
Take Home Points

Alcohol-based Hand Sanitizers

Should contain ethanol or isopropanol

Illicit products contain methanol

Risk for toxicity (poisoning) with misuse
Take Home Points

CVOID and AbHS

Typical Scenario: Intentional Ingestion

Reason: Alcohol Substitute
(ethanol containing AbHS ~ ‘cheap vodka’)

Methanol used in Illicit Manufacturing
Take Home Points

Ethanol

Inebriation and CNS Depression

Synergistic Respiratory Depression

Hypoglycemia, Dehydration, Malnutrition

Trauma and Withdrawal
Take Home Points

**Isopropanol**

Significant CNS depression

Severe Gastritis

Ketosis (Acetone) without Acidosis

Supportive (Ventilatory) Support
Methanol - Take Home Points

Methanol

CNS and Ocular Toxicity

Metabolic Acidosis

Alcohol / 4-MP and Hemodialysis

Stroke

Folate
US Poison Control Centers

Never Hesitate to Call Us

800-222-1222

www.aapcc.org