Mosquitoes and Mosquito Repellents: A Clinician's Guide

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This paper is intended to provide the clinician with the detailed and scientific information needed to advise patients who seek safe and effective ways of preventing mosquito bites. For this review, clinical and analytical data were selected from peer-reviewed research studies and review articles, case reports, entomology texts and journals, and government and industry publications. Relevant information was identified through a search of the MEDLINE database, the World Wide Web, the Mosquito-L electronic mailing list, and the Extension Toxicology Network database; selected U.S. Army, U.S. Environmental Protection Agency, and U.S. Department of Agriculture publications were also reviewed.

N,N-diethyl-3-methylbenzamide (DEET) is the most effective, and best studied, insect repellent currently on the market. This substance has a remarkable safety profile after 40 years of worldwide use, but toxic reactions can occur (usually when the product is misused). When DEET-based repellents are applied in combination with permethrin-treated clothing, protection against bites of nearly 100% can be achieved. Plant-based repellents are generally less effective than DEET-based products. Ultrasonic devices, outdoor bug "zappers," and bat houses are not effective against mosquitoes. Highly sensitive persons may want to take oral antihistamines to minimize cutaneous reactions to mosquito bites.

This paper is also available at http://www.acponline.org.

Ann Intern Med. 1998;128:931-940.

The quest to make humans less attractive to mosquitoes has fueled decades of scientific research on mosquito behavior and control. In the United States, mosquito bites are mostly a nuisance. Worldwide, however, mosquitoes transmit disease to more than 700 000 000 people annually and will be responsible for the deaths of 1 of every 17 people currently alive (1). Malaria results from infection with a protozoan carried by mosquitoes and, according to reports from the World Health Organization, causes as many as 3 000 000 deaths annually (2). Mosquitoes transmit the arboviruses responsible for yellow fever, dengue hemorrhagic fever, epidemic polyarthritis, and several forms of encephalitis (some of which are found in the United States). Bancroftian filariasis is caused by a nematode transmitted by mosquito bite.

Historically, the strategies for reducing the incidence of mosquito-borne disease have been two-pronged, centering around habitat control (through chemical and biological means) and the use of personal protection in the form of insect repellents. This paper reviews the scientific data on chemical (synthetic) and natural (plant-derived) insect repellents currently available, debunks some of the popular myths about alternative repellents, reviews effective techniques for reducing mosquito populations in the local environment, and provides the clinician with the practical information needed to advise patients on how to safely and effectively reduce their likelihood of being bitten by mosquitoes.

Methods

By doing a MEDLINE search with the keywords *DEET, insect repellents, mosquito, citronella,* and *permethrin,* pertinent articles published in English-language journals between 1966 and 1997 were identified and reviewed. The World Wide Web and the Extension Toxicity Network database were also searched for toxicology data and other pertinent information. Selection from the bibliographies of relevant articles augmented the database search. Major distributors of natural insect repellents were contacted and asked to provide scientific data, if available, supporting the efficacy of their products.

The Mosquito Life Cycle

Mosquitoes are found all over the world, except in Antarctica. These two-winged insects belong to the order Diptera. Members of the genera *Anopheles*, *Culex*, and *Aedes* are most commonly responsible for bites in humans. There are approximately 170 species of mosquitoes in North America alone.

To develop, mosquitoes require an environment of standing water. As a group, they have adapted to complete their life cycle in diverse aquatic habitats, including fresh water; salt water marshes; brackish water; or water found in containers, old tires, or tree holes. The life cycle of the mosquito has four stages. The female mosquito lays her eggs, up to several hundred at a time, on the surface of the water or in an area subject to flooding. Unhatched eggs of some species can withstand weeks to months of desiccation, remaining viable until the right conditions for hatching occur. The eggs of most species hatch in 2 to 3 days, and the larvae feed on organic matter in the water for about a week until they change into pupae. The pupae live at the surface of the water for 2 to 3 days before metamorphosing into adult mosquitoes.

Only female mosquitoes bite. Male mosquitoes feed primarily on flower nectar, whereas female mosquitoes require a blood meal to produce eggs. They usually feed every 3 to 4 days; in a single feeding, a female mosquito typically consumes more than its own weight in blood (3). Certain species of mosquitoes prefer to feed at twilight or nighttime; others bite mostly during the day.

Some mosquito species are zoophilic (preferring to feed on animals) and others are anthropophilic (showing a preference for human blood). In some mosquito species, seasonal switching of hosts provides a mechanism for transmitting diseases from animal to human. (It is worth noting, however, that mosquitoes cannot transmit HIV because the virus neither survives nor replicates in mosquitoes and the blood from the last bitten person is not flushed into the next person during subsequent feeds. In addition, the circulating viral load of most HIV-infected persons is so low that the theoretical risk that a mosquito bite would transmit HIV is estimated to be less than 1 in 10 000 000 [4, 5].)

Stimuli That Attract Mosquitoes

The factors involved in attracting mosquitoes to a host are complex and are not fully understood (6–11). Mosquitoes use visual, thermal, and olfactory stimuli to locate a host. Of these, olfactory cues are probably most important. For mosquitoes that feed during the daytime, movement of the host and the wearing of dark-colored clothing may initiate orientation toward a person (3, 12). Visual stimuli seem to be important for in-flight orientation, particularly over long ranges, whereas olfactory stimuli become more important as a mosquito nears its host.

It has been estimated that 300 to 400 compounds are released from the body as by-products of metabolism and that more than 100 volatile compounds can be detected in human breath (9). Of these odors, only a fraction have been isolated and fully characterized. Carbon dioxide and lactic acid are the two best-studied mosquito attractants. Carbon dioxide, released mainly from breath but also from skin, serves as a long-range airborne attractant and can be detected by mosquitoes at distances of up to 36 meters (3, 13–15). Lactic acid, in combination with carbon dioxide, is also an attractant. Mosquitoes have chemoreceptors on their antennae that are stimulated by lactic acid. These same receptors may be inhibited by N,N-diethyl-3-methylbenzamide (DEET)–based insect repellents (16).

At close range, skin temperature and moisture serve as attractants (3, 9, 17). Different species of mosquitoes may show strong biting preferences for different parts of the human body (such as the head or feet), which may be related to local skin temperature and eccrine sweat gland output (18, 19). Anhidrotic persons show markedly decreased attractiveness to mosquitoes (6). Other volatile compounds, derived from sebum, eccrine and apocrine sweat, or the cutaneous microflora bacterial action on these secretions, may also act as chemoattractants (6, 20, 21). Whole-host odors are more attractive than carbon dioxide and lactic acid alone (22). Floral fragrances from perfumes, soaps, lotions, and hair-care products may also attract mosquitoes (23).

The attractiveness of different persons to the same or different species of mosquitoes varies substantially (17, 24). In general, adults are more likely to be bitten than children (17, 25), although adults may become less attractive to mosquitoes as they age (6). Men are bitten more readily than women (3, 26). Larger persons tend to attract more mosquitoes, perhaps because of their greater relative heat or carbon dioxide output (27).

Insect Repellents

Despite the obvious desirability of finding an effective oral mosquito repellent, no such agent has been identified (28, 29). Thus, the search for the perfect topical insect repellent continues. This ideal agent would repel multiple species of biting arthropods, remain effective for at least 8 hours, cause no irritation to the skin or mucous membranes, cause no systemic toxicity, be resistant to abrasion and rub-off, and be greaseless and odorless. No available insect repellent meets all of these criteria.

Efforts to find such a compound have been hampered by the numerous variables that affect the inherent repellency of any chemical. Repellents do not all share a single mode of action, and surprisingly little is known about how repellents act on their target insects (30, 31). Moreover, different species of mosquitoes may react differently to the same repellent (32).

To be effective, a repellent must show an optimal degree of volatility, making it possible for an effective repellent vapor concentration to be maintained at the skin surface without evaporating so quickly that it loses its effectiveness. Many factors play a role in how effective any repellent is, including the frequency and uniformity of application, the number and species of the organisms attempting to bite, the user's inherent attractiveness to blood-sucking arthropods, and the overall activity level of the potential host (33). Abrasion from clothing, evaporation and absorption from the skin surface, wash-off from sweat or rain, higher temperatures, or a windy environment all decrease repellent effectiveness (17, 34–37). Each 10 °C increase in temperature can

Table 1. Repellents That Contain DEET*

Manufacturer, Location, Telephone Number	Product Brand Name	Available Forms	Concentration of DEET, %†
Amway Corp., New York, New York			
800-544-7167	HourGuard 8	Aerosol spray	25.0
	HourGuard 12	Cream	35.0
Minnetonka Brands, Inc., Eden Prairie, Minnesota			
800-243-2929	Skedaddle Insect Protection for Children	Lotion	6.5
	Skedaddle for Children with Sunscreen (SPF 15)	Lotion	6.5
	Skedaddle 4-Hour Insect Protection	Lotion	10.0
Sawyer Products, Tampa, Florida			
800-940-4464	DEET Plus	Lotion, pump spray	17.5
	Sawyer Gold	Lotion, pump spray	17.5
	Sawyer 30	Lotion	30.0
	Deet Plus	Spray aerosol	38.0
	Maxi-DEET	Solution, pump spray	100.0
S.C. Johnson Wax, Racine, Wisconsin			
800-558-5566	OFF! Skintastic for Kids Unscented	Pump spray	5.0
	OFF! Skintastic Unscented	Pump spray	7.0
	OFF! Skintastic Fresh Scent	Lotion	7.5
	OFF! Skintastic Unscented	Lotion	7.5
	OFF! Unscented	Aerosol spray	15.0
	Deep Woods OFF! Unscented	Aerosol spray	30.0
	Deep Woods OFF! for Sportsmen	Aerosol spray	30.0
	Maximum Protection Deep Woods OFF!	Pump spray	100.0
	Deep Woods OFF! for Sportsmen	Pump spray	100.0
Tender Corp., Littleton, New Hampshire			
800-258-4696	Ben's Backyard	Lotion, pump spray	24.0
	Ben's Wilderness	Aerosol	27.0
	Ben's Max 100	Lotion, pump spray	100.0
United Industries Corp., St. Louis, Missouri			
800-767-9927	Cutter Just for Kids	Pump spray	5.0
	Cutter Pleasant Protection with Sunscreen (SPF 15)	Aerosol, pump spray	7.0
	Cutter Unscented	Aerosol spray	10.0
	Cutter Lotion with Sunscreen (SPF 15)	Lotion	10.0
	Cutter Backwoods Unscented	Aerosol spray	23.0
	Cutter Outdoorsman Unscented	Aerosol spray, lotion, stick	30.0
Wisconsin Pharmacal Co., Jackson, Wisconsin			
800-558-6614	Repel Soft Scented	Gel	7.0
	Repel Camp Lotion for Kids	Lotion	10.0
	Repel Soft Scented	Pump spray	18.0
	Repel Family Formula	Pump spray	18.0
	Repel Sportsman Formula	Pump spray	18.0
	Repel Unscented Sun Block (SPF 15)	Lotion	20.0
	Repel Sportsman Formula	Lotion	20.0
	Repel Soft Scented	Lotion	20.0
	Repel Family Formula	Aerosol	23.0
	Repel Classic Sportsman Formula	Aerosol	40.0
	Repel 100	Pump spray	100.0

* DEET = N,N-diethyl-3-methylbenzamide; SPF = sun protection factor.
† Some manufacturers give only the concentration of the m-isomer; others list total concentrations of all DEET isomers. Technical-grade 100% DEET comprises 95% m-isomer and 5% other isomers.

lead to as much as a 50% reduction in protection time (37). The repellents currently available must be applied to all exposed areas of skin; unprotected skin a few centimeters away from a treated area can be attacked by hungry mosquitoes (33, 35).

Chemical Insect Repellents

N,N-Diethyl-3-Methylbenzamide (DEET)

Previously called N,N-diethyl-m-toluamide, N,N-diethyl-3-methylbenzamide (DEET) remains the gold standard of currently available insect repellents. This substance was discovered and developed by scientists at the U.S. Department of Agriculture and was patented by the U.S. Army in 1946. It was subsequently registered for use by the general public in 1957. It is a broad-spectrum repellent that is effective against mosquitoes, biting flies, chiggers, fleas, and ticks. Twenty years of empirical testing of more than 20 000 other compounds has not resulted in another marketed chemical product with the duration of protection and broad-spectrum effectiveness of DEET (30, 33, 38–41). The U.S. Environmental Protection Agency (EPA) estimates that more than 38% of the U.S. population uses a DEET-based insect repellent every year and that worldwide use exceeds 200 000 000 people annually (42).

Formulation of Available Products with DEET

In the United States, DEET is available in 5% to 100% concentrations in multiple formulations, including solutions, lotions, creams, gels, aerosol and pump sprays, and impregnated towelettes (**Table 1**).

Until 1989, the standard-issue insect repellent of

Table 2. Suggested Guidelines for Safe Use of Insect Repellents*

Use just enough repellent to lightly cover the skin; do not saturate the skin
Repellents should be applied only to exposed skin, clothing, or both. Do not use under clothing
To apply to the face, dispense into palms, rub hands together, and apply thin layer to face
Avoid contact with eyes and mouth. To prevent subsequent contact with mucous membranes, do not apply repellent to children's hands
After applying, wipe repellent from the surfaces of the palms to prevent inadvertent contact with eyes, mouth, and genitals
Never use repellents over cuts, wounds, inflamed, irritated, or eczematous skin
Do not inhale aerosol formulations or get in eyes
Frequent reapplication of repellent is unnecessary
Once inside, wash treated areas with soap and water

* Adapted from reference 55.

the U.S. military consisted of 75% DEET in an alcohol base. Complaints about the aesthetic feel of this product and concerns about potential toxicity under long-term daily use led to U.S. Army–sponsored studies to produce new formulations. The 3M Company (St. Paul, Minnesota) developed a slow-release, polymer-based product containing 35% DEET; this has become the repellent provided to all U.S. military personnel. This product is available to the general public exclusively through the Amway Corporation (New York, New York) under the brand name HourGuard (**Table 1**). If lower-strength formulations of extended-release DEET are desired, Minnetonka Brands (Eden Prairie, Minnesota) offers products containing 6.5% and 10% DEET (**Table 1**).

Efficacy

As a general rule, higher concentrations of DEET provide longer-lasting protection. Unfortunately, no guidelines are available to help consumers decide what concentration of DEET is appropriate for their specific needs. The number of variables that affect a repellent's effectiveness precludes assigning an "insect repellent factor" to individual products.

Mathematical models of the effectiveness and persistence of mosquito repellents show that the protection offered by a repellent is proportional to the logarithm of the dose (concentration of the product). This curve tends to form a plateau at higher repellent concentrations, providing relatively less additional protection for each incremental dose of DEET that exceeds a 50% concentration (43, 44). In one laboratory study, 50% DEET provided about 4 hours of protection against *Aedes aegypti* mosquitoes, but increasing the DEET concentration to 100% provided only 1 additional hour of protection (45). In another study, 12.5% DEET provided over 6 hours of protection against *Aedes albopictus*; doubling the DEET concentration to 25% increased the protection time only to about 8 hours (46).

Extended-release formulations of DEET have made it possible to reduce the repellent concentration without sacrificing duration of action. When tested under laboratory and several different environmental and climatic field conditions, the 35% DEET polymer formulation by the 3M Corporation was as effective as 75% DEET in repelling mosquitoes (19, 47–50). The polymer formulation provided up to 12 hours of more than 95% protection, depending on the environmental conditions and species of mosquito tested (46, 48, 49, 51). One study showed that Minnetonka Brands' 6.5% liposphere microdispersion of DEET was effective for up to 2.5 hours and that their 10% product was effective for about 1 hour longer (52).

How To Choose and Apply DEET Repellents

For casual use, a high concentration of DEET is not needed. Products with 10% to 35% DEET will provide adequate protection under most conditions. The American Academy of Pediatrics recommends that repellents used on children contain no more than 10% DEET (53, 54). Products with a DEET concentration of more than 50% are probably best reserved for circumstances in which insect biting pressures are intense and in which other factors, such as high temperature and humidity, may promote rapid loss of repellent from the skin surface. The EPA issued guidelines to consumers about proper application of insect repellents (**Table 2**) (55).

Repellents may be applied directly to the skin or to clothing, window screens, mesh insect nets, tents, or sleeping bags. Persons who are particularly concerned about potential toxicity from DEET may limit application of the repellent to their clothes. If DEET-treated garments are stored in a plastic bag between wearings, the repellent effect can last for many weeks (24).

Repellents containing DEET must be carefully applied because they can damage plastics (such as watch crystals and eyeglasses frames), rayon, spandex, other synthetic fabrics, leather, and painted or varnished surfaces. DEET does not damage natural fibers, such as cotton or wool, and has no effect on nylon. The lay literature contains many accounts of the unpleasant odor or greasy feel of DEET, but careful testing has shown a full spectrum of aesthetic responses to these products (56).

Consumers who apply both a DEET-based insect repellent and a sunscreen should be aware that the repellent may reduce the sunscreen's effectiveness. A limited study in 14 volunteers using the 3M polymer-based 33% DEET repellent and a sunscreen with sun protection factor 15 revealed a mean decrease in sun protection factor of 33.5% when the two agents were applied sequentially (57). Combination products in which the insect repellent and sunscreen

have been formulated together, however, would be expected to provide the sun protection factor stated on the label.

Pharmacology

Numerous studies have evaluated the percutaneous absorption, metabolism, and rate of excretion of DEET (58–61). Initial data suggested that 9% to 56% of the applied dose was absorbed through the skin (59). A carefully conducted study from 1995 that used human volunteers showed that the average dermal absorption of 100% DEET was 5.6%; for 15% DEET in ethanol, an average of 8.4% of the dose was absorbed (58). Because of its lipophilic nature, DEET was rapidly absorbed within 2 hours after application; was eliminated from the plasma within 4 hours after being rinsed off the skin; and was primarily excreted in the urine, mostly within 12 hours. Tape stripping revealed that the chemical does not accumulate in the stratum corneum.

Bioavailability experiments conducted with Minnetonka Brands' 10% DEET liposphere formulation showed that percutaneous absorption was one third of that of a 10% alcohol-based DEET solution (52). In contrast, U.S. Army studies that used an in vitro pigskin model did not show any reduced percutaneous absorption (expressed as a percentage of the applied dose) of the 3M polymer formulation compared with 75% DEET in alcohol (62).

Table 3. Studies Done To Support the Reregistration of DEET with the U.S. Environmental Protection Agency*

Mammalian toxicology studies
Rat, 90-day dermal test
Castrated male rat, 90-day dermal test
Micropig, 2-week dermal dose range–finding study
Micropig, 90-day dermal study
Rat, 90-day multistrain oral administration; done to evaluate renal toxicity
Hamster, 2-week dose range–finding study
Hamster, 90-day dose range–finding study
Rat, 90-day dose range–finding study
Rat, two-generation reproduction study
Rat, long-term toxicity and oncogenicity study
Mouse, 90-day dose range–finding study
Mouse, oncogenicity study
Rat, teratology dose range–finding study
Rat, teratology study
Rabbit, teratology dose range–finding study
Rabbit, teratology study
Rat, short-term oral-dose range–finding study
Rat, short-term neurotoxicity study
Rat, long-term neurotoxicity study
Dog, 2-week diet palatability study
Dog, 8-week dietary dose range–finding study
Dog, 3-week dietary toxicity study
Dog, 2-week oral gelatin capsule administration
Dog, 8-week oral gelatin capsule dose range–finding (first study)
Dog, 8-week oral gelatin capsule dose range–finding (second study)
Dog, long-term toxicity study
Determination of expired volatiles after oral and dermal administration
Pharmacokinetic and comparative dermal absorption tests
Human dermal absorption test
Mutagenicity studies
Ames test
Chromosome aberrations
Unscheduled DNA synthesis
Ecotoxicology studies
Bobwhite quail short-term oral toxicity study
Daphnid short-term toxicity study

* See reference 64. DEET = N,N-diethyl-3-methylbenzamide.

Toxicity

Used by millions of people worldwide for 40 years, DEET has a remarkable safety profile. As part of the 1980 EPA Reregistration Standard for DEET, more than 30 studies were conducted to assess acute, chronic, and subchronic toxicity; mutagenicity; oncogenicity; and developmental, reproductive, and neurologic toxicity (**Table 3**) (42, 63, 64). The results of these studies did not require any change to the product to comply with EPA safety standards, nor did they indicate any new toxicities with normal use. Studies of high doses of DEET orally administered to mice and rats did not reveal any potential in humans for teratogenicity or oncogenicity.

Case reports of potential DEET toxicity exist in the medical literature and are summarized in **Table 4**. The reports of greatest concern involve 14 cases of encephalopathy, 13 of which were in children younger than 8 years of age (63, 66–71, 75). Three of these children died, 1 of whom had an ornithine carbamoyl transferase deficiency (67) that might have predisposed her to DEET-induced toxicity (66). The other children recovered without sequelae. Many of these persons had a history of long-term, excessive, or inappropriate use of DEET repellents, and the details of exposure are frequently poorly documented. Animal studies in rats and mice have shown that DEET is not a selective neurotoxin (42, 61, 63).

Toxicology studies in rats and dogs in which sublethal intraperitoneal injections were used revealed that DEET could induce dose-dependent hypotension and bradycardia; however, these conditions occurred at dosages that would be almost impossible to attain with cutaneous applications of DEET (78). Only one case of bradycardia and hypotension has been documented in the medical literature (79).

Initial repeat-insult patch tests of 100% technical-grade DEET or 50% DEET in ethanol conducted over 21 consecutive days showed no sign of skin irritation (42). Subsequently, 14 cases of contact urticaria and irritant contact dermatitis (mostly in soldiers) have been reported (81–85). The antecubital fossa seems to be particularly sensitive to developing bullous irritant contact dermatitis if DEET products are allowed to remain on this area overnight (86).

A 1994 study reviewed 9086 cases of DEET exposure reported to 71 poison control centers from 1985 to 1989 (76). More than half (54%) of the persons involved had no symptoms at the time of the call to the poison control center. The most

Table 4. Reported Major Signs and Symptoms Attributed to Exposure to DEET*

Affected Area	Signs or Symptoms	Cases	Age	Sex	Concentration of DEET	Details of Use	Outcome	Reference
		n			%			
Central nervous system	Lethargy, confusion, acute manic psychosis	1	30 years	Male	Unknown	Three-week, daily, whole-body application, followed by 2 to 3 hours per day in a sauna	Resolved, no sequelae	65
	Lethargy, headaches, ataxia, disorientation	1	6 years	Female	15	>10 applications	Death (heterozygous for ornithine carbamoyl transferase deficiency)	66, 67
	Acute encephalopathy	1	17 months	Female	20	"Frequent" for 3 weeks	Death	68
	Headaches, disorientation, ataxia, convulsions	1	5 years	Female	10	Nightly for 3 months	Death	69
	Behavioral changes, confusion, tremors, seizures, encephalopathy	10	8 years or younger	Male (n = 6) Female (n = 4)	10–95	Concentration of DEET known in only 5 of 11 cases. Number of applications varied from 2 to 90. Many reports note "daily," "heavy," "frequent," or "whole-body" use	Resolved, no sequelae	63, 69–75
		1	29 years	Male				
	Seizures, hypotension, coma	6	1–33 years	Male (n = 4) Female (n = 2)	47.5–90	Ingested > 50 mL of DEET	3 of 6 patients died Resolved in 3 of 6 patients, no sequelae	76, 77
Cardiovascular	Bradycardia, hypotension	1	61 years	Female	Unknown	"Liberal" application to all exposed skin before gardening	Resolved, no sequelae	78, 79
Cutaneous or allergic reaction	Anaphylaxis	1	42 years	Female	52	Touched companion who had just applied DEET insect repellent	Resolved, no sequelae	80
	Wheals	3	4 years 35 years	Male (n = 2) Female (n = 1)	Unknown	Urticaria developed 10 to 30 minutes after application	Resolved	81–83
	Hemorrhagic bulla and erosions; confined to the antecubital fossa	11	18–20 years	Male	33–50	Military personnel; applied to all exposed skin, then slept outdoors with repellent still on skin	Resolved in 9 of 11 patients; scarring in 2 of 11	84, 85

* DEET = N,N-diethyl-3-methylbenzamide.

commonly reported symptoms were related to spraying repellent in the eyes (DEET is a known eye irritant [42]) or inhaling it. Symptoms were least likely to occur after accidental ingestion of small amounts of the repellent. Although most exposures were in children, there was no evidence that children younger than 6 years of age were more likely than older children or adults to develop adverse effects after use of a DEET repellent. No correlation was found between the severity of symptoms and age, sex, or concentration of applied DEET. Eighty-eight percent of exposed persons did not require treatment at a health care facility. Of the patients who were seen, 81% were sent home, and only 5% required hospitalization. Of the patients in whom follow-up was available, 99% had no long-term sequelae.

In summary, DEET has had a remarkable safety profile during more than 40 years of use by millions of people worldwide. Careful product choice and application of the repellent according to EPA guidelines will greatly reduce the possibility of toxicity. Conservative use of low-concentration DEET products is most appropriate for children.

Questions about the safety of DEET may be addressed to the EPA-sponsored National Pesticide Telecommunications Network, available by telephone every day from 6:30 a.m. to 4:30 p.m. Pacific Standard Time at 800-858-7378 or on the World Wide Web at http://www.ace.orst.edu/info/nptn/.

Skin-So-Soft

Avon (New York, New York) Skin-So-Soft bath oil received considerable media attention several years ago when some consumers reported it to be effective as a mosquito repellent. When tested under laboratory conditions against *Aedes aegypti* mosquitoes, this product's effective half-life was 30 minutes. Against *Aedes albopictus*, Skin-So-Soft oil provided 40 minutes of protection from bites, a duration 10 times less than that of 12.5% DEET (46). It has been proposed that the limited mosquito

repellent effect of Skin-So-Soft oil could be caused by its fragrance or the presence of diisopropyl adipate and benzophenone in the formulation, both of which have some repellent activity (40). Avon now markets products under the Skin-So-Soft label that contain an EPA-recognized repellent (**Table 5**).

Plant-Derived Repellents

Thousands of plants have been tested as potential sources of insect repellents (39, 40, 87). None of the plant-derived chemicals tested to date demonstrate the broad effectiveness and duration of DEET, but a few show repellent activity. Plants whose essential oils have been reported to have repellent activity include citronella, cedar, verbena, pennyroyal, geranium, lavender, pine, cajeput, cinnamon, rosemary, basil, thyme, allspice, garlic, and peppermint (40, 88–91). Unlike synthetic insect repellents, plant-derived repellents have been relatively poorly studied. When tested, most of these essential oils tended to give short-lasting protection, usually less than 2 hours. Readily available plant-derived insect repellents are listed in **Table 5**.

Citronella

Citronella is the active ingredient most commonly found in "natural" or "herbal" insect repellents marketed in the United States. It is registered with the EPA as an insect repellent. Citronella oil has a lemony scent and was originally extracted from the grass plant *Cymbopogon nardus*. Limited data are available from studies that directly compared the efficacy of citronella-based products with that of DEET-based products. In one study, 0.01 μmol of DEET per L of air was sufficient to prevent 90% of mosquitoes from landing on their targets; a 1000-fold higher concentration of citronellol (one of the active chemicals in citronella oil) was required to achieve a similar effect (31).

Studies show that citronella can be an effective repellent, but it provides shorter complete protection time than most DEET-based products. Frequent reapplication of the repellent can partially compensate for this. The manufacturer of Natrapel (Tender Corp., Littleton, New Hampshire) has laboratory data showing that their 10% lotion reduced mosquito bites by 84% during a 4-minute test period. In contrast, 14% DEET reduced biting by 96% in the same test period. Buzz Away (Quantum, Inc., Eugene, Oregon) with 5% citronella oil provided an average protection time of 1.9 hours against *Aedes aegypti* (92). In field testing, Buzz Away Oil provided an average of 88% repellency during a 2-hour exposure. In general, the repellency of Buzz Away was greatest within the first 40 minutes after appli-

Table 5. Plant-Derived Insect Repellents and Permethrin Insecticide Sprays*

Manufacturer, Location, Telephone Number	Product Brand Name	Forms	Active Ingredient
Avon Corp., New York, New York 800-367-2866	Skin-So-Soft Moisturizing Suncare Plus (SPF 8, 15, or 30)	Lotion	Citronella oil, 0.05%
	Skin-So-Soft Bug Guard	Pump spray	Citronella oil, 0.10%
Consep, Inc., Bend, Oregon 800-367-8727	Bite Blocker	Lotion, oil, pump spray	Soybean oil, 2%
Quantum, Inc., Eugene, Oregon 800-448-1448	Buzz Away	Towelette, pump spray	Citronella oil, 5%
	Buzz Away (SPF 15)	Lotion	
Tender Corp., Littleton, New Hampshire 800-258-4696	Natrapel	Lotion, pump spray	Citronella, 10%
All Terrain Co., Encinitas, California 800-246-7328	Herbal Outdoor Protection	Lotion	Citronella oil, 12%; oils of cedarwood, lavender, lemongrass, and peppermint
	Complete Outdoor Protection (SPF 20)	Lotion	
	Herbal Armor	Pump spray	Citronella oil, 15%; oils of clove, cedarwood, eucalyptus, lemongrass, peppermint, and garlic
Green Ban, Norway, Iowa 319-446-7495	Green Ban for People		
	Regular	Oil	Citronella oil, 5%; peppermint oil, 1%
	Double Strength	Oil	Citronella oil, 10%; peppermint oil, 2%
Coulston Products, Easton, Pennsylvania 610-253-0167	Duranon	Aerosol spray, pump spray	Permethrin, 0.5%
Sawyer Products, Tampa, Florida 800-940-4464	Permethrin Tick Repellent	Aerosol spray, pump spray	Permethrin, 0.5%
United Industries Corp., St. Louis, Missouri 800-767-9927	Cutter Outdoorsman Gear Guard	Aerosol spray	Permethrin, 0.5%
Wisconsin Pharmacal Co., Jackson, Wisconsin 800-558-6614	Repel Permanone	Aerosol spray	Permethrin, 0.5%

* SPF = sun protection factor.

cation and decreased over the remainder of the test period (93).

Citronella candles have been promoted as an effective way to repel mosquitoes in the backyard. One study compared the ability of commercially available 3% citronella candles, 5% citronella incense, and plain candles to prevent bites by *Aedes* mosquitoes under field conditions (94). Persons near the citronella candles had 42% fewer bites than controls, who had no protection (a statistically significant difference). However, burning ordinary candles reduced the number of bites by 23%. The efficacy of citronella incense and plain candles did not differ. The ability of plain candles to decrease biting may result from their action as a decoy source of warmth, moisture, and carbon dioxide.

The citrosa plant (*Pelargonium citrosum* 'van Leenii') has been marketed as being able to repel mosquitoes through the continuous release of citronella oils. Unfortunately, when tested, these plants offer no protection against bites (95, 96).

Bite Blocker

Bite Blocker (Consep, Inc., Bend, Oregon) is a plant-based repellent that was released in the United States in 1997. Bite Blocker combines soybean oil, geranium oil, and coconut oil in a formulation that has been available in Europe for several years (97). Studies conducted at the University of Guelph, Ontario, Canada, showed that this product gave more than 97% protection against *Aedes* mosquitoes under field conditions, even 3.5 hours after application. During the same period, a 6.65% DEET-based spray afforded 86% protection, and Avon Skin-So-Soft citronella-based repellent gave only 40% protection (98). A second study showed that Bite Blocker provided a mean ± SD of 200 ± 30 minutes of complete protection from mosquito bites (99).

Permethrin

Pyrethrum is a powerful, rapidly acting insecticide, originally derived from the crushed and dried flowers of the daisy *Chrysanthemum cinerariifolium* (100). Permethrin is a human-made synthetic pyrethroid. It does not repel insects but works as a contact insecticide, causing nervous system toxicity that leads to the death or "knockdown" (out of the air) of the insect. The chemical is effective against mosquitoes, flies, ticks, and chiggers. Permethrin has low toxicity in mammals, is poorly absorbed by the skin, and is rapidly inactivated by ester hydrolysis (101).

Permethrin should be applied directly to clothing or other fabrics (such as tent walls [102] or mosquito nets [103]), not to skin. The spray form is nonstaining, nearly odorless, and resistant to degradation by heat or sun and maintains its potency for at least 2 weeks, even through several launderings (104, 105). The combination of permethrin-treated clothing and skin application of a DEET-based repellent creates a formidable barrier against mosquito bites (19, 106, 107). In a field trial conducted in Alaska, persons wearing permethrin-treated uniforms and a polymer-based 35% DEET product had more than 99.9% protection (1 bite/h) over 8 hours, even under conditions of intense biting pressures; unprotected persons received an average of 1188 bites/h (108).

Permethrin-based insecticide sprays available in the United States are listed in **Table 5**. To apply to clothing, spray each side of the fabric (outdoors) for 30 to 45 seconds, just enough to moisten it. Allow the garment to dry for 2 to 4 hours before wearing it.

Reducing Local Mosquito Populations

Consumers may still find advertisements for small ultrasonic electronic devices that are meant to be carried on the body and purportedly emit sounds that repel mosquitoes. Many studies conducted in the field and laboratory show that these devices do not work against mosquitoes (109–111). Encouraging natural predation of insects by setting up bird or bat houses in the backyard has also been unsuccessful in reducing local mosquito populations (112). Likewise, backyard bug "zappers," which lure and electrocute insects, are ineffective (113). Mosquitoes continue to be more attracted to humans than to the devices. One study conducted in homeowners' backyards showed that of the insects killed by these devices, only 0.13% were female mosquitoes (114). An estimated 71 billion to 350 billion beneficial insects may be killed annually in the United States by these electrocuting devices (114). The most effective way to reduce a local population of mosquitoes is to eliminate sources of standing water, such as old discarded tires, clogged gutters, planters, bird baths, or tree stump holes.

Relief from Mosquito Bites

Cutaneous responses to mosquito bites range from common localized wheal-and-flare reactions to delayed bite papules, rare systemic Arthus-type reactions, and anaphylaxis (115–117). Bite reactions are the result of sensitization to mosquito salivary antigens, which lead to the formation of specific IgE and IgG antibodies (118–121). Immediate-type reactions are mediated by IgE and histamine, whereas cell-mediated immunity is responsible for the delayed reactions.

Several strategies exist for relieving the itch of mosquito bites. Topical corticosteroids can reduce

the erythema, itching, and induration. Topical diphenhydramine and caine-containing derivatives should be avoided because of concerns about inducing allergic contact sensitivity. Oral antihistamines can be effective in reducing the symptoms of mosquito bites. Cetirizine was given prophylactically in a double-blind, placebo-controlled, 2-week, crossover trial to 18 persons who had previously had dramatic cutaneous reactions to mosquito bites (122). Persons who received the active drug had a statistically significant 40% decrease in the size of the wheal response at 15 minutes and the size of the bite papule at 24 hours. The mean pruritus score, measured 0.25, 1, 12, and 24 hours after the mosquito had bitten, was 67% less than that of the untreated controls. These studies have not been done with astemizole, terfenadine, loratadine, or fexofenadine. In highly sensitized persons, prophylactic treatment with nonsedating antihistamines may safely reduce the cutaneous reactions to mosquito bites.

Acknowledgments: The author thanks Donald Baumgartner (U.S. Environmental Protection Agency); Donald Barnard, PhD (U.S. Department of Agriculture); Nigel Hill (London School of Hygiene and Tropical Medicine); and Robbin Lindsay, PhD (Department of Environmental Biology, University of Guelph) for providing data that were not readily available in the medical literature. The author has received no monetary support from any of the manufacturers whose products are mentioned in this paper.

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