

## DEET Insect Repellent Toxicity

### Introduction

DEET (N,N-diethyl-3-methylbenzamide) was developed by the military as an insect repellent in 1946 and introduced for public use in 1957.<sup>1</sup> It has broad-spectrum activity and effectively repels most mosquitoes, biting flies, chiggers, fleas and ticks. It is the most effective insect repellent available for human use.<sup>2</sup> Currently, DEET is formulated in aerosols, pump sprays, lotions, creams, liquids, sticks, roll-ons and impregnated towelettes, with concentrations ranging from 5% to 100%. There is widespread use of products containing DEET due to the increasing incidence of West Nile Virus in the United States and recommendations by the Centers for Disease Control that it is the preferred insect repellent. It is estimated that 30% of the population in the United States applies DEET each year.<sup>1</sup> The widespread use, concern for mosquito-borne viruses, and media attention, have rekindled interest in DEET and its potential toxicities.<sup>3</sup>

### Pharmacology/Pharmacokinetics

DEET is absorbed through the skin. Dermal absorption depends on the concentration and solvents in the formulation. In one study, an average of 5.6% of the total dose was absorbed following the dermal application of 100% DEET. After application of 15% DEET in ethanol, the average absorption was 8.4%. Systemic absorption began within two hours of topical application.<sup>4</sup> Dermal absorption of DEET may also vary by age and body mass. Infants less than 2 months of age have a larger surface area to body mass ratio and can more easily attain elevated plasma concentrations. Absorption can also be increased when DEET is applied to broken skin. When DEET is formulated with ethanol, absorption may also be increased as ethanol enhances permeability of the skin.<sup>3,4</sup> Absorption decreases under conditions of perspiration and elevated body temperature.<sup>2</sup>

DEET distributes into skin and fatty tissues but does not accumulate in the superficial layers of the skin. Following removal of DEET from the surface of the skin, the remaining product in the lower layers of the dermis is absorbed, metabolized and excreted in the urine. The rate of elimination of DEET after topical application is faster than the rate of absorption, and elimination has been found to be complete within 12 hours of removal. Six main metabolites,

none of which are known to be toxic, have been isolated in human urine, however two metabolites predominate. DEET undergoes oxidation by cytochrome P450 2B6 and 1A2 to form N, N-diethyl-m-hydroxymethylbenzamide, while dealkylation by cytochrome P450 2C19 and 3A4 forms N-ethyl-m-toluamide. The primary route of elimination is through the urine, with negligible elimination in the feces.<sup>4</sup> The metabolism of DEET may change in response to large exposures; more of the parent compound is excreted unchanged in the urine and several additional metabolites may be present in the urine.<sup>3</sup>

The concentration of DEET and the protection time it provides are directly related, although the protection time reaches a plateau when the concentration approaches 50%. Controlled-release formulations do not prolong the time of protection, but alcohol-based formulations have been shown to increase time of protection.<sup>2</sup> There is little information available about oral absorption. Severe symptoms have appeared within 30 minutes of ingestion, which implies rapid GI absorption.

### Adverse Effects

DEET has few adverse effects when applied as directed. The most common problem is local skin irritation, including erythema and pruritis, at the site of application. One case of anaphylaxis after brief exposure to DEET has been reported.<sup>1</sup> When the patient was re-exposed to DEET in an emergency department she experienced similar symptoms of anaphylaxis. Many people, including military and forest service personnel, apply high concentrations of DEET on a daily basis and have developed more severe adverse effects due to chronic exposure. These adverse effects included insomnia, muscle cramps, mood disturbances and rashes.<sup>1</sup>

### Clinical Toxicology/Toxicokinetics

The toxicity of DEET is largely dependent upon the route of exposure and dose. The most common unintentional route of exposure is ocular as many DEET formulations are sprays or liquids.<sup>5</sup> DEET causes local irritation and discomfort when introduced into the eyes or oral cavity.<sup>6</sup> DEET has not been shown to cause severe, long-term damage to the eye in animals.<sup>7</sup>

Ingestions of DEET have been associated with nausea, vomiting, hypotension, encephalopathy, seizure, coma, and ataxia.<sup>6</sup> Ingestion of 50 mL of 100% DEET by a 33 year-old woman resulted in hypotension, coma, seizures and death. Ingestion of 25 mL of 50% DEET by a one-year-old child resulted in coma and seizures.<sup>8</sup> Small ingestions of DEET, such as unintentionally spraying the product into the mouth, usually do not cause toxic effects. Excessive dermal application of DEET to large areas of the body over a period of days to weeks, especially in children, has led to seizures, bradycardia, nausea, vomiting, bullous eruptions, lethargy, ataxia, encephalopathy and anaphylaxis.<sup>6</sup>

Neurotoxicity is the most commonly reported systemic toxic effect of DEET and the mechanism is unknown. It has been suggested that DEET may induce neuronal apoptosis or disrupt the permeability of the blood-brain barrier, but neither of these hypotheses have been proven.<sup>3</sup> There are multiple case reports describing seizures after exposure to DEET but many of these cases have few details and too many confounding variables to establish absolute causation.<sup>1</sup> While the majority of reports involve large exposures, there are several reports of seizures following brief exposures to DEET. One case report of seizure following a brief exposure involved a normally healthy 5 year-old boy who applied DEET over his entire body in the form of Muskol® (95% DEET) in the morning and Off® (unknown DEET concentration) later on in the day. The boy experienced a seizure, which was successfully treated with diazepam, and respiratory arrest, which was managed by intubation and ventilation. He recovered without sequelae.<sup>9</sup>

## Pregnancy/Lactation Issues

Animal studies have not shown DEET to be a teratogen even after long-term use. A study performed in Thailand on pregnant women in their second and third trimesters using DEET as malaria protection showed no difference in adverse effects on mother or child between the DEET and placebo group.<sup>10</sup> DEET can cross the placenta when used long-term, but the exposure to the fetus has not proven to be significant.<sup>3,10</sup> The CDC recommends that DEET should be used in pregnant and lactating women to protect themselves and their fetus from potentially life-threatening diseases carried by mosquitoes and other vectors.<sup>3</sup>

## Treatment

Treatment of DEET exposure consists of decontamination and supportive care. Up to 85% of DEET exposures reported to the American Association of Poison Control Centers between 1993-1997 were managed on-site in a non-health care facility.<sup>11</sup> After ocular exposure the eyes should be irrigated

from the eye with lukewarm water for 15 minutes. Patients with persistent eye irritation or pain should be evaluated for corneal injury or chemical conjunctivitis. Following large dermal exposure, the area should be washed 2-3 times with soap and water or an alcohol-detergent solution such as "green soap". Inducing emesis is not recommended, but gastric aspiration via nasogastric tube followed by activated charcoal may be of benefit if large quantities are ingested and the patient presents within one hour of ingestion.

Ingestion or dermal application of DEET rarely causes seizures, but when seizures occur diazepam or another benzodiazepine should be utilized. Other supportive therapies such as anti-emetics for nausea and vomiting, intravenous fluids and vasopressors for hypotension, and antihistamines for severe skin irritation may be useful. There is no specific antidote available for treatment of DEET toxicity.

## Summary

Approximately 30% of the population applies DEET as protection against West Nile Virus and other mosquito-borne viruses and the number of toxic exposures associated with DEET is extremely low in relation to the large number of people who apply it.<sup>1,5,11</sup> Many exposures lead to mild irritation of the skin or eyes and can be managed at home.<sup>5,11</sup> The neurotoxicity associated with DEET is rare but may occur with large exposures.<sup>3</sup> Treatment consists of decontamination and supportive care. DEET is safe to use as directed in the general public, including pregnant and lactating women as well as children 2 months and older.<sup>3,10</sup>

### Recommended Application Guidelines<sup>12,13</sup>

- Apply DEET product only when planning to be outdoors in a mosquito-infested area.
- Use the appropriate concentration of DEET. Children and adults in the general public should use 30% or less. A product with a concentration of 10% or less may be more appropriate for children under 12 years.
- Do not apply DEET to children under 2 months of age.
- When using on children, apply to your own hands and then put it on the child.
- Do not apply to children's hands.
- Do not allow children to handle products containing DEET.
- Do not apply over cuts, wounds, or irritated skin.
- Do not apply near eyes and mouth. Apply sparingly around ears.
- Reapply DEET only as directed by packaging. The effective duration depends on the concentration of DEET in product.

The Utah Poison Control Center expresses its sincere thanks to

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for their generous contribution that allows us to produce and distribute this newsletter.

- Use just enough repellent to cover exposed skin/and or clothing.
- Do not use on skin under clothing.
- Avoid over-application of DEET products.
- After returning indoors, wash treated skin with soap and water.
- Wash treated clothing before wearing it again.
- Do not apply a combination product containing sunscreen and DEET.
- Do not spray aerosol or pump products in enclosed areas.
- Do not apply aerosol or pump products directly to your face. Spray your hands and then rub them carefully over the face, avoiding eyes and mouth.

Marianne Mabey, PharmD

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## Mosquito Repellent Update from the CDC

For the past several years, DEET was the primary insect repellent that the CDC recommended as safe and effective for general public use. On April 22, 2005, the CDC issued a statement adding oil of lemon eucalyptus [p-methane 3,8-diol (PMD)], a plant based repellent in various products, and picaridin (Spectrum Brands Cutter Advanced) to the list. They provide protection similar to repellents with low concentrations of DEET. Oil of lemon eucalyptus should not be used on children under the age of three years. We could find no reported cases of human toxicity to lemon eucalyptus; however, its use has been limited so the incidence and types of adverse effects are not fully studied yet. Ingestion of "oil of

eucalyptus", containing cineole, eucalyptol, and terpenes, is toxic and has resulted in epigastric pain, vomiting and CNS depression within 30 minutes. Bronchospasm, acute lung injury, and seizures may also occur.

<http://www.cdc.gov/ncidod/dbbid/westnile/RepellentUpdates.htm>  
Accessed May 4, 2005

## National Poison Prevention Week Utah Poison Control Center Activities for 2005

The Utah Poison Control Center (UPCC) conducted an extensive statewide poison awareness mailing. Two thousand introductory letters announcing National Poison Prevention Week were sent to pediatricians, pharmacists, health educators, and day care providers. Those letters generated requests for over 76,000 educational publications and over 40,000 stickers and magnets. Many pharmacies conducted their own poison prevention activities using the materials from the UPCC. A press release was distributed statewide. Poison center staff appeared on local TV and radio stations to raise awareness and remind the public of the importance of keeping potential harmful products out of reach of children. The Governor Jon M. Huntsman, signed a proclamation declaring Poison Prevention Week in Utah.



## New Employees

The Utah Poison Control Center is pleased to welcome Julie Gerstner as our new administrative assistant. Julie has been working for the University of Utah Biology Department for the past 13 years. Welcome!

## Meet the UPCC Staff



Mary received her B.S.N. from St. Louis University in 1980 and her M.S. as a Family Nurse Practitioner at the University of Utah in 1996. She has worked for most of her career in critical care, cardiology, dialysis and ER, including several years at the University Hospital on 4 North, the ICU cluster, dialysis and neuro critical care.

For a brief respite from healthcare, she owned and operated a restaurant and microbrewery in Idaho and is still interested in the beneficial uses of bacteria. She recently moved back to SLC from Lake of the Ozarks, Missouri, where she worked as a cardiology nurse practitioner, to be closer to her family. Her interests include reading, cooking, travel, art, home remodeling, and the study of how millionaires and champions succeed. Favorite toxicology situations involve sibling rivalry and getting suicidal patients to the ER.

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\*CSPI denotes Certified Specialist in Poison Information.

## Employment Opportunities

The UPCC has an open position available. You can find out more about this position on our website at <http://uuhsc.utah.edu/poison/employment>.

## M-44 Sodium Cyanide Device

The United States Department of Agriculture, Animal and Plant Health Inspection Service, Bureau of Wildlife Services would like us to remind you that the M-44 sodium cyanide device is used in Utah. The device is tubular and is placed in the ground with 1.5 inches sticking out of the ground baited with meat. This device is used in specific situations to control coyotes, redfox, gray fox and wild dogs. The purpose of the device is to protect livestock, poultry, and endangered species and to prevent the spread of disease. Although this device is primarily used on private lands, it may also be used on federal land in any county in the state. Areas where it is used are marked with signs. While human exposure to this device would be extremely unlikely, it is important to know that this device contains 91% sodium cyanide. Please report any exposure to this device to the Utah Poison Control Center at (800) 222-1222. We thank you in advance for your assistance.

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