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# The Medical Letter®

## on Drugs and Therapeutics

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### ▶ Insect Repellents

Use of insect repellents is strongly recommended by the Centers for Disease Control and Prevention (CDC) and the Environmental Protection Agency (EPA) to prevent infections transmitted by mosquitoes and ticks. Insect repellents applied to exposed skin should be used in conjunction with other preventive measures such as wearing pants and long-sleeved shirts, and avoiding outdoor activities during peak mosquito-biting times.<sup>1</sup> Mosquitoes can transmit Zika, chikungunya, dengue, West Nile, eastern equine encephalitis, and yellow fever viruses, as well as malaria. Ticks can transmit Lyme disease, rickettsial diseases such as Rocky Mountain spotted fever, and viruses such as Powassan virus.

**DEET** — The topical insect repellent N,N-diethyl-*m*-toluamide (DEET) is highly effective against mosquito and tick bites.<sup>2</sup> It also repels chiggers, fleas, gnats, and some flies. DEET is available in concentrations of 5-99%; higher concentrations typically provide longer-lasting protection,<sup>3</sup> but increasing the concentration above 50% has not been shown to improve efficacy. Long-acting polymer-based or liposomal DEET formulations containing concentrations of 30-34% have been shown to protect against mosquitoes for up to 12 hours. The CDC recommends using concentrations  $\geq 20\%$  in adults for protection against both mosquitoes and ticks.

Reviews of the safety and toxicity of topically applied DEET indicate that it is generally safe.<sup>2,4</sup> Toxic and allergic reactions to DEET have been uncommon, and serious adverse effects are rare.<sup>4</sup> Rashes ranging from mild irritation to urticaria and bullous eruptions have been reported. Patients find that some DEET formulations feel uncomfortably oily or sticky on their skin. DEET can damage clothing made from synthetic fibers and plastics on eyeglass frames and watches.

**Children** — The American Academy of Pediatrics recommends using DEET formulations containing concentrations of 10-30% on children and infants >2 months old. Neurologic adverse events have occurred in infants and

#### Summary: Insect Repellents

- ▶ DEET is highly effective against mosquito and tick bites and is generally safe.
- ▶ Picaridin appears to be as effective against mosquitoes as equivalent concentrations of DEET and may be better tolerated on the skin. It also repels ticks.
- ▶ IR3535 at concentrations  $\geq 10\%$  and oil of lemon eucalyptus (OLE) can also be effective in repelling mosquitoes and ticks.
- ▶ Published data on the efficacy of 2-undecanone are limited.
- ▶ Citronella oil-based insect repellents provide short-term protection against mosquitoes, but not ticks. Other essential oils provide limited and variable protection against mosquitoes.
- ▶ Wearing clothing treated with the insecticide permethrin in addition to using DEET or picaridin on exposed skin may provide the best protection against mosquitoes and ticks.
- ▶ Wearable devices such as wristbands are not effective.

children, usually with prolonged or excessive use that sometimes included ingestion of the product.

**PICARIDIN** — Picaridin provides protection against mosquitoes, ticks, flies, fleas, and chiggers. It is available in concentrations of 5-20%; higher concentrations typically provide longer lasting protection.<sup>5</sup> Picaridin appears to be at least as effective against mosquitoes as DEET at similar concentrations.<sup>6</sup>

Picaridin can cause skin and eye irritation, but it appears to be better tolerated on the skin than DEET. It is odorless, non-greasy, and does not damage fabric or plastic, but it can discolor leather and vinyl. In a review of data from US poison centers, ingestion of picaridin-based insect repellents resulted in only minor toxicity (mild oral or skin irritation, mild GI symptoms) that did not require referral to a healthcare facility.<sup>7</sup>

**Children** — The American Academy of Pediatrics recommends formulations of picaridin containing concentrations of 5-10% for use on children as an alternative to DEET.

**IR3535** — IR3535 (3-[N-Butyl-N-acetyl]-amino-propionic acid, ethyl ester), a synthetic version of  $\beta$ -alanine, repels mosquitoes, deer ticks, and flies. It is available in concentrations of 7.5% and 20% in the US (see Table 1). Concentrations  $\geq 10\%$  have been found

Table 1. Some Insect Repellents

Repellent	Formulation	Duration of Protection <sup>1</sup>	Comments
<b>DEET (N,N-diethyl-<i>m</i>-toluamide)</b>			
<i>Cutter All Family Mosquito Wipes</i>	7.15% wipes	2 hrs	Highly effective broad-spectrum repellent; safe on pregnant women and children >2 months old; may feel oily on the skin
<i>Off! Family Care</i>	15% aerosol spray	6 hrs	
<i>Off! Deep Woods VII</i>	25% pump spray	8 hrs	
<i>Sawyer Family Controlled Release</i>	20% lotion	11 hrs	
<i>Ultrathon<sup>2</sup></i>	34% lotion	12 hrs	
<i>Repel 100</i>	98.11% pump spray <sup>3</sup>	10 hrs	
<b>Picaridin</b>			
<i>Cutter Advanced</i>	5.75% wipes	8 hrs	Appears to be as effective against mosquitoes as similar concentrations of DEET; also repels ticks; safe on pregnant women and children >2 months old; odorless, non-greasy
<i>Avon Skin So Soft Bug Guard Plus Picaridin</i>	10% aerosol spray	6 hrs	
<i>Natrapel 8 hour</i>	20% pump spray	8 hrs	
<i>Sawyer Picaridin Lotion</i>	20% lotion	14 hrs	
<b>IR3535 (3-[N-acetyl-N-butyl]-aminopropionic acid, ethyl ester)</b>			
<i>Avon Skin So Soft Bug Guard Plus IR3535<sup>4</sup></i>	7.5% lotion	2 hrs	Concentrations ≥10% effective against mosquitoes; also repels ticks; safe on pregnant women and children >2 months old
<i>Coleman Skin Smart</i>	20% aerosol spray	8 hrs	
<b>Oil of Lemon Eucalyptus (OLE; <i>p</i>-menthane-3,8-diol [PMD])<sup>5</sup></b>			
<i>Off! Botanicals</i>	10% pump spray	2 hrs	Effective for repelling mosquitoes and ticks; avoid on children <3 years old; safe on pregnant women
<i>Coleman Botanicals</i>	30% pump spray	6 hrs	
<i>Repel Lemon Eucalyptus</i>	30% pump spray	6 hrs	
<b>2-undecanone</b>			
<i>HOMS Bite Blocker BioUD Insect Repellent and Clothing Treatment</i>	7.75% pump spray	5 hrs	Limited data available; may have strong odor
<b>Citronella<sup>6</sup></b>			
<i>Buzz Away Extreme</i>	1.0% pump spray <sup>7</sup>	2 hrs	Short-term effectiveness against mosquitoes; probably not effective against ticks
<b>Permethrin</b>			
<i>Sawyer Premium Permethrin Clothing</i>	0.5% pump spray	—	For use on clothing and gear; avoid on exposed skin; effective against mosquitoes and ticks
<i>Repel Permethrin Clothing and Gear</i>	0.5% aerosol spray	—	
<p>1. Approximate duration of protection against mosquitoes for repellents applied to exposed skin, according to protection times approved by the EPA for product labels; for most products, the duration of protection against ticks is expected to be similar (except 2-undecanone, which repels ticks for 2 hours). Products listed in this database are those with an EPA registration number, which indicates the company provided the EPA with technical information on the safety of the product and its effectiveness against mosquitoes and/or ticks. Although this technical information is based on scientific testing guidelines and approved study methods, there are variations in the resulting protection times because of differences in testing conditions. Duration of protection may be affected by ambient temperature, activity level, amount of perspiration, exposure to water, and other factors. Available at: <a href="http://www.epa.gov/insect-repellents/find-insect-repellent-right-you">www.epa.gov/insect-repellents/find-insect-repellent-right-you</a>. Accessed August 15, 2019.</p> <p>2. Long-acting polymer-based formulation developed for the US military.</p> <p>3. There is no evidence that concentrations of DEET above 50% are more effective.</p> <p>4. Contains IR3535 combined with sunscreen; products that contain both an insect repellent and a sunscreen are not recommended because the sunscreen may need to be reapplied more often and in greater amounts than the repellent.</p> <p>5. Oil of lemon eucalyptus (OLE) is not the same as pure, essential oil of lemon eucalyptus, which is not recommended for use as an insect repellent.</p> <p>6. Citronella is also available in a variety of brand name products that are not EPA registered.</p> <p>7. Also contains castor oil (8%), geranium oil (6%), soybean oil (3%), peppermint oil (0.5%), and lemongrass oil (0.25%).</p>			

to be effective against mosquito bites for several hours.<sup>8</sup> Two studies found the 7.5% concentration to be ineffective.<sup>9</sup> IR3535 can cause eye irritation, and it may damage clothing and plastics.

**Children** – According to the EPA, IR3535 is safe for use on children >2 months old.

**OIL OF LEMON EUCALYPTUS** – Oil of lemon eucalyptus (OLE; *p*-menthane-3,8-diol [PMD]), which repels mosquitoes, ticks, flies, gnats, and biting midges, occurs naturally in the lemon eucalyptus plant.<sup>2</sup> It is chemically synthesized for commercial use as a repellent. In field studies against malaria-transmitting mosquitoes, OLE provided up to 6 hours of protection against mosquito bites.<sup>8</sup> It has

demonstrated efficacy equivalent to that of DEET against mosquitoes in some laboratory and field studies.<sup>10</sup> OLE can cause eye and skin irritation, including allergic skin reactions.<sup>11</sup>

**Children** – OLE products are not recommended for use on children <3 years old.

**2-UNDECANONE** – A relatively new insect repellent, 2-undecanone is derived from the wild tomato plant.<sup>12</sup> A synthetic version is commercially available in a 7.75% spray formulation (*BioUD*). Published data on the efficacy of 2-undecanone are limited.<sup>2</sup> According to the product label, *BioUD* is effective for up to 4.5 hours against mosquitoes and up to 2 hours against ticks. It can have a strong odor.

**CITRONELLA** – Citronella oil-based insect repellents provide short-term protection against mosquitoes, but they are probably not effective against ticks. In laboratory studies, various concentrations of citronella oil were less effective than DEET against mosquito bites in duration of protection.<sup>13</sup> The protection times for most citronella oil products are 2 hours or less, and they can cause skin irritation.

**OTHER ESSENTIAL OILS** – Essential oils obtained from raw botanical material, including clove, geraniol, catnip, and patchouli, provide limited and variable protection against mosquitoes. High concentrations can be irritating to the skin.<sup>14,15</sup>

**SUNSCREENS AND INSECT REPELLENTS** – Topical insect repellents can be used with sunscreens; the repellent should be applied after the sunscreen. Applying DEET after sunscreen has been shown to reduce the sun protection factor (SPF) of the sunscreen, but applying sunscreen after DEET may increase absorption of DEET. The CDC does not recommend use of products that combine a sunscreen with an insect repellent because the sunscreen may need to be reapplied more often and in greater amounts than the repellent.

**PERMETHRIN** – A synthetic pyrethroid contact insecticide, permethrin can be sprayed on clothing, mosquito nets, tents, and sleeping bags to repel and kill mosquitoes and ticks. Permethrin-impregnated clothing is available commercially; it remains active for several weeks through multiple launderings with minimal transfer to the skin.<sup>16</sup> An indoor laboratory study found that subjects wearing permethrin-treated sneakers and socks were 73.6 times less likely to be bitten by a tick than those wearing untreated footwear.<sup>17</sup> Studies in outdoor workers in North Carolina wearing uniforms treated with a long-lasting formulation of permethrin using a commercially available factory-based method found that the clothing protected against mosquito and tick bites for at least 1 year.<sup>18,19</sup> No significant adverse effects have been reported from wearing permethrin-treated clothing.<sup>11</sup>

**WEARABLE DEVICES** – Several insect repellents, including DEET, OLE, and citronella, are commercially available in wearable devices such as wristbands. These devices are not effective.<sup>20,21</sup>

**PREGNANCY** – The CDC considers EPA-registered formulations of DEET, picaridin, IR3535, OLE, and 2-undecanone safe for use during pregnancy.<sup>22</sup> According to the EPA, there is no evidence that

exposure to permethrin results in adverse effects in pregnant or nursing women or developmental adverse effects in their children.<sup>23</sup> In its Zika virus prevention guidelines, the American College of Obstetricians and Gynecologists recommended that pregnant women traveling to areas where Zika has been reported use an EPA-registered DEET product and permethrin-treated clothing, cover exposed skin, and stay in air-conditioned or indoor areas.<sup>24,25</sup> ■

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