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USE OF INSECT REPELLENTS IN PREGNANCY

SUMMARY: Pregnant women should avoid travel to areas where a risk of mosquito-borne infection has been identified. In cases where travel is unavoidable non-pharmacological bite-avoidance measures are important.

- Minimise skin exposure between dusk and dawn
- Cover as much of the skin as possible with loose fitting clothing
- Use an insect repellent on areas of exposed skin
- Use insecticide-impregnated mosquito bed nets

Diethyl-m-toluamide (DEET) 20-50% is recommended for travellers to malarial areas. There are limited data on the use of DEET in human pregnancy, especially in the first trimester. No adverse effects on neonatal growth and development have been observed in women exposed to DEET 20% in the second and third trimesters.

Inadvertent exposure to DEET at any stage of pregnancy is not an indication for termination of the pregnancy or invasive diagnostic procedures. The use of DEET is recommended for all pregnant women travelling to a malarial area.

P-menthane-3,8-diol (PMD) and picaridin (icaridin) are used as alternatives to DEET-containing products. There are no data on exposure in human pregnancy, however animal studies have not demonstrated any features of maternal or developmental toxicity.

It is important that insect repellents (especially those containing DEET) are used according to the manufacturer's guidelines. Excessive application of these products should be avoided.

Note: Where travel to a malarial area during pregnancy is unavoidable, additional prophylaxis will be necessary. Please consult the Malaria prophylaxis monograph, or contact NTIS on (0191) 232 1525 for more information.

Diethyl-m-toluamide (DEET)

DEET is one of the most widely used insect repellents and is recommended for travel to areas where a risk of malaria infection has been identified.¹ DEET can be absorbed through the skin and systemic effects have been seen after dermal application. Information on adverse effects is mainly based on cases of ingestion and excessive dermal application and includes central nervous system disorders (e.g. confusion, slurred speech, insomnia and seizures), nausea and vomiting, and hypotension.

Preclinical (animal) data

Initial studies of DEET in rats and chicken embryos demonstrated a high frequency of malformations.^{2,3} However, more recent studies reporting ingestion (up to 750mg/kg/day) and intramuscular injection (300mg/kg) have not demonstrated reproductive or developmental toxicity in rats and rabbits.^{4,5}

DEET did not affect male fertility or induce dominant lethal mutations in treated rats.⁵

Human data

Often, data from observational sources or case reports, including data collected by NTIS, may be confounded by maternal co-ingestion of a number of drugs, at varying doses, and for a range of indications. The severity of the underlying maternal condition, where relevant, is frequently unknown and information on other potential confounding variables may be incomplete. These factors should be considered when interpreting observational human pregnancy data.

One double-blind, randomised trial (n = 897) carried out in the Thai-Burmese border area evaluated the effects of exposure to DEET 20% solution (1.7g of DEET per day) during the second and third trimesters of pregnancy (average use = 18 weeks).⁶ Throughout the study, 741 singleton live births occurred with no significant difference between the DEET and placebo groups with respect to survival, growth and neurological development of the neonates at birth and one year.⁶ There were 12 cases of congenital malformations reported in this study (6 in each group), with no pattern of congenital malformations identified. DEET was detected in the cord blood in 8% of a sub-group of 50 women, indicating the potential for placental transfer.

There are no epidemiological studies evaluating the effects of exposure to DEET in the first trimester of pregnancy. One case report describes coarctation of the aorta in two male cousins after maternal exposure to DEET-containing insect repellent (in addition to several other insecticides) in the first trimester. The authors concluded that the relative contributions of environmental and genetic factors could not be determined in this case.⁷

Longer-term topical application of DEET-containing insect repellent has been reported in one pregnancy which resulted in a single male child with mental retardation, impaired sensorimotor co-ordination and craniofacial dysmorphism. The mother regularly applied insect repellent (25% DEET solution) whilst also taking prophylactic chloroquine throughout the pregnancy.⁸

Risk of neurotoxicity

A number of case reports on the development of neurotoxicity following topical application of DEET in children have been reported.⁹ While neurotoxic effects on the fetus have not been noted following use of DEET in pregnancy, these cases illustrate the potential for the product to cause general toxicity.

Other insect repellents

There are no data on exposure to picaridin (icaridin) or p-menthane-3,8-diol (PMD) during human pregnancy.

Animal studies have found no effect on fertility, pregnancy or lactation with picaridin exposure.^{10, 11} Picaridin is reported to have repellent properties similar to those of DEET, therefore the recommended concentration for travellers to areas where malarial infection has been identified is $\geq 20\%$.¹ To date there are no documented reports of human toxicity associated with use of picaridin.

PMD is a synthetically manufactured ingredient of the lemon eucalyptus plant and is available as an insect repellent. There are no reports on the effects of PMD use in human pregnancy.¹² Animal data is limited to one developmental toxicity study in rats where no treatment-related signs of developmental toxicity or maternal toxicity were observed.¹² PMD gives about the same amount of protection afforded by 15% DEET.¹³ This is less than the HPA recommended concentration for travellers to areas where a risk of malaria infection has been identified (<20% considered inappropriate).¹ However PMD containing products are effective insect repellents and can be used in areas where the risk of mosquito-borne infection is low.

In September 2006 citronella and eucalyptus oil were identified under the Biocidal Products Directive (BPD)(98/8/EC). This means they could no longer be used as insect repellents and has resulted in a number of products being discontinued in the UK.

Paternal exposure

There were no reports found regarding paternal exposure to insect repellents.

Lactation

There were no reports found regarding neonatal toxicity following exposure to insect repellents during lactation.

NTIS Data

NTIS has no follow up data on exposure to insect repellents during pregnancy.

Conclusions

The limited published data do not demonstrate a significant increase in risk of congenital malformations or other adverse fetal effects following the use of any topical insect repellents. The data on all agents are too limited to state that there is no increased risk of adverse outcomes. Given the general toxicity of DEET, less toxic alternatives such as picaridin and PMD may be more appropriate for travel to areas where the risk of malaria is not recognised.

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Completion Date: December 2007

Disclaimer: Every effort has been made to ensure that this monograph is accurate and up-to-date. However it cannot cover every eventuality and the information providers cannot be held responsible for any adverse outcomes of the measures recommended. There is a background incidence of congenital malformations (2-3%) and spontaneous abortions (10-20%) irrespective of any drug or chemical exposure. The final decision regarding which treatment is used for an individual patient remains the clinical responsibility of the prescriber.