Protocol for Naphthalene poisoning management

**Category/Use:** Naphthalene is used as a moth repellent and deodorizer (eg, toilet bowl, diaper pail); has also been used indoors to deter insects and rodents and outdoors to repel other animals or in soil fumigants. Numerous forms of naphthalene products have been developed, including balls, flakes, crystals, and cakes. Naphthalene is also used in scintillation counters and may be a major component of some anointing oils. Additionally, it is used to manufacture several products (eg, celluloid, creosote, dyes, fuels, fungicides, lubricants, naphthalene derivatives, pesticides, plasticizers, preservatives, synthetic resins, tanning agents). Abused solvents (eg, model cement) may also contain naphthalene.

**Specific substances:** Albocarbon; Camphor Tar; Moth Balls; Moth Flakes; Mothballs; Naftalen; Naphthalin; Naphthene; Tar Camphor; White Tar.

**Range of toxicity:**
- Less than one naphthalene mothball (200 to 500 milligrams) may cause hemolysis, especially in G-6-PD deficient children.
- A lethal dose for a child via oral exposure is 100 mg/kg based on RTECS data.
- Exposure to airborne concentrations of 15 ppm may cause eye irritation.

**Mortality rate:** Not available

**Clinical presentation:**

**Ingestion:** Ingestion is the most common route of exposure to naphthalene. Common signs and symptoms may include nausea, vomiting, abdominal pain, diarrhea, fever, headache, and mental status changes. Patients may also experience hemolysis, hemolytic anemia, and methemoglobinemia. These effects typically occur 1-3 days after exposure and are usually preceded by nonspecific gastrointestinal symptoms. Secondary complications may occur in patients who develop hemolysis, hemolytic anemia, and/or methemoglobinemia, including pulmonary edema, tachycardia, arrhythmias, hypotension, hepatomegaly, renal toxicity, GI bleeding, and seizures.

**Dermal:** Acute exposure may result in a similar clinical presentation as described for ingestion. Select patients may also experience hypersensitivity reactions (eg, dermatitis, erythema). Dermal exposures may occur in patients exposed to naphthalene-treated materials (eg, clothing, diapers), especially in infants.
**Inhalation:** Acute exposure may result in a similar clinical presentation as described for ingestion. Inhalational exposures may occur in patients exposed to naphthalene-treated materials (e.g., clothing, blankets).

**Comprehensive listing by system** (listed alphabetically):

**Central nervous system:** Coma (rare), confusion, euphoria (inhalation), fever, headache, lethargy, malaise, mental status changes, restlessness, seizures (rare), syncope (rare), vertigo (rare)

**Dermatologic:** Dermatitis (dermal), erythema (dermal)

**Gastrointestinal:** Abdominal pain, appetite (decrease), diarrhea, nausea, vomiting

**Genitourinary:** Dysuria (rare), urinary urgency (rare)

**Hematologic:** Aplastic anemia (rare), hematocrit (decreased), Heinz body hemolysis, hemoglobin (decreased), hemolysis, hemolytic anemia, leukocytosis, methemoglobinemia, reticulocytosis

**Ocular:** Blindness (rare), cataracts (rare), conjunctivitis (rare), eye irritant, eye pain (rare), optic atrophy (rare), retinal lesions (rare), vision (decreased; rare)

**Respiratory:** Choking (rare)

**Mechanism of Toxicity:**

Naphthalene metabolites, mainly alpha-naphthol (1-naphthol), are responsible for hemolysis and methemoglobinemia. Metabolites provide oxidative stress and can denature and precipitate hemoglobin, increasing the susceptibility of an erythrocyte to hemolysis. Metabolites may also oxidize an iron atom of hemoglobin from the ferrous (Fe\(^{2+}\)) state to the ferric (Fe\(^{3+}\)) state, thus forming methemoglobin. Methemoglobin impairs oxygen delivery to tissue as ferric (Fe\(^{3+}\)) irons are unable to transport oxygen and additional hemoglobin of the tetramer in the ferrous (Fe\(^{2+}\)) state exhibits increased oxygen affinity. Hemolysis and methemoglobinemia can manifest independently or simultaneously in normal or population-susceptible patients. Infants are more susceptible to hemolysis, likely due to insufficient conjugation of toxic metabolites and methemoglobinemia because of decreased activity of nicotinamide adenine dinucleotide (NADH) methemoglobin reductase (cytochrome b5 reductase) and increased susceptibility of hemoglobin F. Individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency are more susceptible to hemolysis and methemoglobinemia due to reduced glutathione stores. G6PD deficiency can affect both sexes and all races, but is more prevalent in males and individuals of African, African American, Asian, and Mediterranean descent.

**Pharmacokinetics:**

**Absorption:** Oral: Continued absorption over several days as moth repellent dissolves
Dermal, Oral: Absorption may be enhanced by lipid-soluble compounds (eg, oil, milk)

**Metabolism:** Hepatic, via CYP450 to 1,2-naphthalene oxide followed by further metabolism to alpha-naphthol (1-naphthol) and other metabolites; CYP1A2 appears to be the most efficient isoform for producing 1-naphthol; metabolism may also occur in human lung tissue.

**Excretion:** Urine (primarily as metabolites); feces (primarily as unabsorbed naphthalene)

**Criteria for hospital admission:**
Symptomatic patients who are more susceptible to naphthalene-induced toxicities, including infants and patients with known or suspected G6PD deficiency, sickle cell anemia, or sickle cell trait. Patients with hemolysis, hemolytic anemia, or methemoglobinemia. Patients who cannot be closely monitored and managed on an outpatient basis

**Monitoring parameters:**

**First aid measures:** Same as decontamination method explained in treatment part

**Treatment:**

**Oral exposure:**

**Stabilization**
Initially, evaluate and correct immediate life-threatening complications (eg, airway, breathing, and circulation). The most serious complications include hemolysis, hemolytic anemia, methemoglobinemia, and associated complications.

**Decontamination method:**
All contaminated clothing and belongings should be bagged in liquid-occlusive containers and removed from patient care areas to protect healthcare providers from exposure. **Note:** To prevent further exposure, contaminated clothing should be discarded as naphthalene is generally not completely removed through washing.

**Emesis:** Emesis is not recommended. Also Cathartics are not recommended.
If the patient presents within 1 hour of ingestion, consider the following decontamination procedure(s):

**Activated charcoal:** Minimum of 240 milliliters of water per 30 grams charcoal.
Adults and Adolescents dose: 25 to 100 grams
Children aged 1 to 12 years: 25 to 50 grams
Infants up to 1 year old: 0.5 to 1 gram/kilogram.
**Gastric lavage:** Gastric lavage is unlikely to be beneficial following a mothball ingestion due to the large size of mothballs relative to the small diameter of the gastric lavage tube. In rare situations when gastric lavage is deemed appropriate, it is most effective if initiated within 1 hour of ingestion; however, gastric aspiration and lavage have not been proven to be beneficial and are not routinely recommended due to the risk of complications and the lack of demonstrated efficacy. Use is contraindicated in patients with an unprotected airway, in patients in whom its use increases the risk and severity of aspiration, and in patients who are at risk of hemorrhage or gastrointestinal perforation due to pathology.

**Inhalation:** Remove the patient from the source of exposure and into fresh air. Monitor for respiratory distress.

**Dermal:** Gently wash exposed skin and/or hair with nontoxic, mild detergent and warm water; rinse thoroughly with water.

**Ocular:** Irrigate with copious amounts of tap water or normal saline for at least 15 minutes; remove contact lenses if easily removable without causing additional trauma to the eye.

**Specific treatment/Antidote:**

**Methylene blue:**

Indication for use: Symptomatic methemoglobinemia or methemoglobin level >30%. Common signs and symptoms of methemoglobinemia may include, but are not limited to, headache, fatigue, cyanosis, and dyspnea.

**Note:** Methylene blue is indicated only for methemoglobinemia. Do not administer in patients who develop other naphthalene-induced toxicities (eg, hemolysis) in the absence of methemoglobinemia. Methylene blue should be used with caution in young patients and individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency as these patients are at an increased risk for paradoxical methemoglobinemia.

Contraindications: Hypersensitivity to methylene blue or any component of the formulation; intraspinal injection; renal insufficiency

Mechanism of action: Upon administration, methylene blue is reduced to leukomethylene blue which accelerates the conversion of methemoglobin to hemoglobin. At high doses (>7 mg/kg), methylene blue acts as an oxidizing agent by converting ferrous iron in hemoglobin to ferric iron, causing paradoxical methemoglobinemia. Glucose is required for the reduction of methemoglobin to hemoglobin; therefore, if insufficient glucose is available, methylene blue may not be effective.
Dosage: I.V.: Note: Repeat dosing may be required; high doses may cause paradoxical methemoglobinemia. Doses may be immediately followed by a 15-30 mL flush in an effort to reduce local pain.

Neonates: 0.3-1 mg/kg

Children and Adults: 1-2 mg/kg or 25-50 mg/m² over 3-5 minutes; may be repeated in 30-60 minutes if necessary; maximum dose: 7 mg/kg

Supportive Treatment:

Control of seizures: First-line therapy with benzodiazepines (eg, diazepam); additional agents may be added if needed (eg, phenobarbital). In patients without I.V. access, treatment with I.M. midazolam is recommended. Phenytoin is not generally useful in the management of poison-induced seizures; routine use is not recommended.

Diazepam: I.V.:

Infants 30 days to Children: 0.1-0.3 mg/kg (maximum: 10 mg/dose) slow I.V. (maximum rate: 5 mg/minute); may repeat every 5-10 minutes as needed (Hegenbarth, 2008)

Adults: 5-10 mg slow I.V. (maximum rate: 5 mg/minute); may repeat every 5-10 minutes as needed (maximum total dose: 30 mg)

Lorazepam: I.V.:

Infants and Children (unlabeled use): 0.05-0.1 mg/kg (maximum: 4 mg/dose) slow I.V. (maximum rate: 2 mg/minute); may repeat every 5-15 minutes as needed (Hegenbarth, 2008; Sabo-Graham, 1998)

Adults: 4 mg (0.1 mg/kg) slow I.V. (maximum rate: 2 mg/minute); may repeat in 5-15 minutes; usual maximum dose: 8 mg

Phenobarbital: I.V.:

Infants and Children: 15-20 mg/kg (maximum: 1000 mg/dose) infused over 10 minutes (rate: <100 mg/minute); may repeat dose after 15 minutes as needed (maximum total dose: 40 mg/kg)

Adults: 10-20 mg/kg infused over 10 minutes (rate: <100 mg/minute); may repeat dose in 20-minute intervals as needed (maximum total dose: 30 mg/kg)

Midazolam: I.M.:

Infants and Children: 0.2 mg/kg (maximum: 6 mg/dose); may repeat every 10-15 minutes as needed

Adults: 0.15-0.3 mg/kg (usual dose: 5-15 mg); may repeat every 10-15 minutes as needed

Supportive Treatment:

Transfusion: Blood transfusion may be considered in patients with severe hemolysis and anemia. Exchange transfusion has been performed in severe cases; however, routine use is not recommended.
**Oxygen:** Oxygen supplementation may be necessary for patients with symptomatic methemoglobinemia.

**Elimination enhancement method:** None of the elimination enhancement methods are useful

**Criteria for emergency department discharge:**
Some experts recommend that patients who remain asymptomatic and are not known or suspected to be G6PD deficient may be considered for discharge following 2-4 hours of ED observation. Close follow-up may be required (eg, daily laboratory studies, clinical evaluation) in select patients.

Some experts recommend that patients who remain asymptomatic and are known or suspected to be G6PD deficient may be considered for discharge following 4-6 hours of ED observation and collection of baseline laboratory studies; close follow-up of these patients is required (eg, daily laboratory studies, clinical evaluation).

**Complications of Exposure:** No information available

**Contraindications:** No information available

**References:**
3. www.lexi.com