

# A Dangerous Encounter with Naphthalene

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**N**aphthalene is a polycyclic, aromatic, crystalline, white hydrocarbon composed of two fused benzene rings (molecular formula,  $C_{10}H_8$ ) that is toxic to humans if ingested, inhaled, or absorbed by the skin. Its most frequent use is as a raw material in the industrial production of phthalic anhydride used to manufacture polyvinyl chloride piping, vanity tops, and boat hulls, as well as in the manufacturing of synthetic resins, solvents, and lubricants.<sup>1</sup> Major commercial products made from naphthalene are moth repellants and toilet deodorant blocks. This article reports the case of a 67-year-old woman who developed altered mental status after ingesting a substance containing naphthalene. The epidemiology, pathophysiology, diagnosis, and treatment of naphthalene toxicity are discussed.

### CASE PRESENTATION

#### Patient Presentation and History

A 67-year-old woman of Colombian origin with a history of Parkinson's disease and major depression was brought to an emergency department in Florida by her son and daughter because of an episode of syncope and a recent change in mental status. The daughter reported that on their recent trip to New Jersey to visit relatives, her mother developed congestion and rhinorrhea, which she attempted to relieve by inhaling a substance purchased at a local alternative health store. While on the airline flight back to Florida, the daughter noticed her mother eating the substance; at that time, the mother admitted to occasionally using the substance in the past as an analgesic balm for muscle pain but contended that she never before this trip had inhaled or ingested it. Five days after their return, the son and daughter noticed their mother becoming progressively more lethargic and confused and vomiting with meals. The mother then admitted inhaling the substance in the past and ingesting approximately 3 g of it during the previous 5 days. Examination of the packaged substance—a dry, waxy, white, cake-like

material—revealed the ingredient naphthalene in small print on the label.

#### Physical Examination

On initial examination, the patient appeared to be a lethargic woman who was unable to answer questions appropriately in either English or Spanish. She was mildly tachypneic but otherwise in no apparent distress. Her blood pressure was 130/88 mm Hg, heart rate was 98 bpm, and respiratory rate was 22 breaths/min. Ophthalmoscopic examination revealed a small cataract. The patient's neck was supple, and she had no palpable masses. Her lungs were clear to auscultation, and examination of her heart revealed only tachycardia. Abdominal examination revealed hyperactive bowel sounds with no hepatomegaly or splenomegaly. Neurologic examination revealed minimal rigidity in both upper extremities with a fine resting tremor. The patient was awake but not oriented. She had no palpable lower extremity cords, and there was no rubrous discoloration of her limbs. Results of her rectal examination were heme negative.

#### Laboratory and Diagnostic Studies

Results of laboratory studies obtained on the case patient's admission to the hospital are presented in [Table 1](#). Serum levels of sodium, potassium, chloride, bicarbonate, and calcium were all normal. Serum lactate dehydrogenase level was elevated, and an increased level of indirect bilirubin suggested hemolytic anemia. Urinalysis revealed proteinuria; lead levels were not detected. An electrocardiogram showed sinus tachycardia. Results of chest radiography were normal,

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**Table 1.** Laboratory Values of the Case Patient

Leukocyte count, $11.3 \times 10^3/\text{mm}^3$ (normal, $4.0\text{--}11.0 \times 10^3/\text{mm}^3$ )
Hemoglobin level, 12 g/dL (normal, 12.0–16.0 g/dL)
Hematocrit, 38% (normal, 37%–47%)
Creatinine, 1.7 mg/dL (normal, 0.7–1.5 mg/dL)
Aspartate aminotransferase, 827 U/L (normal, 7.0–40.0 U/L)
Alanine aminotransferase, 22 U/L (normal, 7.0–40.0 U/L)
Arterial blood gases
Paco <sub>2</sub> , 28.5 mm Hg (normal, 35.0–40.0 mm Hg)
Pao <sub>2</sub> , 60.7 mm Hg (normal, 80–100 mm Hg)
Oxygen saturation, 86% on room air (normal, $\geq 95\%$ )

and a computed tomographic scan of the patient's head showed neither acute bleeding nor edema. Bilateral Doppler ultrasonography of the lower extremities revealed no deep venous thromboses.

#### Treatment and Outcome

The patient was given 50 g of activated charcoal and 50 mL of sorbitol in the emergency department. She was transferred to the intensive care unit for intravenous administration of fluids, supplemental oxygenation, and vigilant cardiopulmonary monitoring. A ventilation-perfusion scan revealed bilateral mismatches consistent with pulmonary emboli; she was subsequently placed on heparin and warfarin therapy. Within 6 hours, she became unresponsive, her respirations were shallow, and she was emergently intubated to ensure appropriate respiratory support. Over the next 8 days, her daily liver enzyme levels progressively increased to a maximum aspartate aminotransferase level of 1200 U/L and an alanine aminotransferase level of 633 U/L. Her hemoglobin level fell to 7 g/dL; transfusion brought the level up to 11 g/dL, where it remained stable. An assay for glucose-6-phosphate dehydrogenase (G6PD) deficiency was negative. Because she was minimally responsive to external stimuli, it was difficult to wean her from the ventilator, despite no prior pharmaceutical sedation. On day 8 of her hospital stay, results of her urinalysis were positive for the presence of naphthols.

Subsequent arterial blood gas analyses revealed a worsening metabolic acidosis, and urinalyses confirmed an increasingly alkaline pH, which suggested renal tubular acidosis. The patient's methemoglobin level remained normal throughout her hospitalization. She was given 150 mmol of bicarbonate intravenously and remained in stable condition. On hospital day 9, she became more responsive and was successfully weaned from the ventilator. Her serum creatinine level steadily

decreased to a baseline of 0.7 mg/dL, and her liver enzyme levels returned to normal. After day 10, she was moved to the telemetry unit and began physical therapy. Despite some lingering confusion, she was able to recognize all of her family members, as well as engage in active conversation with the house staff. On day 14, she was transferred to a rehabilitation facility for active physical therapy and further convalescence. After 10 days of rehabilitation, she returned home with her children, who subsequently reported that their mother's health had returned to baseline.

#### DISCUSSION

Naphthalene can be absorbed by oral, inhalational, transplacental, and transdermal routes. The typical air concentration of naphthalene in cities is approximately 0.0007 ppb; the lethal level is 10 ppm. Naphthalene can be detected (ie, smelled) by humans at a concentration of 84 ppb. Most of the naphthalene that is released into the environment comes from the burning of wood and fossil fuels in the home. The second greatest release comes from moth repellants. Naphthalene is not typically found in water; rather, it is predominantly found in soil. Several medical reports from the United Kingdom show that infants dressed in clothing that had been stored in naphthalene mothballs can develop liver problems and hemolytic anemia.<sup>2</sup> Patients with G6PD deficiency are especially susceptible to naphthalene-induced hemolytic anemia secondary to glutathione depletion.<sup>3</sup>

#### Sources of Exposure to Naphthalene

Mothballs are easily obtainable, and exposure to naphthalene is quite common. Presently, commercial mothballs are composed of either naphthalene or non-toxic paradichlorobenzene. Paradichlorobenzene mothballs will not melt in a water bath; naphthalene requires a water bath of 80°C (176°F) to melt. Paradichlorobenzene is described as "wet and oily," whereas naphthalene is described as having a dry appearance.<sup>3</sup>

Although inhalation exposure can occur over the course of years with regular use as a moth repellant in closets, most persons do not accrue enough naphthalene exposure to be symptomatic. Despite this observation, the compound is evidently not benign.<sup>4</sup> Persons who work with naphthalene or tar distillation are exposed to rather low concentrations of naphthalene, methylated naphthalene, and naphthols,<sup>5</sup> but it has been reported that workers exposed to vapors of naphthalene and coal tar can develop laryngeal carcinomas or neoplasms of the pylorus and cecum. The di-, tri-, and tetramethylnaphthalene contaminants of coal tar

were found to be carcinogenic when applied to the skin of mice, but naphthalene alone was not.<sup>4</sup> Pica during the early months of pregnancy can lead to intentional ingestion of naphthalene with resultant fetal death (caused by hemolytic anemia within days after transplacental diffusion).<sup>5</sup> Naphthalene was the principal ingredient of the product bought as a cold remedy by the case patient, which she reported is a common product in her Latin American culture.

#### **Pathophysiology of Naphthalene Toxicity**

Following a one-time ingestion of naphthalene, the highly soluble compound is absorbed immediately into the brain and body fat, as seen in rabbit organ tissue assayed after exposure. What occurs next is uncertain. The substance may then diffuse back into the bloodstream (at an unknown rate), become conjugated within the erythrocytes and liver, and then be renally excreted. Toxic effects are secondary to exposure to naphthalene itself or its metabolites. Metabolism of naphthalene in bacteria proceeds through formation of an epoxide, which undergoes conjugation with glutathione or can spontaneously be converted to the water-soluble *cis*-1,2-dihydroxynaphthalene.<sup>6</sup> This may be one model of how naphthalene is eliminated in humans, utilizing the bacterial flora of the intestines. In animals (including humans), naphthalene can also be converted to 1,2-naphthoquinone, which binds irreversibly to proteins in the lens of the eye, causing cataracts.

#### **Diagnosis of Naphthalene Toxicity**

Acute exposure to naphthalene by inhalation, ingestion, and dermal contact is associated with hemolytic anemia, damage to the kidneys, and cerebral infarcts.<sup>7</sup> Reported systemic effects, in order of noted frequency, are shown in **Table 2**.

The most common toxic effect observed in the laboratory following oral ingestion or inhalation of naphthalene is hemolytic anemia, evidenced by a rapid decrease in hemoglobin and hematocrit levels, an elevated reticulocyte count and serum bilirubin level, and the presence of Heinz bodies on a peripheral blood smear.

One source recommends obtaining a baseline complete blood cell count, electrolyte and G6PD levels, liver and renal function tests, urinalysis, and a urine dipstick test to detect hemoglobinuria in patients with suspected naphthalene exposure. Measurements of urinary metabolites (1-naphthol or mercapturic acid) may help confirm the diagnosis. Abdominal radiographs may show the presence of mothballs if exposure is questioned.<sup>8</sup>

Naphthalene and its breakdown products can be measured in fat, urine, and feces.<sup>4,6,9</sup> Naphthols and

**Table 2.** Systemic Effects of Naphthalene Exposure

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#### **Gastrointestinal effects**

Nausea, vomiting, abdominal pain, diarrhea

#### **Renal effects**

Increased creatinine level, increased serum urea nitrogen level, hematuria, renal tubular acidosis

#### **Respiratory effects**

Congestion, acute respiratory distress syndrome (noted at 2 ppm)

#### **Neurologic effects**

Confusion, lethargy, vertigo, fasciculations, convulsions, anesthesia, cerebral edema, coma (coma is noted at 0.05 mg/kg body weight per day)

#### **Hepatic effects**

Jaundice, hepatomegaly, elevated liver enzyme levels (noted at 0.02 mg/kg per day)

#### **Ocular effects**

Optic nerve atrophy, bilateral cataracts with chronic exposure

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Data from US Environmental Protection Agency. Health and environmental effects profile, naphthalene EPA/600/X-86/241. Cincinnati (OH): Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development; 1988 and from EPA health effects notebook for hazardous air pollutants—draft, EPA-452/D-95-00, PB95-503579, December 1994. Available at <http://www.epa.gov/ttn/atw/hapindex.html>. Accessed 1 Oct 2002.

1,4-naphthoquinone identified in the urine are usually diagnostic of naphthalene exposure.

#### **Treatment of Naphthalene Ingestion and Toxicity**

In patients with acute naphthalene ingestion, the recommended treatment of 50 mL of sorbitol followed by 50 g of activated charcoal usually averts subsequent toxicity.<sup>10,11</sup> There have been no careful studies suggesting a specific mechanism of clearance. Charcoal and sorbitol are standard for the treatment of most poison ingestions (including overdosing of illegal, over-the-counter, and prescription drugs). However, sorbitol is not recommended for use in children, because the catharsis may result in profound dehydration. The information on activated charcoal is scarce, but adsorption is thought to occur. Methylene blue is recommended if methemoglobin levels are elevated. (In the case patient, they were not.)

The case patient, who had been ingesting the substance containing naphthalene for at least 5 days, was immediately symptomatic. We hypothesize that as the substance diffused from her corporeal fat, she developed the observed hepatic failure and renal toxicity. Her case

**Table 3.** First Aid Procedures in the Home

In the eye: Hold eye open and rinse slowly and gently with water for 15–20 minutes. Remove contact lenses. Call poison control center for further instructions.

On the skin: Take off contaminated clothing and rinse skin immediately for 15–20 minutes. Call poison control center.

If swallowed: Call poison control center. Have person sip a glass of water if able to swallow. DO NOT induce vomiting if patient has evidence of central nervous system depression or lethargy. Give nothing to an unconscious person. Respond to the nearest emergency department or urgent care center.

Data from Material safety data sheet. Conclude G herbicide. Agricultural Products Group, BASF Corporation. Available at <http://www.cdms.net/ldat/mp0DQ003.pdf>. Accessed 2 Oct 2002.

was complicated by pulmonary emboli, which we believe developed from venous stasis during her airplane trip and were not attributable to naphthalene toxicity.

Unfortunately, no safe substances are available that can hasten the excretion of naphthalene in the body. Like most poisons ingested, there is no antidote. Thus, supportive treatment is the only measure available. Mothballs dissolve slowly, and gastric decontamination should be considered even in patients presenting late after ingestion.<sup>8</sup> The course of hospitalization is variable and usually not fatal, except in the case of G6PD deficiency.<sup>3,4,11</sup>

## CONCLUSION

The product used by the case patient, similar to mothballs, is a commonly purchased material and, therefore, often assumed to be benign. By many accounts of patients with pica, naphthalene has a sweet taste, and the odor is not unpleasant. This may explain why the majority of cases of naphthalene exposure involve young children and pregnant women. First-aid procedures for exposure to naphthalene in the home are listed in **Table 3**. Caregivers of elderly persons with dementia, as well as parents of small children, should make mothballs and other naphthalene-containing products inaccessible in the house and respond immediately with emergency care should ingestion be suspected. Health care workers should take a careful history of possible poison exposure and act quickly when told of possible mothball or toilet-deodorant ingestion. **HP**

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