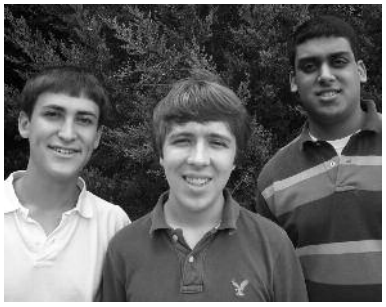

The accompanying commentary is the culmination of a journey commenced by three thoroughly individualistic writers who slowly but surely learned how to write as an effective team. In our Writing 20 class, "Science versus the Mosquito," Dr. Cary Moskovitz helped us to develop our scientific writing skills, beginning with group work, to produce both a scientific Review and Commentary.

The groups of three worked intensely to improve their writing, and ultimately to produce polished pieces that would be considered ready for publication. We spent countless hours writing, revising and meeting with Dr. Moskovitz to hone this scientific commentary. The beauty of group writing is that many of us were unaccustomed to collaborating with anyone else on written works. Each of us had been successful individual authors but none of us knew the most effective way to surrender our egos for the benefit of our group in order to achieve our common goal. Through group exercises and research we gradually learned to work as one and were able to logically piece all of our ideas together on paper. The outcome was the final version of the commentary accompanying this note.

Many college students are skeptical of writing group papers — they do not want to jeopardize their final grades because of concern about possible unequal participation among the group's members. GPAs are all too important in college, but without this Writing 20 class many of us may not have learned effective cooperative writing techniques, and the valuable skills of group scientific research. ►

Is DEET Past its Prime? New Recommendations for Travelers in Malarial Regions

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Writing 20 (Spring 2009): Science versus the Mosquito
Professor Cary Moskovitz

American health authorities have long recommended DEET-based repellents to travelers seeking protection from mosquitoes that carry malaria; however, a new repellent called picaridin may be a better option.

Malaria, a mosquito-borne illness, is a worldwide pandemic affecting approximately 350 to 500 million people each year[1]. Most cases of malaria occur in impoverished regions of the world, including sub-Saharan Africa, South Asia, Central America, and parts of South America[2]. However, the disease also poses a threat to travelers from countries such as the United States, where malaria is not widespread. For example, in 2003, 15.9% of American Peace Corps volunteers located in Madagascar reported signs of malaria[3]. In total, an estimated 30,000 international travelers contract the disease each year[4]. Visitors from other countries are particularly vulnerable to malaria because they lack the protective immunity that residents of the regions usually possess. Although travelers can take anti-malarial drugs to compensate for this deficiency, the drugs can cause adverse effects, and many strains of malaria are now resistant to the most common medications[5]. Preventing malaria-transmitting mosquitoes from biting travelers in the first place is crucial. Bed nets are cheap and effective[5], but not portable. The most viable forms of protection, especially during the daytime, are mosquito repellents. Health organizations, researchers, and even ordinary citizens have been immersed in a continuous debate over which mosquito repellent is most effective. Recently, the dynamic of this debate has transformed as new repellents with promise have emerged.

Recommendations from health authorities

When Americans think of mosquito repellents, they think of DEET. Most of the major health authorities in the United States claim that DEET products are the best choice for protection against mosquitoes. Developed by the United States military in 1946, it was released to the public in 1956 and soon spread worldwide; it is now the most extensively used repellent on the market[6]. The American Academy of Family Physicians (AAFP), the American Academy of Pediatrics (AAP), and the Centers for Disease Control and Prevention (CDC) advise travelers to use DEET products against virtually all species of mosquitoes[7,8,9]. An AAFP article entitled "Prevention of Malaria in Travelers" claims that "repellents containing [DEET] in concentrations of approximately 30 percent are effective and safe." In fact, the AAFP did not mention

any alternatives to DEET[7]. The CDC also indicated that travelers should use DEET products when traveling to any malarial region, though it mentioned alternative repellents (picaridin, oil of lemon eucalyptus, and IR3535) in some portions of its website[10,11]. On the whole, American health authorities endorse DEET-based products for protection against mosquitoes that are vectors of malaria.

In contrast to American health agencies, the World Health Organization (WHO) recommends picaridin as the best repellent for protection against malaria-carrying mosquitoes due to its safety, effectiveness, and cosmetic properties[12]. Picaridin (also known as icaridin, Bayrepel, Saltadine, and KBR 3023) is relatively new, developed by the German chemical company Bayer in the 1980s and used worldwide since 1998[13]. The Environmental Protection Agency (EPA) registered picaridin for commercial use in 2001 and products containing picaridin entered the U.S. market in 2006. Picaridin concentrations above 15% are not readily available in the U.S. However, the EPA does not stipulate a legal limit of concentration at which picaridin must remain below[14,15]. Although picaridin is much newer than DEET and less prevalent in the U.S., it has enjoyed commercial success in places such as Europe and Australia[6]. For this reason, much of our evidence is based on the picaridin's evaluation in other parts of the world.

The most prominent health authorities in the world have proposed conflicting recommendations to individuals traveling to malarial regions. The major American health agencies heavily endorse DEET, while the WHO endorses picaridin. In light of this, which repellent should travelers choose? We allege that American health authorities may be inaccurate in their assessment that DEET is the most viable repellent against all mosquitoes. Consequently, we intend to argue that picaridin is the better choice for travelers seeking to shield themselves from malaria for three reasons: (1) it is just as effective, if not more effective, than DEET; (2) DEET's perceived health risks deter consumers; and (3) picaridin does not irritate the skin.

Potency and persistence of repellent compounds

Two measurements determine the efficacy of a repellent for preventing mosquito bites: the percentage of mosquitoes that the repellent prevents from biting immediately after application (initial potency), and the length of time before this protection wears off (persistence). In order to examine the first measurement, one must consider the species of mosquitoes that are vectors for malaria. There are thirty to forty carriers of the illness worldwide, all of which are members of the genus *Anopheles*[16].

One significant member of the genus is *Anopheles gambiae*, a common species throughout sub-Saharan Africa and one of the most destructive vectors of malaria worldwide[17]. Several studies indicate that picaridin and DEET are equally potent against this species. In a field test performed by Costantini et al. in Burkina Faso, researchers assessed the effectiveness of three repellents, notably KBR 3023 (picaridin) and DEET, against *An. gambiae* and other *Anopheles* species. The researchers measured the initial potency of repellents by tracking effective dose (ED) concentrations—the amounts of repellent needed to keep 50% and 95% of mosquitoes from biting. They found that the most effective dose concentrations were almost identical for picaridin and DEET. The results were similar for other *Anopheles* species in the region (*An. nili*, *An. funestus*, and *An. pharoensis*), though these made up less than 5% of all mosquitoes captured[18,19]. It is important to acknowledge that this study used a small number of subjects, all young males, and that it only tested the strains of *An. gambiae* present in a very limited area. However, its findings on potency are supported by a 2004 lab study conducted by a previous member of Constantini's team—Badolo. As with Costantini's team, Badolo and his colleagues found no statistically significant difference in effective doses between DEET and picaridin against *An. gambiae*[20].

The second major species assessed was *An. farauti*, a mosquito from northern Australia. A 2004 field study by Frances et al. examined the effects of DEET and picaridin against this carrier. This study measured potency via percentage protection—the percentage of mosquitoes prevented from biting at the given repellent concentrations. In this case, the measurements were taken over a period of seven hours. The study concluded that the differences in potency between the two repellents were statistically insignificant, at least at the relatively low doses tested (19.2% picaridin versus 20% and 35% DEET)[21]. These results, similar to those of the *An. gambiae* studies, demonstrate equal effectiveness between DEET and picaridin.

A lab test performed by Klun et al. in 2003 focused on a third species: *An. stephensi*, a mosquito found along the east coast of the

Although picaridin is much newer than DEET and less prevalent in the U.S., it has enjoyed commercial success in places such as Europe and Australia.

Furthermore, Dr. Moskovitz taught us that joining forces on a group writing project is equally important in all fields, not just scientific. He helped us realize that working in partnership is a valuable tool that we can use throughout our lives, and not just for writing.

Finally, Dr. Stephanie Jeffries provided invaluable assistance to us in revising and polishing our writing even further, specifically to allow our writing to be ready for publication to a wider academic audience. Cheers to everyone in Dr. Moskovitz's Writing 20 class who benefited from this shared experience. Our final commentary has evolved dramatically from our original draft. While we have come a long way in the development of this piece and are proud of the final product, as much as anything we all have learned and matured tremendously simply as a result of our journey.

We allege that American health authorities may be inaccurate in their assessment that DEET is the most viable repellent against all mosquitoes.

Although persistence plays an important role in determining repellent efficacy, only one study thoroughly examined this property in a tropical climate, where malaria is most pervasive.

This study measured potency via percentage protection—the percentage of mosquitoes prevented from biting at the given repellent concentrations.

Arabian Peninsula and throughout the Indian subcontinent. This study also used a percentage protection method to assess potency; however, its period of measurement was only two minutes. As in the other studies, the differences in potency between DEET and picaridin were statistically insignificant[22]. In short, picaridin matches DEET in potency across multiple species of the *Anopheles* genus.

Although persistence plays an important role in determining repellent efficacy, only one study thoroughly examined this property in a tropical climate, where malaria is most pervasive. The aforementioned study by Costantini et al. found that picaridin lingered on the skin for significantly longer than DEET, with a half-life of 4.1 hours, compared to DEET's 2.9 hours. This made picaridin significantly more effective at preventing mosquito bites overall[18,19]. The fact that picaridin persists longer on the skin is not dependent on the species of mosquito, so this is a claim of effectiveness that can be extrapolated to other species of mosquitoes that thrive in tropical climates.

After analyzing the previous studies, we are confident that picaridin, at the very least, is as effective as DEET in preventing bites from mosquitoes that are vectors for malaria. However, picaridin may not offer sufficient protection when diseases besides malaria are factored in; several studies demonstrate that DEET is more effective against other mosquito species such as *Aedes aegypti*, which is known to carry yellow fever[23,24]. Travelers may still want to use DEET in areas where multiple mosquito-borne illnesses are prevalent.

Health risks associated with DEET and picaridin

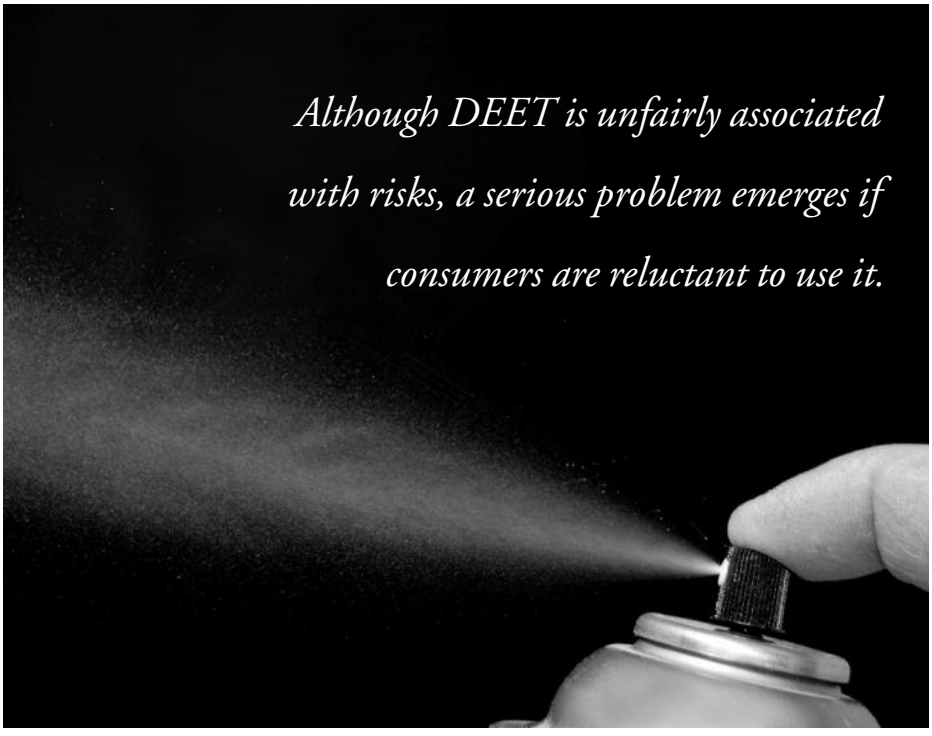
When comparing DEET and picaridin, one must also examine the health implications that stem from the use of repellents. Our analysis suggests that although DEET has a remarkable safety profile, its perceived risks have an impact on whether consumers will actually use it, whereas picaridin not only matches DEET in safety, but is also free from any perceived risk.

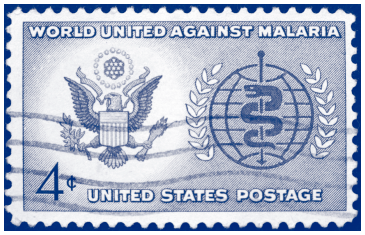
For decades, DEET has faced public scrutiny regarding the health risks it poses to consumers. However, several studies indicate that DEET has a remarkable safety profile. For instance, a lab study conducted by Antwi et al. found that there were "no significant toxicological risks from typical usage of [DEET and picaridin]"[25]. Furthermore, a safety re-assessment conducted by the Environmental Protection Agency in 1998 deemed that "the normal use of DEET does not present a health concern to the general population"[26]. Much of the controversy associated with DEET comes from its safety record concerning children. The Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ASTDR), states that seventeen cases of significant toxicity from DEET exposure have been reported during the period between 1961 and 2002. Fourteen of these cases occurred in children under the age of eight—the most frequently reported symptoms were lethargy, headaches, tremors, involuntary movements, seizures, and convulsions[27]. Although these cases should in no way be deemphasized, they are likely attributed to inappropriate usage such as repellent ingestion[27]. Additionally, the number of reported cases is miniscule for a forty-year span.

Unlike DEET, picaridin has not been extensively evaluated in the United States, since it is a relatively new repellent. However, picaridin is widely available in other parts of the world; hence, most of the relevant safety data comes from abroad. An article published in the *Medical Letter* concluded that in places such as Australia and Europe, no major health concerns have been reported regarding picaridin[28]. Furthermore, the aforementioned study conducted by Antwi et al. found picaridin to be free from toxicological risk[25]. On the whole, DEET and picaridin are reasonably safe repellents.

Aside from the actual risks associated with DEET and picaridin, it is imperative to consider their perceived risks. We previously noted that the CDC recommended DEET for those traveling to any malarial region; however, in some portions of their website we noticed that alternative repellents including picaridin were recommended, especially for pregnant women and infants. We presume that the CDC considers DEET safe, yet they understand that there are consumers who have are wary of using it. As a result, the agency may have exercised caution by equally recommending three repellents in addition to DEET on web pages that target pregnant women and children. In his book entitled *Travel Medicine for Health Professionals*, Larry Goodyer states, "The use of DEET has been the subject of controversy because of perceived disadvantages involving adverse reactions and contraindications in both pregnancy and young children." Goodyer concludes that most of these fears are unfounded[29]. According to Emily Zielinski-Gutierrez, a behavioral scientist in the Division of Vector-Borne Infectious Diseases at the CDC, most Americans report infrequent or no use of DEET-based repellents in their lives because it is perceived as risky, irritates the skin, and has an undesired smell. Furthermore, Americans have a difficult time conceptualizing that a single mosquito bite can be fatal or life changing[30]. Thus, many are unwilling to take a "risk" by using DEET to prevent against something that is "insignificant." Although DEET is unfairly associated with risks, a serious problem emerges if consumers are reluctant to use it. Fortunately, picaridin is free from such perceived risks, making it much more viable.

After analyzing the previous studies, we are confident that picaridin, at the very least, is as effective as DEET in preventing bites from mosquitoes that are vectors for malaria.





American travelers such as volunteers, study-abroad students, and vacationers should not be restricted to DEET products or insufficient concentrations of picaridin when traveling to malaria-prone regions of the world.

Cosmetic appeal

The final criterion that factors into choosing the best overall repellent is cosmetic appeal. Several case studies conducted by the ATSDR conclude that although exposure to DEET rarely leads to health concerns, skin irritation occurs quite often. One study was conducted on 143 Everglades National Park employees in order to determine the effects of DEET on varying use groups. At the conclusion of the study, 25% of the employees reported health effects that were attributed to DEET—some of which include "rashes, skin or mucous membrane irritation, transient numb or burning lips, dizziness, disorientation, and difficulty concentrating"[31]. Furthermore, the previously mentioned article in the *Medical Letter* stated that "Unlike DEET it [picaridin] is odorless, does not feel greasy or sticky, is less likely to irritate the skin and does not damage plastics or fabrics"[28]. Finally, the *Journal of Drugs in Dermatology* in its January-February 2004 publication reinforces these claims by stating that picaridin is "as effective and less irritating than DEET"[32]. All in all, perhaps consumers may be less hesitant to apply picaridin when necessary.

Policy decisions and availability of picaridin

Picaridin appears to be a promising repellent due to its effectiveness, high safety profile, and cosmetic appeal. Furthermore, the difference in cost between picaridin and DEET is negligible*. That said, why do the most prominent American health agencies continue to endorse DEET? One explanation is that DEET dominates the American repellent market, and only picaridin formulations up to 15% concentration are readily available—a concentration far lower than the ones found effective in several studies[14]. This creates a kind of circular propagation: travelers do not buy picaridin because the government tells them to buy highly-concentrated DEET products; manufacturers do not bother to provide higher concentrations of picaridin because the lower concentrations are not popular; and the government does not bother recommending high concentrations of picaridin because they are unavailable. Another possibility is that DEET is a better all-purpose repellent, warding off many different kinds of mosquitoes. As mentioned before, it is more effective than picaridin against *Aedes aegypti*, and it may be more effective against other species as well. It is possible that health organizations intentionally make blanket recommendations such as this to avoid confusion among consumers, rather than suggest different products for different situations. However, if evidence demonstrates that picaridin is more effective than DEET in certain situations, a "one size fits all" mentality does not make much sense.

Though DEET is undoubtedly a viable repellent, we believe that American health authorities should reconsider their recommendations. If research suggests that picaridin is superior to DEET, then authorities must collaborate with manufacturers for the purpose of bringing higher concentration products to consumers. American travelers such as volunteers, study-abroad students, and vacationers should not be restricted to DEET products or insufficient concentrations of picaridin when traveling to malaria-prone regions of the world. Picaridin can give them the protection they need, safely, without the odor or irritation that can turn people away from repellents. Our citizens deserve both access to this repellent and knowledge of its abilities, so that they may be well armed in the fight against malaria.

Acknowledgments

We would like to thank Dr. Cary Moskovitz, our peers in the "Science versus the Mosquito" Writing 20 seminar, and Dr. Craig Singer for their assistance in developing this commentary. ■

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