Moth repellent toxicosis
Camille DeClementi, VMD

Between 2002 and 2004, ASPCA Animal Poison Control Center (APCC) staff members consulted on 158 cases of moth repellent ingestion. In most instances, the exposure was oral, but dermal and inhalation exposures were also reported. Naphthalene was the active ingredient in 83% of the cases, and paradichlorobenzene was the active ingredient in 17%. Naphthalene, a bicyclic aromatic hydrocarbon, is a natural component of fossil fuels, such as petroleum and coal. It is also produced when wood and tobacco are burned. Paradichlorobenzene, an organochlorine insecticide, is considered to be half as toxic as naphthalene. Many moth repellent products contain nearly 100% naphthalene or paradichlorobenzene. The products can be formulated into balls, crystals, or flakes.

Pharmacokinetics

Naphthalene evaporates easily and has a strong odor that repels moths. People can detect it in the air at concentrations of 84 ppb. Naphthalene can be inhaled, ingested, or absorbed transdermally. It is soluble in oils and fats, so dermal absorption is increased if oils have been previously applied to the skin. Similarly, oral absorption increases when naphthalene is coadministered with a fatty product such as corn oil. Paradichlorobenzene also has a characteristic penetrating odor and is well-absorbed orally and by inhalation. As with naphthalene, drinking milk or eating a fatty meal after oral exposure to paradichlorobenzene increases its absorption. Mothballs of either type may take several days to dissolve in the gastrointestinal tract, so prolonged absorption is possible.

Naphthalene is carried to other organs once it enters the bloodstream, regardless of the absorption route. After a single dose of naphthalene in pigs, the highest concentration of naphthalene was found in adipose tissue. The kidneys, liver, and lungs contained the next highest concentrations, respectively. But pigs given multiple doses of naphthalene had the highest concentrations in the lungs with little in adipose tissue. The highest tissue concentrations of paradichlorobenzene are found in adipose tissue. Both naphthalene and paradichlorobenzene are found in milk and are able to cross the placenta.

The metabolism of naphthalene is complex. The initial metabolite, a 1,2-oxide, is produced in the liver by the monooxygenase enzymes (P450). Naphthalene 1,2-oxide can then form epoxides or quinones that may cause cellular damage, or it can be conjugated with glutathione to nontoxic metabolites. Additionally, some metabolites are conjugated with sulfate or glucuronic or mercapturic acid. Paradichlorobenzene is oxidized to phenolic compounds and then undergoes rapid conjugation with sulfate and glucuronide. The metabolites of both naphthalene and paradichlorobenzene are excreted primarily through urine, but some metabolites are excreted in bile.

Toxicity

Paradichlorobenzene is considered less toxic than naphthalene. In rats, the oral LD₅₀ of naphthalene is 1.8 g/kg, whereas the oral LD₅₀ of paradichlorobenzene is 3.8 g/kg. Dogs ingesting 1.5 g/kg of paradichlorobenzene did not develop clinical signs of toxicosis, but hemolytic anemia was reported in a dog that received a single 1.525-mg/kg dose of naphthalene and in another dog that received about 263 mg/kg/day naphthalene for seven days. One mothball of either type weighs about 5 g. Less than one naphthalene mothball may cause clinical signs of toxicosis in children, but accidentally ingesting up to one paradichlorobenzene mothball is generally well-tolerated.

Clinical signs of toxicosis

Naphthalene
Hematologic effects have been reported in dogs after naphthalene ingestion, and cataracts have developed in laboratory animals. In the ASPCA APCC database, the most commonly reported clinical signs after ingesting naphthalene-containing moth repellent products were vomiting, lethargy,
and anorexia (ASPCA APCC Database: Unpublished data, 2004). Seizures and methemoglobinemia were also reported.

In people, oral exposure to naphthalene can cause gastrointestinal signs, including vomiting, nausea, abdominal pain, and diarrhea. Hemolytic anemia and cataract formation have also been reported. An association exists between glucose-6-phosphate dehydrogenase deficiency and the hematologic effects of naphthalene. Inhaling naphthalene can also cause hemolysis and gastrointestinal effects in people.

Paradichlorobenzene

In the ASPCA APCC database, the clinical signs reported after ingestion of paradichlorobenzene-containing moth repellent products were vomiting and trembling (ASPCA APCC Database: Unpublished data, 2004). A bird that had inhaled paradichlorobenzene showed depression, head bobbing, weakness, and anorexia. The bird recovered with symptomatic treatment including force-feeding, thermoregulation, and confinement. Long-term oral exposure studies in laboratory animals showed no hematologic or ocular effects with paradichlorobenzene, but liver and renal changes were noted. Additionally, neurologic signs including weakness, ataxia, and tremors were noted in rats receiving doses between 770 and 1,200 mg/kg/day for at least five days.

In people, paradichlorobenzene ingestion can cause nausea and vomiting. Hepatotoxicity is also possible but uncommon after large oral exposures. Paradichlorobenzene vapors are irritating to the nose and eyes, and central nervous system depression may occur at concentrations that are extremely objectionable. With dermal contact, the solid material produces a burning sensation but causes only slight skin irritation. Paradichlorobenzene has less potential for hematologic damage than naphthalene, but methemoglobinemia was seen in one pediatric patient, and anemia has been seen with long-term exposures. Paradichlorobenzene may cause cataract formation.

Treatment

When treating moth repellent exposure, assess and stabilize the patient. If the patient is dyspneic, provide supplemental...
oxygen and place an intravenous catheter. Initiate decontamination procedures if the patient is stabilized and provide supportive care. Fluid therapy is recommended in symptomatic animals. Induce emesis only in asymptomatic patients and only if ingestion occurred less than two hours before presentation and no contraindications to inducing emesis exist. Dogs, cats, ferrets, and potbellied pigs can vomit, but rodents, rabbits, birds, horses, and ruminants cannot. After the vomiting has subsided, administer activated charcoal (1 to 2 g/kg orally) and a saline cathartic (250 mg/kg magnesium sulfate or sodium sulfate orally).\textsuperscript{9} Administering activated charcoal with a cathartic may be beneficial up to 24 hours after mothball ingestion because mothballs dissolve slowly in the gastrointestinal tract.\textsuperscript{2}

In general, naphthalene ingestion requires more aggressive treatment than paradichlorobenzene. If the type of mothball ingested is unknown and the owner has brought in a sample, perform the following test. Add three heaping tablespoons of table salt to tepid water, and mix vigorously until the salt will no longer dissolve. Place the mothball in the saturated salt water. Naphthalene mothballs float, and paradichlorobenzene mothballs sink.\textsuperscript{10}

Obtain a baseline complete blood count and serum chemistry profile. Address any gastrointestinal signs. Vomiting may be controlled by administering metoclopramide hydrochloride (dogs and cats 0.2 to 0.5 mg/kg orally, intramuscularly, or subcutaneously t.i.d.\textsuperscript{11}) or another standard antiemetic. Sucralfate (1 g for large dogs, 0.5 g for small dogs orally t.i.d.; 0.25 g orally b.i.d. to t.i.d. for cats\textsuperscript{11}) can be used to relieve gastrointestinal irritation. Additionally, consider adding a medication to decrease gastric acid production, such as the H\textsubscript{2} antagonist famotidine (dogs and cats 0.5 to 1 mg/kg orally, subcutaneously, or intramuscularly once or twice a day\textsuperscript{11}) or proton-pump inhibitor omeprazole (dogs 0.5 to 1 mg/kg orally once a day; cats 0.7 mg/kg orally once a day\textsuperscript{11}).

Seizures may be controlled with diazepam (dogs and cats 0.5 to 1 mg/kg intravenously to effect\textsuperscript{11}). Blood transfusions or polymerized bovine hemoglobin glutamer-200 (Oxyglobin—Biopure) (dogs single dose of 30 ml/kg intravenously at a rate of up to 10 ml/kg/hr; not labeled for use in cats\textsuperscript{11}) may be needed in patients with severe methemoglobinemia.

Methemoglobinemia occurs when oxidative injury to hemoglobin leads to conversion of the heme from the ferrous to the ferric state. Methemoglobin is incapable of carrying oxygen. The blood of patients with methemoglobinemia is a characteristic chocolate-brown color, and their mucous membranes may appear brown. Methemoglobinemia is reversible, and the body has enzyme systems that reduce methemoglobin back to hemoglobin. Treatment is required when the body’s enzyme systems become overloaded and clinical signs of hypoxia develop. Patients become symptomatic when 20% to 30% of their hemoglobin has been converted to methemoglobin.\textsuperscript{12}

Methemoglobinemia has been treated in dogs and cats with ascorbic acid (20 mg/kg orally, intramuscularly, or subcutaneously up to every six hours\textsuperscript{[10,13]} or methylene blue (1.5 mg/kg slowly intravenously as a 1\% solution\textsuperscript{[10,14]}). Ascorbic acid is thought to reduce methemoglobin to hemoglobin by a nonenzymatic reserve mechanism that the body uses when the enzyme systems normally responsible for the reduction are overloaded.\textsuperscript{13} This conversion is relatively slow,\textsuperscript{10} so ascorbic acid may not be useful for seriously affected patients unless it is used in conjunction with other treatments. Methylene blue acts rapidly and works through its conversion to leucomethylene blue in the tissues. Leucomethylene blue acts as a reducing agent in the conversion of methemoglobin to hemoglobin. Because methylene blue is an oxidizing agent, increased methemoglobinemia is a possible adverse effect.\textsuperscript{11}

Cats are reported to be at an increased risk for this adverse effect because of their unusual hemoglobin structure, so methylene blue use in cats is considered controversial.\textsuperscript{11,12}

\textit{N}-Acetylcysteine may also be helpful in treating naphthalene- or paradichlorobenzene-induced methemoglobinemia, but it has not been recommended in the literature for this purpose. Acetylcysteine is a precursor in the synthesis of glutathione, or it can be oxidized to organic sulfate that is used in the sulfate conjugation pathway. Acetylcysteine is regularly administered to patients with acetaminophen toxicity to reduce methemoglobinemia by providing an alternative substrate for conjugation with the metabolites of acetaminophen and maintaining glutathione concentrations\textsuperscript{[11,15]} Based on its mechanism of action, acetylcysteine may also help maintain glutathione and sulfate concentrations during naphthalene or paradichlorobenzene toxicosis. Acetylcysteine is available in 10\% and 20\% solutions; it should be diluted to a 5\% solution, using 5\% dextrose solution or sterile water, before use. Administer an initial loading dose of 140 mg/kg, followed by 70 mg/kg orally every six hours for seven treatments. When given orally, acetylcysteine may cause gastrointestinal upset.\textsuperscript{11} Proper dilution can decrease the chances of gastrointestinal upset developing. Acetylcysteine is not labeled for intravenous use, but it...
can be given intravenously in severely affected patients or patients showing signs of gastrointestinal upset. Administer intravenous acetylcysteine slowly over 15 to 20 minutes through a bacteriostatic (0.2-µ) filter.10

Prognosis

The prognosis for patients exposed to naphthalene- or paradichlorobenzene-containing moth repellents is favorable if the clinical signs are treated and no underlying patient factors, such as liver disease or conditions causing anemia, are present. Therapy and monitoring should continue until the clinical signs have resolved and complete blood count and serum chemistry profile results have returned to normal.

REFERENCES

14. Rumbeha WK, Oehme FW. Methylene blue can be used to treat methemoglobinemia in cats without inducing Heinz body hemolytic anemia. Vet Hum Toxicol 1992;34:120-122.