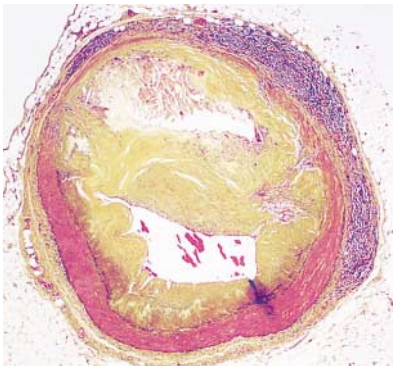
This Week in the Journal

July 4, 2002



Widespread Coronary Inflammation in Unstable Angina

Inflammation within a vulnerable coronary plaque may cause unstable angina by producing erosion or rupture. This study used measurements of neutrophil myeloperoxidase to assess neutrophil activation in blood from the aorta, femoral vein, and great cardiac vein. The data support the concept that in unstable angina there is widespread inflammation in the coronary bed, not just in a single vulnerable plaque.

These findings add to a growing body of evidence that unstable coronary disease is associated with an inflammatory reaction throughout the coronary tree. There may be important therapeutic implications, since treatment of a single unstable plaque may not address the problem of widespread coronary inflammation.

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"DEET-based repellents remain the standard of protection under circumstances in which it is crucial to be protected against arthropod bites that might transmit disease."

Comparative Efficacy of Insect Repellents against Mosquito Bites

Insect-borne diseases are a major cause of illness and death worldwide. Insect repellents can reduce the risk of being bitten. In this study, volunteers inserted their arms into standardized mosquito-containing cages, and investigators calculated the elapsed time until the first bite in order to evaluate which repellent products available to consumers in the United States offered the most complete, reliable protection. Products containing high concentrations of *N,N*-diethyl-3-methylbenzamide (DEET) were most effective, with other products containing IR3535 or botanicals offering far less protection.

Only DEET-based repellents provide adequate, long-lasting protection. Non–DEET-based repellents are unreliable in environments in which mosquito-borne diseases pose a substantial threat.

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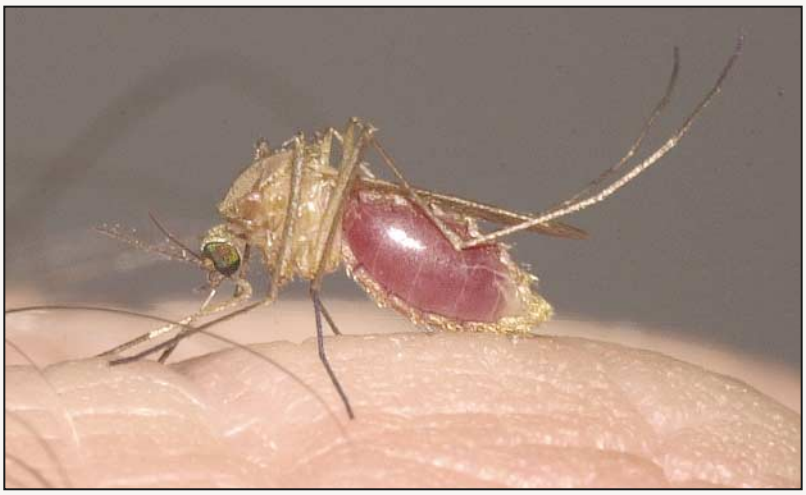
PERSPECTIVE

Repelling Mosquitoes



Culex pipiens, or the Northern House Mosquito, Thought to Be the Main Enzootic Vector of West Nile Virus (Photograph Courtesy of Gary Alpert).

Concern about mosquitoes, ticks, and the pathogens that they transmit grows annually in temperate parts of the world with the leafing of the trees. The arrival of West Nile virus in North America in 1999 has added to anxieties about arthropods (see Figure). Residents of relatively urban sites in the Mid-Atlantic and southern New England states where vector-borne infections tended to be infrequent before the recent emergence of Lyme disease are affected the most. While various hematophagous arthropods increasingly violate our privacy at home, similar worries accompany travel to many tropical sites where malaria and dengue threaten visitors and take a steadily increasing toll on human health. Thus, repellents that effectively deter mosquitoes and ticks have assumed ever greater importance, promising bodily comfort and providing personal protection against emerging and established diseases around the globe.

Consumers face a bewildering array of "repellent" formulations that contain diverse active ingredients and are sold in packages that bear extraordinary claims. What "works"? What is "safe"? How do "natural" products compare with "synthetic" preparations? How can one make an informed decision about what to purchase?

In this issue of the *Journal,* Fradin and Day (see pages 13–18) clearly demonstrate that not all repellents are created equal by showing that some protect only transiently or not at all. Under ideal laboratory conditions, products containing *N,N*-diethyl-*m*-toluamide (now called *N,N*-diethyl-3-methylbenzamide and known as DEET) protect considerably longer than other synthetic and botanical repellents. Although concentrated DEET formulations protect longer than those that are more dilute, little improvement is offered by concentrations of the active ingredient higher than 50 percent. The transient protection offered by dilute preparations, however, can be extended by reapplication.

Few people willingly thrust their arms into small cages filled with hungry mosquitoes, as subjects in this study did. So how relevant to the real world are the observations made in such studies? Failure of a candidate repellent under laboratory conditions, of course, virtually ensures failure in the field, but success in the laboratory may not translate to success in the field. Although DEET-based preparations powerfully deter many biting arthropods — including the mosquito that carries yellow fever (*Aëdes aegypti*), the species tested by Fradin and Day — they are less effective against various other types of mosquitoes, including certain of the anopheline mosquitoes that transmit malaria.

DEET is far less toxic than many people believe. Adverse effects, though documented, are infrequent and are generally associated with gross overuse of the product. The risk of DEET-related adverse effects pales in comparison with the risk of acquiring vector-borne infection in places where such diseases are endemic. Users should avoid the temptation to apply the most concentrated formulation available and, when using a more dilute product, should reapply it as protection wanes. Alternative "natural" products generally fail to live up to their reputations for greater safety and effectiveness and offer their users a false sense of security.

Various mass-marketed devices are advertised as "most effective" in distracting mosquitoes from people. Such contraptions are said to protect against pests and vector-borne disease either by repelling blood-feeding insects or by attracting and trapping them. These claims rely heavily on subjective testimonials and have not been well documented in peer-reviewed studies. The attractants in such devices may even increase the local density of mosquitoes. A $10 bottle of a DEET-based repellent is more cost effective and eminently more portable than such elegantly constructed machinery.

In the United States, the sale of

"We did not find increased risks of intrauterine growth restriction in association with maternal polymorphisms."

Polymorphisms Associated with Thrombophilia

It is uncertain whether thrombophilia polymorphisms in women are associated with an increased risk of intrauterine growth restriction in their offspring. In this large case–control study, the presence in the mother or newborn of polymorphisms for methylenetetrahydrofolate reductase (MTHFR) C677T or A1298C, factor V Leiden G1691A, or prothrombin G20210A was not associated with an increased risk of intrauterine growth restriction (defined as birth weight below the 10th percentile).

In contrast to a previous report in the Journal *involving a smaller sample, the present findings do not indicate that there are associations between several polymorphisms associated with thrombophilia in the mother and a risk of intrauterine growth restriction; such polymorphisms in the newborn also do not appear to confer an increased risk of intrauterine growth restriction.*

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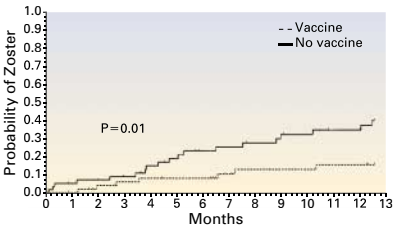

Inactivated Varicella Vaccine in Hematopoietic-Cell Recipients

The efficacy of a heat-inactivated varicella vaccine in recipients of hematopoietic-cell transplants was evaluated in a randomized trial in which vaccination was compared with no vaccination. Patients who received the vaccine had a significantly lower incidence of zoster than patients in the control group and recovered clinically significant T-cell immunity against varicella–zoster virus earlier than did the patients who received no vaccine.

This trial differs from previous attempts to prevent zoster in recipients of hematopoietic-cell transplants in that the first dose of vaccine was given before, rather than after, transplantation. The results indicate that protective memory T cells evoked by the vaccine can persist despite a myeloablative preparatory regimen.

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insect repellents is regulated by the Environmental Protection Agency (EPA). Registration requirements are more stringent for products for which health benefits are claimed than for those that are simply labeled as repellents. Results of assays such as those reported by Fradin and Day might motivate the EPA and perhaps the Federal Trade Commission to scrutinize these products and their manufacturers' claims more closely. What is needed is realistic labeling that offers at least a modicum of guidance as to how much repellent to apply and its expected duration of protection.

Concentrated DEET formulations (≥35 percent) may be appropriate for those who are exposed for many hours to numerous black flies or mosquitoes or who work in tick-infested areas. Less concentrated products might be used where more transient protection is desired. Although the susceptibility of children to DEET-related toxic effects remains uncertain, the use of a relatively dilute product might be prudent. DEET does irritate mucous membranes, and concentrated formulations dissolve plastic. As Fradin and Day nicely demonstrate, we currently have access to effective insect repellents that are safe when used judiciously.

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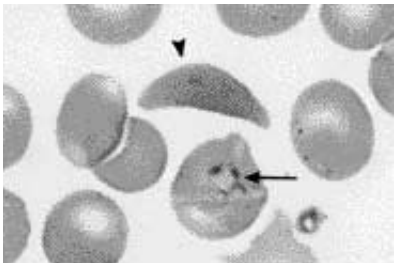
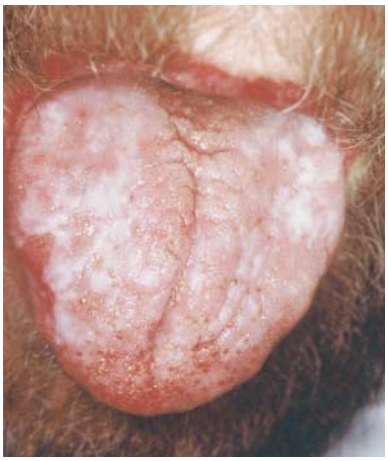


Images in Clinical Medicine (Web only): **Malaria and Sickle Cell Disease**

Although hemoglobin S is considered to be protective against *P. falciparum,* this is not always the case.



Clinical Practice: **Long-Term Care after Hematopoietic-Cell Transplantation**

A 35-year-old man who underwent allogeneic hematopoietic-cell transplantation two years earlier for acute myeloid leukemia has recently moved to a new town. He comes in for a general checkup because he tires easily and has frequent bouts of sinusitis. Physical examination reveals small central cataracts, some patches of vitiligo, and a dry mouth. What are the major issues in the long-term follow-up of patients after successful hematopoietic-cell transplantation?

Currently, more than 20,000 patients are alive more than five years after hematopoietic-cell transplantation, and many such patients are followed by primary care providers. This article reviews medical problems specific to this population and approaches to management.

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"The decision to institute hypocapnia should be undertaken only after careful consideration of the risks and benefits."

Medical Progress: **Hypocapnia**

Hypocapnia, defined as low partial pressure of arterial blood carbon dioxide, is usually well tolerated and often has no apparent effects. Although transient induction of hypocapnia can be lifesaving in patients with severe intracranial hypertension or neonatal pulmonary-artery hypertension, prolonged hypocapnia may adversely influence outcome. In this article, Laffey and Kavanagh review the prevalence and pathogenesis of hypocapnia, as well as the role of hypocapnia in clinical medicine.

The authors present a strong case for reconsidering previous recommendations for the induction of profound or prolonged hypocapnia.

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