Personal protection measures against mosquitoes

A brief history and current use of repellents by the Australian Defence Force

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A selection of mosquito repellents.

Synopsis

- Personal protection measures are the first line of defence against mosquito-borne diseases, such as malaria and dengue.
- The main active ingredient in mosquito repellents is *N,N*-diethyl-*3*-methylbenzamide (deet). Deet has a broad spectrum of effectiveness against a variety of arthropods, including mosquitoes.
- There is little risk of adverse effects due to the use of deet. However, it is recommended that the chemical be used appropriately and not excessively for prolonged periods.
- The Australian Defence Force has a repellent formulation containing 35% deet in a gel. This formulation is effective against mosquitoes, but is not used widely by soldiers, primarily because it feels sticky and uncomfortable on the skin and melts plastic and some synthetic fibres. Many soldiers prefer commercially available spray-on repellents.
- There are relatively few alternatives to deet. New active ingredients, such as picaridin and the piperidine AI3-37220, are being evaluated and may prove to be equally effective in providing a broad spectrum of activity against mosquitoes.

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ARTHROPODS CAN CAUSE major problems for exercising or operationally deployed defence personnel. A recent survey conducted with US Army soldiers showed that, as pests, arthropods could "obstruct movement and field positions, prevent concealment and cover, disrupt manoeuvres and cause panic".[1] Additionally, there is the cost of lost work time, treatment and hospitalisation.[1] However, it is as vectors of disease that arthropods are most dangerous: typhus, scrub typhus, malaria, dengue and yellow fever are just some of the arthropod-borne diseases that have had a major impact on military operations over the last 100 years.

The role of the Australian Army Malaria Institute (AMI) is to provide the Australian Defence Force with the best available protection against arthropod-borne diseases. Of these, malaria and arboviruses such as dengue are currently the most relevant, with 471 cases of malaria and 234 cases of dengue diagnosed in ADF personnel over the last two years.[2] The vectors of both these diseases are various species of mosquitoes.

Although malaria no longer occurs on the Australian mainland, the region surrounding Australia is highly malarious and over the last decade all major deployments involving the ADF — Cambodia, Somalia, Rwanda, Bougainville and East Timor — have been in malarious areas. Malaria protection is partly provided by using antimalarial drugs.[3,4] However, the drugs currently available are not 100% effective and *Plasmodium vivax* relapses are a continuing problem for ADF personnel following their return from malarious areas.[5]

A vaccine is available for Japanese encephalitis virus, but there are no vaccines or drugs available for protection against many other mosquito-borne viruses, such as dengue, Murray Valley encephalitis, Ross River virus and Barmah Forest virus.

The first, and in some cases the only, line of defence against these diseases is to lessen the likelihood of being bitten by mosquitoes. This can be achieved by several methods which, where possible, should be used concurrently. One method is to reduce the number of biting mosquitoes by controlling the larval and adult populations through source reduction and insecticide treatment of larval habitats, and fogging and spraying of insecticides to kill adults. A second method is the use of bed nets as a barrier against biting mosquitoes. These two methods are useful in base locations, but there are limitations on the areas that can be kept under regular control and nets are only

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1: Examples of mosquito repellents containing deet available in Australia*

Product	Type	Concentration of deet	Manufacturer
Bushman	Gel 75 g	80%	North Queensland Laboratories
ADF	Gel 75 mL	35%	Colbar Laboratories
Aerogard	Lotion 125 mL	17%	Reckitt Benckiser
RID	Lotion 125 mL	16%	Thorley Laboratories
Skintastic	Lotion 125 mL	7%	S C Johnson

*Partly obtained from Reference 17.

effective while the person is under them. The treatment of uniforms with compounds such as permethrin has been found to be effective in reducing the number of mosquito bites. However, the most effective method is individual personal protection using repellents.

The ADF currently has recommendations for repellent use.[6] This article will focus on the history, aspects of safety and current use of repellents against mosquitoes and other arthropod vectors of disease.

Repellents

Over the last 50 years many types of natural and synthetic compounds have been evaluated for their repellent activity against arthropods, primarily mosquitoes.[7-13] Of the natural compounds, most are plant oil extracts such as citronella, eucalyptus, tea tree, cedarwood and neem. The success of these products has been limited due to adverse skin reactions, unpleasant odours, batch variability and short protection times (S P Frances, unpublished data).[12-13] Several products containing these oils are available on the Australian market and offer an alternative to synthetic chemicals, although, to be effective, they need to be applied more frequently. The systemic use of high doses of vitamin B1, long advocated as having mosquito-repellent properties, is totally unfounded and lacks any scientific validity.[14]

Of the synthetic chemical compounds, the first to gain wide acceptance were dimethyl phthalate and dibutyl phthalate, both patented in the USA in 1929. The former was used extensively by the allied forces in the Pacific during World War II and proved to be quite effective.[7] By the end of the war dimethyl phthalate, ethyl hexanediol and Indalone (butyl-3,3-dihydro-2,2-dimethyl-4-oxo-2H-pyran-6-carboxylate) were widely used as effective repellents. These compounds were later combined to exploit their best individual features. The combined formulation was called the 6-2-2 repellent (dimethyl phthalate, ethyl hexanediol and Indalone in the proportions 6:2:2). This product fell out of favour in the early 1990s when ethyl hexanediol was linked to adverse effects on fetal development.

The most important synthetic repellent, discovered in 1954, is the chemical *N,N*-diethyl-*3*-methylbenzamide. This compound, also called diethyl toluamide and commonly known as **deet**, is the most effective and widely used repellent to date. It is estimated that 15 million people in the UK, 78 million people in the USA[15] and 200 million people globally use deet each year.[16] In Australia, deet is the active ingredient in most of the commercially available products, many of them containing less than 20% deet (Box 1).[17]

Effectiveness of deet

Although deet is effective against many arthropods, including mosquitoes, the response of different mosquito species varies.[18] The principal species used throughout the world for repellent testing in the laboratory is *Aedes aegypti*, since it is easily reared, a good biter, highly anthropophilic and a vector of two important human diseases, dengue and yellow fever.[19]

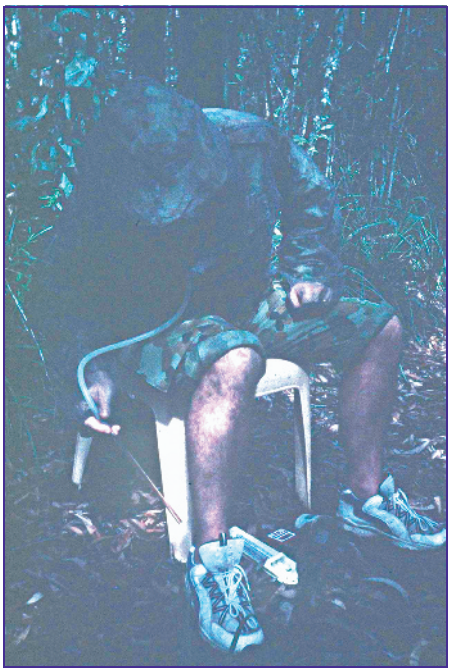
The assessment of many repellent formulations is often based on the response of this single species. However, during the last 20 years, laboratories have been assessing the effectiveness of potential repellent chemicals against other mosquito species. Laboratory studies are essential in the preliminary assessment of repellents, but ultimately field testing of repellent chemicals using human volunteers is needed to provide information on their effectiveness against pest and vector species.

Studies in several laboratories have shown a tolerance of some malaria vectors to repellent chemicals. In laboratory tests with *Anopheles dirus*, a vector of malaria in Thailand, concentrations of less than 35% deet and 30% dimethyl phthalate provided protection for 90 minutes or less. In contrast, *Aedes albopictus* was more sensitive to these formulations, which provided protection from bites for more than 180 minutes.[20] In a subsequent field trial in southeastern Thailand, 25% deet in ethanol provided less than 90% protection two hours after repellent application against *An. dirus*.[21] In another trial in northeastern Thailand, 50% deet and 75% deet provided complete protection for six hours against *An. dirus* and *Culex vishnui*.[22]

In laboratory tests with *An. farauti*, a vector of malaria in the southwest Pacific, concentrations of 5%–50% deet provided up to 130 minutes protection. However, in a field trial in northern Queensland, a formulation of 25% deet in ethanol provided greater than 95% protection against *An. farauti* for five hours.[23] In a similar field trial in Lae, Papua New Guinea, 25% deet provided protection for at least four hours.[24] These studies have shown the importance of conducting laboratory and field studies against a variety of potential vector species, as different mosquito species vary in their response to deet.

The studies described above have mainly used active ingredients dissolved in ethanol. The use of sustained-release technology has provided extended protection against biting

mosquitoes in the laboratory.[25] In field trials in the southern Philippines, an extended-duration repellent formulation containing 32% deet formulated in a polymer cream was significantly more effective than 71% deet in ethanol for 6 to 12 hours after repellent application.[26] However, sustained-release cream formulations containing 33% deet and 41% deet were no more effective than the then standard military formulation which contained 75% deet in ethanol against several species of Australian mosquitoes, including *An. farauti*.[27] In this study, the volunteers applied repellents according to label instructions and applied what each individual considered sufficient. An analysis of variance of the actual amount of each formulation applied by the volunteers showed highly significant differences. However, due to the differences in deet concentrations, there were no significant differences in the amount of active ingredient applied by the participants.[27] Although sustained-release repellent formulations are not yet available in Australia, possibly due to their cost of production and ultimate cost to consumers, they may become available in the future.



Major Frances evaluating insect repellents in the field at Cowley Beach Training Area, northern Queensland.

Synthetic repellents other than deet have also been evaluated in the last 10 years. A piperidine compound, AI3-37220, developed by the US Army, was shown to be equal to or better than deet in protecting people from malaria vectors (*Anopheles* spp.) in Thailand,[21] Kenya,[28] Australia[23] and Papua New Guinea.[29]

Effectiveness of picaridin, a new repellent

AMI is currently evaluating a repellent formulation containing a new active ingredient called picaridin, 1-(1-methylpropylcarbonyl)-2-(2-hyroxyethyl)-piperidine. A formulation containing 9.3% picaridin became commercially available in Australia in November 2000, and is called Autan Repel (Bayer). Another formulation containing 19.3% picaridin in ethanol also became available for evaluation. Both formulations are reported not to dissolve plastics and synthetic fibres, and to be less irritating to the skin than deet.

AMI conducted a comparative evaluation of repellents containing either picaridin or deet against pest and vector mosquitoes at Cowley Beach Training Area in April–May 2001.[30] In nighttime tests, 19.2% picaridin provided greater than 95% protection for at least nine hours and the ADF 35% deet repellent provided greater than 95% protection for seven hours. The 9.3% picaridin formulation provided greater than 95% protection for only two hours. In daytime tests, a 20% controlled-release deet formulation (Sawyer, 20% deet) provided greater than 95% protection for six hours, and both 19.2% picaridin and the US Army extended-duration repellent formulation (which contains 33% deet in a polymer) provided greater than 95% protection for eight hours.

In both nighttime and daytime tests, 19.2% picaridin provided protection better than or similar to formulations of deet.[30] Following additional work on its effectiveness against *Anopheles* mosquitoes, it is hoped that this product may provide an alternative to deet.

Safety and toxicity of deet

In the late 1980s concerns were raised regarding the safety of repellents containing deet.[31] Qiu et al. reviewed the safety of deet and listed the reported severe adverse events associated with skin exposure to deet.[32] These included several cases of encephalopathy and three deaths. The deaths involved two six-year-old children and one 17-month-old infant and were believed to be the result of excessive and prolonged external use.

The first large scale systematic study of the adverse effects of deet in humans was reported in 1994 by Veltri and colleagues.[33] They examined the reports of adverse effects from exposure to deet-containing repellents submitted to 71 poison control centres from 1985 to 1989. These centres participated in the American Association of Poison Control Centers national data collection system. Most of the 9086 reports involved young children who had accidentally ingested the product, although symptoms were usually quite mild. Sixty-six individuals experienced symptoms of moderate severity, but they all resolved without becoming life threatening or resulting in permanent ill effects. They were usually the result of children spraying the product in the eye(s) or inhaling it. Only five children were reported to have experienced major effects from exposure, and one child died nine days after intentionally drinking eight ounces (240 ml) of insect repellent containing deet.

The major adverse effect of deet in adults ranges from mild skin irritation to urticaria. However, Lamberg and Mulrennan[34] reported a more severe condition involving bullous eruptions of the antecubital fossa when deet was applied before sleeping. To investigate this they applied 75% deet to the antecubital fossa of 77 volunteers; of these, 37 (48%) developed blisters followed by local necrosis and late scarring. The authors suggested that this condition was the result of deet exposure and the occluded and macerated nature of this part of the arm during sleeping.[34] Reuveni and Yagupsky report that 18–24 hours after the use of 50% deet, 10 Israeli soldiers developed burning, erythema, and blisters of the antecubital fossa, followed by ulceration and

scarring.[35] Other isolated cases of local allergic reactions in the form of contact urticaria have been reported.[36]

Snodgrass et al., working on rabbits, rats and dogs, reported that the absorption of deet would be expected to be less than 10% of the applied dose.[37] Recently, Selim et al. measured the absorption, metabolism and excretion of deet in human volunteers.[38] They concluded that when deet was applied to the skin it was absorbed at a steady rate and rapidly eliminated in the urine. Less than 10% of the applied dose was absorbed, and there was complete elimination of deet and its metabolites within four hours of application.[38] Mack suggested that increased transcutaneous absorption may occur through sunburnt or damaged skin.[39]

Some recent studies that have investigated the safety of deet concluded that there is very little risk of serious adverse effects provided that it is used appropriately and not excessively for prolonged periods.[15,32,39-41] However, due to possible toxicity problems, most countries now advocate the use of repellents containing less than 50% deet.

The use of deet has been implicated as a possible contributing factor in the condition known as "Gulf War syndrome".[42] The simultaneous exposure to pyridostigmine bromide (an anti-nerve-gas agent), deet and permethrin (a synthetic pyrethroid insecticide) was found to increase neurotoxicity compared with a combination of two of the compounds. There was minimal toxicity when just one of these compounds was used.[43] The combination of these chemicals resulted in a decrease in their breakdown and elimination and an increase in their availability to the nervous system.[43] However, these findings should be interpreted with caution due to the high concentrations of deet and permethrin (500 mg/kg/day for two months administered subcutaneously) needed to elicit this response.[43] This is 60 times the normal dose of deet used by soldiers in the Gulf War.[15] The average amount of deet normally applied to cover face, neck, forearms and hands is 1.03–1.35 g (about 17 mg/kg for a 70 kg person).[27] Other studies have found no toxic synergism between deet and permethrin, even when high doses far exceeding those recommended were used.[41]

Repellent use in the ADF

A formulation containing 95% deet in ethanol was introduced into the ADF in the early 1970s. This formulation was found to be effective against several species of Australian and PNG mosquitoes, a number of which were vectors of malaria and arboviruses.[44] At the time, the standard US Army repellent formulation was 75% deet in alcohol. Concerns for adverse side effects associated with using high concentrations of deet prompted a collaborative research study between the US Army and AMI to evaluate a 33% deet sustained-release formulation.[27] This concentration was found to be just as effective in repelling mosquitoes and, after improvements were made to the formulation, a 35% deet gel formulation was placed into service in Australia in 1992. The gel formulation was designed to allow more deet to remain on the treated skin for longer than ethanol formulations and with less intradermal absorption. This formulation has been shown to be effective in protecting people against mosquitoes in PNG[29] and Australia.[30]

2: Type of repellent formulation preferred by soldiers on deployment to East Timor

Repellent type	3 RAR	5/7 RAR	1 RAR
Liquid	79 (16.5%)	122 (17.3%)	97 (17.4%)
Lotion/cream	48 (10.0%)	131 (18.5%)	62 (11.1%)
Aerosol spray	227 (47.3%)	314 (44.4%)	282 (50.5%)
Roll on	112 (23.3%)	114 (16.1%)	82 (14.7%)
Gel	14 (2.9%)	26 (3.7%)	35 (6.3%)
Totals	480	707	558

Despite the efficacy of this product in repelling mosquitoes it was poorly accepted by ADF personnel. It is not the use of a repellent *per se* that is the issue, as soldiers will readily buy and use commercial products containing deet.[45] As repellent use is an important component of a soldier's personal protection against arthropod-borne diseases, it is essential that service personnel have a product that they are willing to use.

Questionnaire regarding repellent use

To obtain information on soldiers' perceptions of insect repellents, AMI investigators asked members of the 3rd Battalion, Royal Australian Regiment (3 RAR), 5/7 RAR and 1 RAR to complete a questionnaire on their use of repellents during deployment in East Timor. 3 RAR and 5/7 RAR were deployed between September 1999 and May 2000, and 1 RAR was deployed between October 2000 and May 2001. Sixty per cent of the soldiers were privates, 22% junior NCOs, 10% senior NCOs and 8% officers. Questionnaires were completed on return from deployment by 1457 soldiers: 386 from 3 RAR, 569 from 5/7 RAR and 502 from 1 RAR.

The results showed that most soldiers did not use the ADF-issue repellent, and disliked it because it did not feel good on the skin and melted plastic. Only 290 soldiers (20%) used ADF repellent during their deployment, whereas 550 (38%) used Aerogard (containing 16%–19% deet), 756 (52%) used Rid (16% deet) and 230 (16%) used Bushman (80% deet). Many of the soldiers in this group used more than one formulation of insect repellent during their deployment of several months. Only 296 soldiers (20%) said they used repellents all the time, while 232 (16%) said they rarely or never used repellents. Most soldiers used repellents occasionally (929/1457; 64%). The main reason given for non-compliance was because they felt that there was no need, as mosquitoes were not a problem. In response to a question regarding the preferred type of repellent, 47% of soldiers preferred an aerosol spray formulation, while only 4% preferred a gel formulation (Box 2).

3: User acceptability of two repellent formulations by Australian soldiers during operations in East Timor*

Repellent formulation	Number (%) of responses		
	Mild, uncomfortable (sticky, oily)	Actual irritation (burning sensation)	No particular feeling
Autan (Bayer, 19.2% picaridin)	10 (2.8%)	42 (11.9%)	98 (27.7%)
ADF gel (35% deet)	112 (31.7%)	79 (22.3%)	12 (3.4%)

*Percentage based on a total of 353 responses.

Comparison of 35% deet (in a gel) with 19.2% picaridin (aerosol spray)

In early 2001, 150 soldiers deployed to East Timor were asked to compare the ADF 35% deet gel formulation with 19.2% picaridin applied as a non-pressurised pump action spray. The soldiers were asked to use each formulation for one week, applying it twice a day. At the end of two weeks, they were asked to complete a questionnaire.

The results of this survey supported the earlier findings with 3 RAR and 5/7 RAR, with 94% (141/150 responses) preferring the aerosol pump action spray over the gel. The results of the comparison of adverse effects following application are shown in Box 3. Significantly more soldiers reported mild discomfort and irritation with the use of ADF deet compared with 19.2% picaridin.

Conclusions

The use of personal protection measures, such as applying chemical repellents to the exposed skin, will continue to be the first line of defence against mosquito-borne diseases such as malaria and dengue. For repellents to be effective, they have to be used consistently, so the search for more acceptable repellent formulations is important. New active ingredients such as picaridin and the piperidine AI3-37220 are being evaluated. If they prove to be equally effective in providing a broad spectrum of activity against mosquitoes, their greater acceptability to soldiers may make them a better alternative.

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Fitness

Body mass index of Australian Army reservists and the Australian population — is there a difference?

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Synopsis

Objective: To investigate the existence of a difference in the body mass index (BMI) of Australian Army Reserve (ARES) personnel and the Australian population.
Design: Cross-sectional study of ARES personnel and secondary analysis of data presented in the Australian Diabetes, Obesity and Lifestyle Study conducted by the International Diabetes Institute in 1999–2000.
Participants: 562 ARES personnel of both sexes aged 17 and over based in Perth and 704 Perth residents of both sexes aged 20 and over selected randomly from the Commonwealth electoral roll.
Main outcome measures: BMI based on measured height and weight.
Results: ARES males aged 17–29 had a lower BMI than the Australian male population aged 20–29, and their mean BMI was in the healthy weight range (BMI 20–24.9). The mean BMI of ARES males aged 30–54 was in the overweight category (BMI, 25–29.9) and was no different from the mean BMI of the Australian male population aged 30–54. There was no difference in BMI between ARES females aged 17–44 and the Australian female population aged 20–44. The mean BMI for women was in the healthy weight range up to the age of 34, and in the overweight category for age 35–44.
Conclusion: ARES males aged 17–29 have a lower BMI than the Australian male population and a BMI in the healthy weight range, possibly due to a selection effect. ARES males aged 30–54 have the same overweight BMI as Australian males aged 30–54. Membership of the ARES does not have any impact on the BMI of males aged 30–54.

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THE BODY MASS INDEX (BMI) of the Australian population is increasing, with more people entering the overweight and obese categories.[1] By late 1995, over 64% of Australian men and 49% of Australian women aged over 18 were overweight or obese.[2] This contrasts with figures from 1989 showing that 52% of Australian men and 38% of Australian women aged over 20 were overweight or obese.[3]

Maintaining BMI within the healthy weight range of 20–25 kg/m^2 is important, as this range is associated with the longest high quality life expectancy and the lowest death rate.[4] A BMI in the overweight or obesity category is associated with increased mortality[5,6] and/or morbidity from type 2 diabetes, hypertension, gallbladder disease, some types of cancers and coronary heart disease.[4] Overweight men (BMI, 25–30) have 1.7 times the risk of coronary heart disease as those in the healthy weight range.[7] Overweight and obesity are caused by a combination of low activity,[8] high caloric intake[4] and genetic factors.[9]

The men and women of the Australian Army Reserve (ARES) are a subset of the Australian population who, while working in the ARES on a part-time volunteer basis, must nonetheless fulfil and maintain all the health and fitness