SHORT REPORT: THE SAFETY AND TOXICITY OF INSECT REPELLENTS

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Abstract. In recent years, concerns have been raised regarding the safety of diethyltoluamide (DEET), one of the most widely used and reliable insect repellents available. This paper summarizes the recent evidence and concludes that concerns over safety appear largely unfounded.

Increasing tourism to tropical regions and the changing patterns of vector-borne disease have led to a reassessment of personal protection measures that can be taken against insects. Methods for avoiding bites, which include the use of insect repellents, are an important element of strategies for reducing infection with malaria, dengue, filariasis, and other insect-borne diseases. Concerns have been raised over the safety of the most popular repellent, diethyltoluamide (DEET), and have resulted in travelers experimenting with natural plant repellents as an alternative. We felt it was appropriate to examine the safety profile of DEET in the light of recent evidence to provide facts on the toxicity of repellents when advising travelers.

Diethyltoluamide has been extensively used in Europe and the United States following its introduction as a repellent in the 1950s. Manufacturers' estimates and consumer research figures indicating that 30% of the population in the United States (S. C. Johnson and Sons, Racine, WI, unpublished data) and 25% of the population in the United Kingdom (Taylor-Nelson AGP, unpublished data) apply a DEET-containing product at least once a year. The most comprehensive published review of toxicity associated with the use of DEET was gathered from poison control centers across the United States by analyzing the 3,098 exposures to DEET reported by the public to the centers between 1985 and 1990. The exposures included DEET taken orally, by topical application, or inhalation, or by accidental contamination of the eye. The survey found that only 44 exposures resulted in a hospital admission, and five led to a serious adverse reaction. The most severe poisonings were following inhalation or ocular contact and were unrelated to the concentration of DEET in the preparation. In the United Kingdom, of the 25 reports received by the National Poisons Centre (London, United Kingdom) in 1996 (unpublished data), most were consequent to ingestion by children and all resulted in mild symptoms only.

The rat oral 50% lethal dose (LD50) of DEET is 2–4g/kg, and although toxicity data indicate a high oral absorption, bioavailability following oral ingestion in humans has not been described. It is not unexpected that intentional or accidental oral ingestion of large volumes of DEET may cause toxicity, and this has led to hypotension, respiratory, central nervous system depression, and rarely, death. Some of these symptoms, however, may be related to the alcohol carrier of DEET. Systemic toxicity following topical application of DEET in adults is very rare with only two case reports; one resulting in psychosis and the other in cardiovascular complications.

As with many topically applied preparations, local reactions, urticaria, and contact dermatitis are occasionally reported. Of particular interest are reports of bullous eruptions observed in the antecubital fossae of soldiers who applied DEET to this area of the body before retiring at night. The air-tight occlusion of the ante-cubital fossa from a flexed elbow during sleep may be the explanation of this skin abnormality, and applying DEET to flexures just before retiring should be avoided.

Concerns over the potential encephalopathic toxicity of DEET in children are based on only 12 case reports in the literature, some of which cannot be positively attributed to DEET usage alone. Based on early animal and limited human studies, this toxicity was attributed to a theoretically excessive cutaneous absorption and prolonged excretion from children who have a larger body surface area than adults. However, a recent pharmacokinetic study with radiolabeled DEET at normal dosage in adults by Selim and others reported that only a small proportion (8%) of topically applied DEET is absorbed and along with its metabolites is then completely eliminated within 4 hr of application. With such a small proportion of the applied dose absorbed, it is questionable whether a greater amount would be absorbed in children and whether this amount would be toxicologically significant, although such studies have yet to be performed.

Diethyltoluamide has been proposed as contributing to the Gulf war syndrome, but doses in a chicken model examining topical DEET toxicity used doses that were 60-fold higher than those used by soldiers in the Gulf. Its toxicity in combination with other agents used in this situation has yet to be confirmed.

The use of non-DEET repellents based on plant extracts have become more popular because of the unfounded reputation and cosmetic features of DEET. These substances are by no means free of toxicity and adverse reactions. For instance, Citronella, one of the most popular ingredients in natural repellents, caused the death of a 21-month-old child after ingestion of 15 ml of the oil. Eucalyptus oil has an LD50 within the same range as DEET; oral ingestion has resulted in two deaths and several reports of poisonings. Unlike DEET, limited experience with natural oils used as insect repellents means their true safety profile has yet to be determined.

Considering the widespread use of DEET, there appears to have been remarkably few problems. The encephalopathy in children has not been substantiated by detailed surveillance. Since DEET is considered the most reliable repellent for those visiting the tropics, travelers should not be deterred against its use because of concerns over safety. However,
recommendations regarding careful application, particularly in children, should nonetheless be followed.\textsuperscript{19} There appears to be no good evidence for a correlation between the concentration of DEET in a product and the incidence of adverse effects, but application of the lowest effective dose of approximately 30\%, depending on formulation, would be a sensible policy.

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