
Prevention of arthropod-related disease

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Arthropods of medical importance include vespids, ticks, mosquitoes, mites, flies, and fleas. They spread illness as disease vectors, are associated with lethal allergic reactions, and produce potentially deadly toxins. Strategies for prevention of illness include avoidance, vector reduction programs, chemoprophylaxis, and repellents. Strategies must be tailored to regional risks. (J Am Acad Dermatol 2004;51:947-54.)

Recently, vector-borne disease has featured prominently in the popular press, with news of leishmaniasis among US troops in Iraq and mosquito-borne outbreaks of West Nile fever in several states. Rocky Mountain spotted fever (RMSF) remains the most lethal vector-borne illness in North America,¹ but many other illnesses can be transmitted by mosquitoes, flies, ticks, and fleas. In several regions of the United States, mosquitoes carry West Nile fever, St Louis encephalitis, and equine encephalitis. Dengue is once again a problem in southern Texas,² and even malaria has resurfaced as an endemic infection.³ Ticks in the United States carry Lyme disease, RMSF, ehrlichiosis, babesiosis, Colorado tick fever, relapsing fever, and tularemia. Sandflies in Texas transmit leishmaniasis, and fleas in the Southwest transmit plague and endemic typhus. This article will review strategies for the prevention of arthropod-related illness (Table I), to include anaphylaxis, mosquito-borne disease, diseases associated with ticks and mites, and fleas and ticks on pets. Most of the strategies discussed are applicable worldwide. Guidance for particular geographic regions may be obtained at <http://www.cdc.gov/travel/> or <http://healthlibrary.stanford.edu/resources/internet/bodysystems/infectious.html>.

THE BURDEN OF ARTHROPOD-RELATED DISEASE

Arthropod-borne diseases are major causes of death and morbidity throughout the world. Malaria kills thousands every year. Dengue, sleeping sickness, leishmaniasis, Chagas' disease, and viral hemorrhagic fevers remain important threats in much of the world. Citizens of most developed countries

suffer much lower rates of infection, even when they travel abroad. US travelers who follow Centers for Disease Control and Prevention guidelines are unlikely to become infected. Of the 891 US civilians who acquired malaria abroad in 2001, only 180 (20.2%) reported that they had followed the recommended chemoprophylactic drug regimen.⁴ Proper use of chemoprophylaxis, repellents, mosquito netting, and protective clothing reduce the incidence of disease when traveling.^{5,6} At home, public health measures control the prevalence of mosquito-borne illness in endemic areas. State health departments administer highly successful mosquito control programs. When used properly, insecticides used for vector control have a low incidence of adverse effects and save many lives each year.⁷ Our affluent indoor lifestyle affords us a large measure of protection. Window screens and air-conditioned indoor living provide significant protection, as evidenced by the recent outbreak of dengue fever along the US—Mexican border. Although the vector, *Aedes aegypti*, was more abundant in Laredo, Tex, the incidence of disease was much higher in Nuevo Laredo, Mexico.⁸

Despite this, many US citizens still die every year from arthropod-related illnesses. The recent outbreaks of West Nile fever demonstrated just how fragile our defenses can be. We do not live sealed inside our homes. We live in the world, and the world is full of disease-carrying pests. Even at home, our pets bring disease-carrying arthropods into the house. Thus, despite our affluent, air-conditioned lives, we face the challenge of controlling arthropod-borne illness. Among those less fortunate, poverty and homelessness contribute significantly to the spread of vector-borne disease. Those who must sleep outdoors are at much greater risk for mosquito-borne illnesses. Louse and flea infestation also plays a significant role in the spread of disease. Homeless patients who have a history of ectoparasite infestation have a high prevalence of infection with *Bartonella quintana*, a cause of endocarditis.⁹⁻¹¹

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Table I. Prevention strategies for arthropod-borne illnesses

Arthropod-related illness	Prevention strategies
Anaphylaxis	Bees and vespids: Desensitization Avoid bright clothing, perfume, and sites where wasps congregate. Removal of bee and vespid colonies. Immunotherapy. Fire ants: Desensitization Bait insecticides, growth regulators, avermectins, spinosyns, pyethrin derivatives, botanicals, parasitic microsporidia (<i>Thelohania solenopsae</i>), and phorid flies.
Mosquito-borne diseases such as malaria, dengue, and viral encephalidites	Malaria chemoprophylaxis, repellents, mosquito netting, protective clothing, insecticides, screens, drainage of stagnant water, mosquito traps, fish or turtles to consume larvae
Fly-borne diseases such as leishmaniasis, bartonellosis, and sleeping sickness	Repellents, netting, protective clothing, insecticides, screens
Tick-associated diseases such as Rocky Mountain spotted fever, Lyme disease, and tick paralysis	Primary: Tick inspections and early tick removal, permethrin-treated fabric, repellents, leaf removal, acaricide sprays, bait boxes, treated feed for hosts, host exclusion, mulching of border beds, parasitic wasps, nematodes, fungi, encourage bird populations, vaccines Secondary: Antibiotic prophylaxis
Mite-borne disease such as scrub typhus	Primary: Permethrin-treated fabric, repellents, acaricide sprays Secondary: Antibiotic prophylaxis
Bug-borne disease such as Chagas' disease	Screens, repair of mud and daub, permethrin-treated surfaces, insecticide sprays
Flea-borne disease such as endemic typhus and plague	Host exclusion, insecticidal sprays, growth regulators and boric acid Prophylaxis of pets as recommended by a veterinarian (including lufenuron, fipronil, imidacloprid, selamectin, and nitenpyram)
Web sites for regional threats	http://www.cdc.gov/travel/ http://healthlibrary.stanford.edu/resources/internet/bodysystems/infectious.html

Both primary and secondary prevention play valuable roles in controlling arthropod-associated disease. Primary prevention includes drainage of stagnant water, insecticide-spraying programs, programs for the homeless, arthropod avoidance, use of repellents, prompt tick removal, and vaccination. Secondary prevention and treatment include antibiotic prophylaxis, early treatment of illness, and the use of epinephrine bee sting kits to treat anaphylaxis.

Anaphylaxis

Anaphylaxis-related deaths can be prevented by the prompt administration of epinephrine.

Anaphylaxis is most commonly related to hymenopterid stings.¹² This order of insects includes bees, wasps, hornets, and ants. Patients with hypersensitivity to insect stings are more likely to be atopic, and some have underlying mastocytosis.¹³

All patients with a history of sting hypersensitivity should carry injectable epinephrine.¹⁴ They should also avoid bright clothing and perfume. Many stings occur at picnic grounds and other sites where wasps congregate at trash cans. Avoidance of these sites can prevent many stings. Epipens (Dey Laboratories, Napa, Calif) deliver a single intramuscular injection of 0.3 mL of epinephrine in a 1:1000 dilution. The Epipen Jr (Dey Laboratories) contains a half-strength

solution. Patients should be referred to an allergist for immunotherapy.

Fire ants can be controlled with bait insecticides, containing hydramethylnon and sulfuramid. These are spread in the form of bread crumb—like granules. A wide variety of other fire ant control products are marketed including insect growth regulators, avermectins, spinosyns, pyrethrin derivatives, and various botanicals. Parasitic microsporidia (*Thelebania solenopsae*) have shown promise for the control of fire ants.^{15,16} Phorid flies also shows promise as a form of biologic control.¹⁷ Immunotherapy is indicated. Patients should be referred to an allergist.

Mosquito and sandfly-borne diseases

Prevention of mosquito and sandfly bites requires the use of protective clothing and chemical repellents, and methods to reduce the numbers of flies and mosquitoes in a given area. As the anophelini mosquitoes that carry malaria bite mostly at night, retiring to the indoors in the evening plays a major role in disease prevention. Transmission is also prevented by repellents and pyrethroid-impregnated mosquito netting. All travelers to malaria-endemic areas should take the recommended chemoprophylaxis. In contrast to anophelini mosquitoes, mosquitoes that carry dengue tend to bite during the day. Any traveler to south Texas soon becomes aware that day-biting mosquitoes exist. Repellents and protective clothing are especially important to prevent transmission in dengue-endemic areas.^{18,19} Control of standing water, stocking of ponds with fish to consume mosquito larvae, area spraying, and mosquito traps are helpful for area control of mosquitoes. Mosquitoes are generally attracted to traps by the use of carbon dioxide, although light, heat, and chemical attractants such as octenol and butanone are commonly used.²⁰⁻²² Many mosquitoes respond best to combinations of attractants, although this varies by species, and some *Culex* mosquitoes are repelled by octenol.²³⁻²⁵ The traps may use adhesives, nets, or air counterflow to trap the mosquitoes until they desiccate. Many such traps are now marketed. In general, propane-powered units provide superior results. Prospective buyers should consult consumer magazines or World Wide Web sites and local health departments for advice on the best control methods for their geographic area. A good evaluation of various models was performed by the US Department of Agriculture and published in the *Journal of Vector Ecology* in 2002.²⁶

Applications of insect repellents remain an important part of vector-borne disease prevention. Deet (N,N-diethyl-3-methylbenzamide, previously called N,N-diethyl-m-toluamide) remains a highly

effective repellent for the prevention of mosquito and sandfly bites and has a good safety record.^{27,28}

The American Academy of Pediatrics recommends concentrations of 30% or less in products intended for use in children. The lowest effective concentration should be used. Adults can use higher concentrations, but 10% to 30% extended-release products are preferred over higher concentrations of deet because they provide sustained levels and are less likely to cause systemic toxicity or deet dermatitis. High concentrations of deet have a strong early peak effect, but the effect wanes quickly. Concentrated deet can occasionally produce dramatic bullous eruptions.²⁹ Anaphylaxis has rarely been reported.³⁰

Deet can be applied both to exposed skin and to clothing. The duration of efficacy of deet is dependent on the formulation, the dose applied, and the sex of the individual. Girls and women demonstrate less protection, independent of serum estradiol levels.³¹ Efficacy is significantly reduced by the presence of skin abrasions.³² The combination of a deet-containing repellent and permethrin-treated clothing has proved highly effective against a wide range of biting arthropods, and should be considered the standard against which other regimens are measured.^{33,34}

A recently published arm box study evaluated the duration of efficacy of various popular repellents.³⁵ The study has several limitations, the greatest of which is that it did not include field evaluation of the agents. Nevertheless, it provides some indication of the duration of action of various available agents. The study showed excellent results for 23.8% deet (mean complete protection 301.5 min), 20% deet (234.4 min), 6.65% deet (112.4 min; Off! Skintastic, SC Johnson, Racine, Wis), soybean oil (94.6 min; Bite Blocker for Kids, Homs LLC, Clayton, NC), and 4.75% deet (88.4 min; Off! Skintastic for Kids, SC Johnson). Poorer results were noted for IR3535 (22.9 min; Skin So Soft Bug Guard Plus, Avon, New York, NY), citronella (19.7 min; Natrapel, Tender Corp, Littleton, NH), citronella (10.3 min; Skin So Soft Bug Guard, Avon), Skin So Soft Oil (9.6 min; Avon), and Gone Original Wristband (0.2 min; Solar Gloooooo, Glen Head, NY).

Citronella candles and incense have little documented efficacy.³⁶ Neemos (neem oil) has proven efficacy as a mosquito repellent in areas endemic for malaria.³⁷ Travelers to such areas should still carry and use a deet repellent. New repellents are being developed. Although field trials remain the gold standard for evaluation of any new repellent, arm box studies and in vitro predictive values such as the van der Waals surface electrostatic potential, the

atomic charge at the amide nitrogen atom, and the dipole moment are useful to identify new agents for field testing.³⁸ One-piperidinecarboxylic acid, 2-(2-hydroxyethyl)-, 1-methylpropylester (KBR 3023, Picaridin, Bayrepel[Bayer AG, Leverkusen], and Autan [SC Johnson]) was as effective as deet in field trials against a variety of mosquitoes in Queensland, Australia,³⁹ and Africa.⁴⁰

Preventing disease from ticks and mites

In parts of Asia, chiggers carry scrub typhus. In North America, tick-borne diseases have a wide distribution. *Ixodes scapularis*, the principal vector for Lyme disease, also transmits human granulocytic ehrlichiosis and human babesiosis. Lyme disease remains the most common tick-borne illness in North America. Despite the perceived public threat, an effective Lyme vaccine proved to be a commercial failure and was voluntarily withdrawn from the market in February 2002. We must, therefore, rely on other means to prevent tick-borne disease. Tick-borne diseases in the United States include Lyme disease, RMSF, ehrlichiosis, babesiosis, Colorado tick fever, relapsing fever, and tularemia. Tick paralysis is related to a neurotoxin produced by the tick. In Australia, *Ixodes* ticks are an important cause of human tick paralysis, but in North America, *Dermacentor* ticks are the only significant cause. *Dermacentor* ticks preferentially attach to the head and neck, and are often hidden by hair. Tick paralysis closely resembles Guillain-Barré syndrome and carries a 10% mortality.⁴¹⁻⁴⁴ The tick is often found at autopsy or by the mortician.

Permethrin, the active ingredient in Elimite and Nix, has been marketed as a spray tick repellent. It is effective for a broad range of crawling arthropods and can be used in conjunction with a deet-based repellent to provide superior protection against ticks and chiggers.^{33,34} Once applied to clothing, it is stable through a number of wash cycles.⁴⁵ It can be used on clothing, tents, sleeping bags, and mosquito netting, and has demonstrated efficacy against a broad range of North American and European ticks. Some Southwest Asian and North African hard ticks have demonstrated innate resistance to permethrin. In these ticks, permethrin can provoke a pheromone-like attachment response.⁴⁶ Fortunately, this phenomenon appears to have a limited geographic distribution, and is not a problem in North America.

Tick exclusion and prompt tick removal remain critical strategies for the prevention of tick-borne illness. Ticks enter yards, golf courses, and playing fields by crawling and by attaching to an intermediate host. Most ticks are acquired in nonwooded

areas, but recreational areas and yards that abut green belts have higher rates of infection.⁴⁷⁻⁴⁹ A safe perimeter around recreational areas can be created by several means. Deer fencing can be combined with removal of leaf debris at the edge of the woods, and planting of border beds with wood-chip mulch.⁵⁰ These efforts deter deer, and keep people from entering the adjacent woods. Hard ticks are susceptible to dehydration if they cannot descend into a moist shaded layer of leaf debris.^{51,52} The presence of leaf debris in backyard play areas has been shown to be a risk factor for tick attachments in children.⁵³ The density of ticks decreases, and the efficacy of acaricidal sprays is improved, when leaf debris is removed. Homeowners should be reminded that landscaping and clearing of leaf debris are high-risk activities in terms of tick exposure. Tick inspections are mandatory after such activities, as after other outdoor activities.⁵⁴

Exclusion of deer has been shown to be effective in reducing the number of disease-carrying ticks.^{55,56} This method only reduces the numbers of ticks that use the deer as a host. Smaller hosts, such as the white-footed mouse, are harder to exclude by fencing, so the protection is incomplete. Bait boxes and deer feeding stations have been outfitted to deliver topical acaricides, such as amitraz or permethrin, to the coats of mice and deer.⁵⁷ This type of strategy has proved effective in reducing tick numbers.^{58,59} Ivermectin has also been added to feed corn to control tick populations.⁶⁰ Mouse bedding material impregnated with an acaricide can also be effective.^{61,62} Targeted use of acaricides may have less environmental impact than widespread spraying. A variety of biologic control strategies have been proposed.⁶³ Parasitic wasps, such as *Ixodiphagus hookeri*, provide biologic control of tick populations in some areas of New England. Unfortunately, to sustain wasp populations, the deer population must be maintained at a density of approximately 10 to 20/km².⁶⁴ When the deer population decreases, the wasps disappear. This makes an otherwise attractive method of control financially risky. Nematodes have been used commercially to control termite infestation, and show potential for the control of tick populations as well.⁶⁵ Entopathogenic fungi, and foraging ants and birds, have also demonstrated some potential for use in the control of tick populations.⁶⁶ Biologic control methods have the appeal that they could potentially be self-sustaining in the environment, but all of these alternatives are expensive when compared with simple exclusion of deer with fencing. Some will fare no better than the Lyme vaccine did in the marketplace. None has yet proven to be a commercial success, and most

communities and homeowners will take much more modest steps to control tick populations.

Ticks are unlikely to transmit disease when they have been attached for less than 24 to 36 hours.⁶⁷⁻⁶⁹ Therefore, prompt tick removal has been promoted as first-line prevention of disease transmission. When removing a tick, care should be taken not to squeeze the abdomen.⁷⁰ Gentle traction tends to result in more complete removal, whereas a twisting motion may leave a single small mouth part in many cases.^{71,72} Gloves should be worn when possible, and hands should be washed after contact with the tick. Several inexpensive plastic tick removal devices are marketed. The Tick Nipper includes a plastic magnifying lens to aid in tick removal. A similar device, without the magnifying lens, can be made by cutting a narrow slot in a plastic spoon. Even removal with tweezers generally gives good results.⁷³ Applications of isopropyl alcohol, fingernail polish, petroleum jelly, and hot matches do not work well and may result in patient injury.⁷¹

Despite the efficacy of early tick removal, this strategy is only effective if tick inspections are routinely performed. Comprehensive inspections, including the genital area and scalp, must be performed after every possible exposure. Casual inspection is inadequate, and inspections only after outings in the woods will miss many tick attachments, as ticks are often encountered in the backyard, rather than the woods. Tick habitats include grassy areas, caves, old cabins, and scrubland. In disease-endemic areas, adult ticks are found and removed within 36 hours of attachment only 60% of the time. Smaller nymphal ticks are only removed in 10% of patients within the first 24 hours of tick feeding.⁷⁴ Prolonged tick attachment, long enough for disease transmission to occur, is more common in children.⁷⁵ Patients also tend to underestimate the duration of tick attachments, and measurements of tick engorgement may be more reliable than estimating hours of attachment.⁷⁶

Because a significant population will experience long durations of tick attachment, many patients will require antibiotic treatment of symptomatic disease. Most tick-borne organisms respond to tetracycline, and the cost and risks associated with a course of doxycycline are relatively low. In the case of RMSF, a significant delay in the initiation of antibiotic therapy can prove fatal.⁷⁷ In heavily endemic areas, a tetracycline should be considered for anyone with fever and a headache, regardless of the history of a tick bite or the presence of rash.^{78,79} In children, doxycycline is recommended by the pediatric red book, as staining of teeth is unlikely with a short course of tetracycline and chloramphenicol is not as active against *Rickettsiae*.

Antibiotic prophylaxis after tick bites remains controversial. Secondary prevention with an antibiotic may be reasonable in some heavily endemic areas in patients who have many attached ticks or a heavily engorged tick. In such settings, the risk-benefit ratio may favor prophylaxis.⁸⁰⁻⁸² To prevent disease, the dose must be sufficient and the timing must be appropriate.⁸³ In the case of RMSF, a single dose administered early in the course of incubation may delay the onset of clinical symptoms and cloud the diagnostic picture. If given within 48 hours before expected onset of disease, even a single dose can be effective in preventing disease, but as the incubation period varies, timing can be tricky.⁸⁴ There is no evidence that a 10-day course of a tetracycline given before the onset of disease is any less effective than a full course given after the onset of disease. For this reason, I have never prescribed single-dose prophylaxis.

Although prophylaxis before the onset of symptoms may be justified in some circumstances, most tick-borne diseases are quite responsive to antibiotic therapy if it is started soon after the onset of symptoms, and it is difficult to justify the cost and risks of widespread use of antibiotics for every tick bite.⁸⁵ Asymptomatic infection with the Lyme spirochete is rare in the United States.⁸⁶ When faced with an anxious patient who requests antibiotic prophylaxis, it is now my practice to provide a prescription for a 10-day course of antibiotic. The patient is carefully counseled about the signs of infection and the efficacy of antibiotics when started promptly after the onset of signs and symptoms. The patient is advised not to fill the prescription unless signs or symptoms occur. The patient rarely fills the prescription. The same practice can be applied to RMSF and scrub typhus.

Fleas and ticks on pets

Fleas are important vectors of plague and endemic typhus. Exclusion of the rats and opossums that serve as the intermediate host is difficult. Most cost-effective efforts are targeted at the family pet and the home environment. Lufenuron, a maturation inhibitor that prevents fleas from becoming fertile, is marketed in oral and injectable formulations for cats and dogs. It does not prevent flea attachment, but prevents reproduction. Fipronil is marketed as a topical agent for the prevention of flea and tick infestation. For a dog, monthly applications are recommended for tick prevention, whereas applications every 3 months may be sufficient for flea control.⁸⁷ Monthly applications have been shown to reduce the risk of canine monocytic ehrlichiosis.⁸⁸ Fipronil has also been used to treat mud bricks for

the control of triatome bugs carrying Chagas' disease. Although it demonstrates some efficacy in this setting, its duration of action is inferior to that of other available insecticides.⁸⁹ On the skin, the agent has a long duration of action, and limited evidence of toxicity. Available data suggest an excellent safety profile, although adverse endocrine effects have been noted in rats treated with fipronil.^{90,91} As fipronil is still a relatively new agent, pet owners are advised not to handle the wet liquid, and to avoid excessive exposure to impregnated fur.^{92,93} The current recommendations are likely to be modified as more information becomes available. As a variety of agents are now available, the choice should be discussed with a veterinarian. Agents such as fipronil, imidacloprid, selamectin, lufenuron, and nitenpyram appear to offer efficacy with favorable toxicology profiles.⁹⁴⁻⁹⁷ Insecticides, growth regulators such as pyriproxyfen, and boric acid may be useful for treatment of the infested environment.⁹⁸ Environmental treatment should be discussed with an exterminator.

Summary

Arthropod-related diseases continue to be a worldwide problem. Many patients present with cutaneous manifestations, and products applied to the skin are commonly used for prevention. The dermatologist needs a working knowledge of primary and secondary strategies for prevention of arthropod-related illness. Repellents and environmental treatments are useful for the control of mosquito- and sandfly-related diseases. Repellents, topical acaricides, and prompt tick removal are effective strategies for the prevention of tick-borne illness. Other strategies, including the use of biologic control, show promise. Most tick-borne diseases respond to a tetracycline, and treatment should not be delayed. In some high-risk settings, there may be role for antibiotic prophylaxis, although treatment can generally be delayed until signs or symptoms occur. Flea-borne illness is best controlled by targeted treatment of family pets. A knowledgeable veterinarian should be consulted.

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