### Linking Practice & Research

**Cough Drops: Cause For Concern?**

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**1 - Clinical Vignette**

- One of the authors (RM) observed that patients didn’t usually admit cough drop use even when asked about OTC medications and some patients with prolonged unexplained coughs took large amounts of cough drops.
- After following his recommendation to cease excessive cough drop use, the cough resolved in several patients.
- RM contacted the Wisconsin Research & Education Network (WREN) to help research cough drop use causing worsening cough.

**2 - Methods**

- **Literature search**: Menthol toxicity¹,²,³
- **Research Question**: Do menthol-containing cough drops adversely affect cough severity and/or duration?
- **Survey construction**: Cross-sectional prevalence survey in 5 rural, suburban and urban clinics of adolescents and adults with acute/subacute cough (<60 days duration).

**Survey Questions × 10**

- **Clinical Vignette**
- **Age, Sex**
- **Smoking Status**
- **Cough Drop Use**
- **Cough Duration**
- **Cough Severity**

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**3 - Analytic Framework**

1. Cough drop use is likely associated with increased cough severity/duration because patients will likely seek more relief if they are sicker.
2. Menthol dose is not readily apparent on the packaging. A dose-response relationship between daily menthol dose and cough severity would support a possible causal association because it seems less plausible that sicker patients would intentionally seek higher menthol doses.

A DOSE-RESPONSE ASSOCIATION WOULD BE INFORMATIVE, IF PRESENT.

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**4 - Results**

- 2/3 used cough drops; 90% contained menthol

**COUGH DROP USERS V NON-USERS**

<table>
<thead>
<tr>
<th></th>
<th>Cough Drop Users (n=343)</th>
<th>Non-Cough Drop Users (n=195)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough Severity</td>
<td>6 (4–6)</td>
<td>5 (4–6)</td>
<td>0.0885</td>
</tr>
<tr>
<td>Cough Duration</td>
<td>9 (5–17)</td>
<td>7 (4–14)</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

* Median (25 – 75 %ile), 1-point scale (1=very mild, 5=very severe)

**MENTHOL V NON-MENTHOL**

<table>
<thead>
<tr>
<th></th>
<th>Menthol (n=269)</th>
<th>Non-Menthol (n=31)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough Severity</td>
<td>6 (4–6)</td>
<td>6 (4–6)</td>
<td>0.65</td>
</tr>
<tr>
<td>Cough Duration</td>
<td>10 (6–20)</td>
<td>6 (5–14)</td>
<td>0.101</td>
</tr>
</tbody>
</table>

* Median (25 – 75 %ile), 1-point scale (1=very mild, 5=very severe)

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**5 - DOSE-RESPONSE**

Cough severity was associated with:

- **Average menthol dose per cough drop** (R = 0.19, P = 0.007)
- **Number of daily cough drops consumed** (R = 0.20, P = 0.002)
- **Average daily menthol dose** (R = 0.21, P = 0.003)

**FIGURE**

The total daily menthol dose consumed by some patients approached 100 mg daily.

Doses of this magnitude can cause respiratory physiologic pathology in an animal model.

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**6 - Conclusions**

- Two-thirds of patients with cough used cough drops; 90% of cough drops contained menthol.
- Cough severity in some individuals may be negatively influenced by the amount of menthol consumed via cough drops.
- Clinicians should include cough drop use in history taking of patients with persisting cough illnesses.
- Further research into potential mechanisms is warranted.

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**References**