Summary Wilderness Meeting 3/28/16

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* “**Chemical and Plant-Based Insect Repellents: Efficacy, Safety, and Toxicity.”**
	+ James Diaz, MD, MPH&TM, DrPH
	+ Published in *Wilderness &Environmental Medicine*, 2016
	+ Review article examining arthropod-borne infectious diseases and prevention.
* Methods
	+ Online search through multiple websites (pubmed, medline, Ovid, Cochrane, etc) for articles that meet any of the following criteria
		- * Describe burden of arthropod-borne diseases
			* Differentiate insecticides from repellants
			* Compare efficacies and toxicities
* Results
	+ Definitions:
		- Insect repellant: chemical or organic agent that makes atmosphere within 4 cm so noxious to insects that they are discourage from biting or contact
		- Insecticide: chemical or organic agent, often plant derived, that kills insects, usually by neurotoxin.
	+ Why use insect repellants
		- 3 major reasons
			* New threats to human health posed by emerging and imported arthropod-borne infectious diseases
			* Dominance of new, competent insect vectors of infectious diseases
			* Inability to primarily prevent transmission of most arthropod diseases by vaccinations (except yellow fever vaccine and few others)
		- Arthropod-borne disease threats
			* Arthropod-borne infectious disease primarily transmitted to humans through extensive reservoirs in birds and mammals via bites from mosquitoes, midges, flies, fleas, ticks.
			* Most common arthropod-borne disease in U.S. and Europe is Lyme disease by the tick, Borrelia burgdorferi
			* Most common mosquito-borne disease in U.S. is West Nile Virus, an arbovirus from Culicine mosquitoes.
				+ Usually asymptomatic, sometimes meningoencephalitis
			* Ticks are more versatile insect vectors than mosquitoes and can transmit variety of pathogens, including bacteria, viruses, and parasites, sometimes concurrently.
		- Emerging competent arthropod vectors
			* Mosquitos

responsible for most arthropod-borne diseases worldwide.

Malaria- most deaths worldwide

* + - * + Temperate and tropical regions harbor 2 competent mosquito vectors for dengue and chikingunya

Aedes aegypti

Aedes albopictus-Asian tiger mosquito imported to U.S. from SE Asia now replaced A. aegypti as dominant mosquito in many areas, especially southeastern U.S.

* + - * + Most cases of chikingunya and dengue in U.S. and Europe imported from travelers, but there has occurred local transmission in both.
			* Ticks
				+ Dominant vectors of infectious disease transmission within U.S. and Europe

14 tick-transmitted diseases in U.S., 3 new.

* + - Properties of ideal insect repellants
			* Must be effective, save, and pleasant to apply in children, adults, and during pregnancy without damaging skin or clothes
	+ Insect repellants
		- 2 Categories: synthetic chemicals and plant-derived oils and synthetics
		- Chemical Repellants:
			* DEET (N-diethyl-3-methylbenzamide)
				+ Used by U.S. army in 1946
				+ Used by public by 1956
				+ Available in aerosols, creams, lotions, sprays, gels, sticks, wipes

Concentrations vary from 5-100%

* + - * + Human studies have confirmed plateau effect when concentration exceeds 50%
				+ DEET concentrations in 10-35% will provide adequate insect bite protection.
				+ Under 2 yrs old should use concentrations under 30%
				+ Will not damage cotton, wool, or nylon clothing
				+ Will damage rayon, spandex, leather, and dissolve plastic, vinyl upholstery
				+ Toxicity

DEET crosses placenta, but no developmental toxicity ever described.

FDA recommends applying sunscreen before DEET as applying DEET before sunscreen can lead to increased absorption.

Between 1956-2008 there were 43 confirmed case reports DEET toxicity

25 CNS involvement

lethargy, Headache, confusion, disorientation, ataxia, tremors, seizures, acute encephalopathy, and psychosis

1 Cardiovascular effect

orthostatic hypotension and bradycardia

17 allergic or cutaneous manifestations

urticarial reactions, hemorrhagic vesiculobullous erosions an topical preparations above 50%

6 deaths

3 intentional ingestions

1 in child with ornithine transcarbamylase deficiency

2 cases occurred in children with convulsive CNS reactions after repeated overapplications.

* + - * Picaridin
				+ Developed in Europe in 1990’s
				+ Several advantages over DEET

Lack chemical odor

Non-sticky or greasy feeling

Doesn’t damage clothing or plastics

* + - * + Mechanism unknown
				+ Effective against mosquitoes, flies, chiggers, and ticks
				+ Available as lotions, sprays, and wipes in strengths of 7-20%
				+ May provide greater protection and longer duration than DEET against ticks.
				+ Not recommend in childen under 2 yrs old
				+ Toxicty

No dermal, solid organ, or reproductive toxicity in human field and animal investigations.

* + - * IR3535 (ethyl butylacetylaminoproprionate)
				+ Initially marketed as skin emollient and moisturizer (avon skin so soft)
				+ Greater efficacy and duration of action than DEET against onchocerciasis-transmitting black flies, leishmaniasis-transmitting sandflies, and biting midges
				+ Toxicity

Not demonstrated developmental toxicity

* + - Plant-derived insect repellants
			* Oil of lemon eucalyptus (p-menthan-3, 8-diol)
				+ Extract of the leaves of lemon eucalyptus or synthetic version of its major repellent component, PMD (8-diol)
				+ Available in pump sprays in concentrations 10-40%
				+ Mosquito repellant effectivity and duration comparable to DEET.
				+ May offer better protection than DEET against ticks.
				+ Not recommended in children under 3 years of age
			* Citronella (3,7-dimethyloct-6-en-1-al)
				+ Natural plant oil from several species of Cymbopogon lemongrass.
				+ Available as a lotion, oil, or solid wax in candles and flame pots in concentrations 0.5-20%
				+ Highly volatile with a short duration of action of 2 hours.
				+ Ineffective against flies, fleas, biting midges, and ticks.
			* Permethrin
				+ Derived from crushed dried flowers of Chrysanthemum cinerarifolium
				+ Not absorbed topically
				+ Requires direct contact to be effective
				+ Mechanism:

Initial excitation of insects CNS by Na channel blockade followed by acetylcholinesterase inhibition and fatal paralysis

* + - * + Applied to clothing, bed nets, tents, sleeping bags
				+ Provide very lethal protection against mosquitoes, flies, biting midges, chiggers, fleas,sandflies, and ticks
				+ Should retreat products treated with permethrin after 5-70 washings
				+ Provides better protection than DEET and picaridin against ticks
				+ Toxicity

Neurotoxicity after massve ingestion

ataxia, hyperactivity, hyperthermia, seizures, paralysis

No known developmental toxicity (Pregnancy B cat)

Avoid in patients allergic to chrysanthemums

* + - * Garlic: a double-blinded, placebo controlled trial showed garlic to be ineffective
	+ Paper recommends a combination of insect repellant (DEET or picaridin) on skin with permethrin or other synthetic pyrethroid-impregnanted clothing.
	+ If encountering ticks, biting midges, sandflies, or black flies, consider IR3535, picaridin, or PMD instead of DEET as they offer better protection
	+ Area and barrier chemical insect repellants
		- Permethrin treate fabrics are highly effective adjuncts to topical repellants.
		- Electric insecticide vaporizers that release permethrin can be used to inhibit mosquitoes, but no evidence of prevention of transmission of arthropod borne diseases.
		- Mosquito coils when can smoke for hours, discouraging mosquitoes
			* Repeated exposures may pose significant risk factors for lung disease/lung cancer.
		- Plant oil-base candles may reduce mosquitoes and fly bites
			* No evidence to support them over arthropod avoidance, topical insect repellants, and permethrin impregnated blinds and curtains
		- Non-chemical measures
			* CDC recommends long sleeved shirts, hats, boots, covered shoes.
			* Ticks should be removed for expert identification within 24 hours.
				+ Removal should be done with forceps or fine-tipped tweezers
				+ Grip at point closest to skin attachment, use gentle steady traction
				+ Avoid using fingers (can crush ticks causing regurgitation of pathogens), burn with matches, or painting with adhesives, solvents, nail polish, or nail polish remover.