Look What's Out There

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MOSQUITOES AND MOSQUITO REPELLENTS

The following information was extracted from the Annals of Internal Medicine, 1 June 1998. 128:931-940. Mark S. Fradin, MD.

Worldwide 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. 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. Mosquitoes transmit the arboviruses responsible for yellow fever, dengue hemorrhagic fever, epidemic polyarthritis, and several forms of encephalitis. Mosquitoes cannot transmit HIV.

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.

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. 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. Some mosquito species prefer to feed on animals and others show a preference for human blood.

Mosquitoes use visual, thermal, and olfactory stimuli to locate a host. Of these, olfactory cues are probably most important. 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 human body as by-products of metabolism and that more than 100 volatile compounds can be detected in human breath. 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. Mosquitoes have chemoreceptors on their antennae that are stimulated by lactic acid. At close range, skin temperature and moisture serve as attractants.

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 sweat gland output. Other volatile compounds, derived from sweat, or the cutaneous microflora bacterial action on these secretions, may also act as chemoattractants. Floral fragrances from perfumes, soaps, lotions, and haircare products may also attract mosquitoes. In general, adults are more likely to be bitten than children, although adults may become less attractive to mosquitoes as they age. Men are bitten more readily than women. Larger persons tend to attract more mosquitoes, perhaps because of their greater relative heat or carbon dioxide output.

Despite the obvious desirability of finding an effective oral mosquito repellent, no such agent has been identified. Thus, the search for the perfect topical insect repellent continues.

Repellents do not all share a single mode of action, and surprisingly little is known about how repellents act on their target insects. Moreover, different species of mosquitoes may react differently to the same repellent. 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. 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. Each 10 °C increase in temperature can lead to as much as a 50% reduction in protection time.

N,N-diethyl-m-toluamide also called N,Ndiethyl-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 broadspectrum 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. The U.S. Environmental Protection Agency (EPA) estimates that more than 38% of the U.S. population uses a DEETbased insect repellent every year and that worldwide use exceeds 200,000,000 people annually.

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.

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 also available to the general public. As a general rule, higher concentrations of DEET provide longer- lasting protection.

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. Extended-release formulations of DEET have made it possible to reduce the repellent concentration without sacrificing duration of action. 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.

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. 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.

Consumers who apply both a DEET-based insect repellent and a sunscreen should be aware that the repellent may reduce the sunscreen's effectiveness. 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. 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. The reports of greatest concern involve 14 cases of encephalopathy, 13 of which were in children younger than 8 years of age. Three of these children died. 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. 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. A 1994 study reviewed 9086 cases of DEET exposure reported to 71 poison control centers from 1985 to 1989. More than half (54%) of the persons involved had no symptoms at the time of the call to the poison control center. The most commonly reported symptoms were related to spraying repellent in the eyes (DEET is a known eye irritant) 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 followup was available, 99% had no long-term sequelae.

Avon 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.

Thousands of plants have been tested as potential sources of insect repellents. 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. 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.

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. 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. 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. 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 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.

Bite Blocker 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. 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.

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. Encouraging natural predation of insects by setting up bird or bat houses in the backyard has also been unsuccessful in reducing local mosquito populations. Likewise, backvard bug "zappers," which lure and electrocute insects, are ineffective. 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% where female mosquitoes. An estimated 71 billion to 350 billion beneficial insects may be killed annually in the United States by these electrocuting devices. 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. (AIM, 6/98)

Pesticide News

* U.S. health officials were cited as saying on May 8 that a recent cluster of food poisonings in Michigan likely was caused by a nicotine-laced pesticide deliberately added to ground beef bought at a supermarket. The study published by the U.S. Centers for Disease Control and Prevention says that nearly 100 people developed diarrhea, burning in the mouth, vomiting and other symptoms consistent with food poisoning early this year after eating meat from an unidentified store in the state. The tainted meat was recalled in January after members of four families notified the store of their illnesses. Tests conducted by a private laboratory later identified nicotine as the source of the contamination. A former supermarket employee has since been indicted for allegedly poisoning 200 pounds of ground beef with an insecticide that contained nicotine. (SPDN letter of 5/12/03).

* The Washington Apple Commission closed its doors April 10 following a federal court ruling that the commission's mandatory fee collection is unconstitutional. The Wenatchee-based body was established in 1937 to promote the state's top crop by assessing growers a fee for every apple box marketed. Washington produces more than half the nation's crop. Whether the commission can reconstitute in some way is not clear, nor is the future of other state commoditypromoting commissions. (CropLife America *Spotlight*, 4/25/03).