**Introduction:**
Diphenhydramine (DPH) is an over the counter, first generation, ethanalamime-derived antihistamine discovered in 1960’s. Massive abuse of DPH is not well described. Some users claim that it gives them a clarity of thought unlike any other substance of abuse.

**Case Report:**
61 yo F with long history of substance abuse and addiction to opiates, was brought to the ED in a delirious, agitated state. Her daughter recently discovered that she had been abusing excessive amounts of diphenhydramine (DPH). The daughter discovered pharmacy receipts for the patient’s purchase of 23 bottles, 600 tablets of DPH 25 mg in each, within the past 5 months. The patient admitted taking up to 500 mg (20 tablets) of DPH 3x/day. The patient told the admitting physician that she was taking up to 1.5 gm (60 tablets) every night “to sleep.” The estimated daily DPH use based upon the pharmacy receipts averaged 92 tablets or 2.3 gm/day. The daughter had become very concerned about such excessive DPH use and made her mother stop taking DPH 2 days prior to presentation. One day prior to presentation, the daughter allow her to take DPH 100 mg and the patient seemed fine. On presentation, she was very confused and diaphoretic despite taking another DPH 100 mg.

Medications: Suboxone, Lasix, KCl, Omeprazole
Past Medical History: Insomnia.
Social History: Opiate abuse, compulsive soda drinking; remote history of ethanol abuse.

Pertinent Findings: VS: **HR 95**, RR 15, BP 122/63, ill-appearing in severe distress, **moist skin**, **miotic pupils**, slow mentation, **confused**, slurred speech, **ataxic gait**, non-communicative, flat affect.

**Medical Decision Making:** Severe distress secondary to DPH withdrawal versus DPH toxicity from surreptitious use.

**ED Course:** The ED physician called the Poison Center and asked whether to give physostigmine for DPH toxicity or more DPH for withdrawal. Because physostigmine was felt to be more hazardous, the recommendation was to attempt to control her delirium and agitation with carefully titrated doses of IV DPH. Her symptoms were eventually controlled with IV DPH up to 200 mg every 4-6 hours and she was admitted to the ICU.

**Hospital Course:** Her DPH doses were gradually reduced over 3 days. She refused transfer to drug rehabilitation facility and regional detoxification. Local rehabilitation facilities declined to admit her because of inexperience with this addiction and she was lost to follow up.

**Discussion:**
Usual adult oral DPH dose is 25-50 mg 3 or 4 times daily, not to exceed 300 mg/day. Abuse of anticholinergics is widespread. Many more cases of chronic abuse may go undetected by our current systems. Thomas hypothesized that increases in dopaminergic neurotransmission in mesolimbic brain pathways following antimuscarinic dosing may produce rewarding properties and drug-seeking behaviour.

The first published report of DPH dependence was by Harenko in Scandinavia in 1965. He described chronic DPH abuse that led to dependence in multiple patients who showed signs of parasympathetic blockade during use and abstinence symptoms upon abrupt withdrawal.

The majority of the reported cases (listed below) occurred in patients with chronic schizophrenia. Thomas speculated that in patients treated with antipsychotic medication, anticholinergics may produce rewarding effects associated with a reversal of secondary negative symptoms (induced by antipsychotic treatment), DPH withdrawal manifest resembles cholinergic excess with acute delirium, insomnia, agitation, restlessness, diaphoresis, rhinorrhea, abdominal cramps, vomiting, and diarrhea.

**Table: Published Cases of Massive DPH Abuse**

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Age</th>
<th>Sex</th>
<th>Max Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feldman</td>
<td>1986</td>
<td>34</td>
<td>M</td>
<td>1600 mg</td>
</tr>
<tr>
<td>MacRury</td>
<td>1987</td>
<td>69</td>
<td>M</td>
<td>700 mg</td>
</tr>
<tr>
<td>De Nesar</td>
<td>1996</td>
<td>32</td>
<td>M</td>
<td>2500 mg</td>
</tr>
<tr>
<td>De Nesar</td>
<td>1996</td>
<td>38</td>
<td>M</td>
<td>1250 mg</td>
</tr>
<tr>
<td>Barsoum</td>
<td>2000</td>
<td>33</td>
<td>M</td>
<td>3000 mg</td>
</tr>
<tr>
<td>Cox</td>
<td>2001</td>
<td>34</td>
<td>M</td>
<td>720 mg</td>
</tr>
<tr>
<td>Gracious</td>
<td>2010</td>
<td>15</td>
<td>F</td>
<td>400 mg</td>
</tr>
<tr>
<td>Erbe</td>
<td>2013</td>
<td>40</td>
<td>M</td>
<td>3000 mg</td>
</tr>
</tbody>
</table>

**Conclusion:**
Massive DPH abuse has rarely been reported in past. Abrupt discontinuation of DPH in such cases may lead to withdrawal. Carefully titrated doses of DPH are required for proper detoxification. Drug rehabilitation facilities may not be comfortable managing this type of addiction.

**References:**