

# EXTRA! EXTRA!

## MAN BITES MOSQUITO

Photo by Jim Gathany, CDC

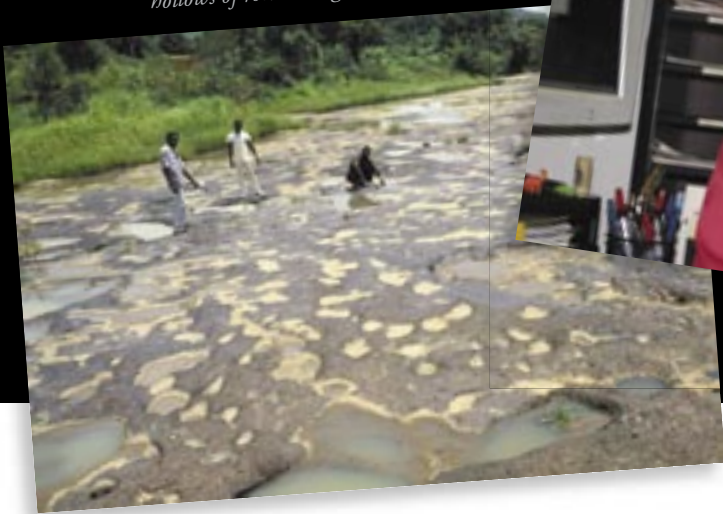
IT IS WORTH OUR TIME TO SUSPEND WHATEVER ILL FEELINGS WE MAY HAVE FOR THE MOSQUITO AND—FOR A MOMENT—MARVEL AT ONE OF MANKIND'S MOST TENACIOUS TORMENTORS. INDEED, IT'S IN OUR BEST LONG-TERM INTERESTS TO PAY DUE RESPECT TO THE MOSQUITO AS A FORMIDABLE AND POTENT ADVERSARY.

Nora Besansky approaches her research at Notre Dame as if she were a spy covertly amassing as much intelligence about an enemy as possible. The foe in her case is *Anopheles gambiae* (*A. gambiae*), the principle carrier of malaria in Africa, and therefore the deadliest malaria vector in the world.

“The question ‘What makes *Anopheles gambiae* so good at transmitting malaria?’ is what motivates my studies,” she says.

This is no small question. *A. gambiae* is driven to the point of obsession to feed on human blood. “Carefully controlled studies in the field have shown that given a choice between a calf and a human, *Anopheles gambiae* will go straight to the human,” Besansky says. This preference leads to at least one million deaths from malaria annually in Africa, most of them children less than five years old.

*A. gambiae* like to breed in the watery hollows of rocks along river sides.



*Notre Dame biologist Nora Besansky*

Consider how this baryonic life form of less than an ounce has found the means and methods to adapt to human environments, treating every new permutation of our own existence as an opportunity to maintain a synchrony with us, and a resource to be exploited. It will do anything—including the biological equivalent of morphing itself—to keep pace with humankind.

Besansky marvels at *A. gambiae*'s capacity to adapt to environments of our own making—entering our homes for shelter as adults, and using our irrigated agricultural plots and flooded excavations or even footprints for rearing their young. All this for a prize: our lifeblood.

Quite literally, *A. gambiae* is bent on stalking us in the dark of night, when the adult females sip our blood as we sleep. As they suck, they spit on us, and adding injury to insult, with the spit is injected the third layer—the actual malaria parasite, *Plasmodium falciparum*. Then consider how the addition of this third element has produced for medical science such a conundrum of daunting complexity. Little wonder why this cycle of transmission involving mosquito, parasite, and man has stymied for decades the efforts of the best minds of science both in research universities and at billion-dollar pharmaceutical companies to halt the spread of malaria.

Theoretically, malaria can be controlled by eliminating the parasites (by parasite-killing drugs or vaccines administered to humans), by eliminating or reducing mosquito densities (using insecticides), or by preventing contact between humans and mosquitoes (using repellants and bednets).

But *A. gambiae* is not easily defeated by such tactics. There is no vaccine for malaria and *A. gambiae* eventually develops resistance to the repellants used in bednets. A far better strategy, Besansky says, is to set a long-term goal of identifying novel targets for mosquito control or behavior modification. “I am looking at how *A. gambiae* adapts to different environments. What are the ecological and environmental cues that this mosquito responds to? And where and how has it changed its genetic code to acquire these adaptations?” she poses.

Understanding the traits that make a good malaria vector is a significant challenge. Of the 4,000 known species of mosquitoes, only *Anopheles* mosquitoes transmit human malaria. Furthermore, of the 500 types of *Anopheles* only 30 or so are involved in transmission. And just a handful of those do most of the damage.

One might guess that these 30 types of *Anopheles* are closely related “but that is not true at all,” Besansky says. “These 30 are dispersed all over the *Anopheles* family tree.”

That only one group of mosquitoes—*Anopheles*—transmits human malaria indicates that there are fundamental physiological factors at work,

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—NORA BESANSKY

probably related to the ability of the parasite to establish an infection in the mosquito and complete its life cycle. But other factors crucial to making a good vector are not stable evolutionarily, as suggested by the fact that major human malaria vectors within *Anopheles* are not very closely related. “It turns out the behavioral traits that lead to efficient malaria transmission—such as preference for all things human—evolve very quickly. And they have evolved repeatedly among different groups of *Anopheles* mosquitoes.”

“This tells you that the ability to be a good vector has evolved independently multiple times,” Besansky says.

But what about the behavioral issues that drive these mosquitoes, especially *Anopheles gambiae*, to pursue humans with such a vengeance?

## “ANOPHELES GAMBIAE SEEMS TO HAVE A POWERFUL ABILITY TO ADAPT TO HETEROGENEOUS ENVIRONMENTS.”

“*Anopheles gambiae* seems to have a powerful ability to adapt to heterogeneous environments,” Besansky says. *A. gambiae* even produces different races, for want of a better term, within its own species. Even to the trained eye they seem identical. “These ‘races’ are closely related to each other,” Besansky says. “They do not interbreed for the most part, although they are capable of interbreeding. They can be considered like a subspecies. So *Anopheles gambiae* has spawned a number of certain races that are exploiting a variety of habitats.”

There are *A. gambiae* that love breeding in pools of water in the hollows of rocks along river sides. Other races of *A. gambiae* take to breeding in the watery pools made by hoofprints or tire tracks.

“The landscape is a mosaic of different breeding sites for *A. gambiae*,” she says. To the extent that *A. gambiae* can use its environment more efficiently, it can reduce competition among its various populations. Reduced competition results in higher mosquito densities and longer-lived mosquitoes that are better at transmitting more cases of malaria.

One would suppose that *A. gambiae*’s efficiency as a malaria vector evolved over the eons. In fact, this has occurred recently—in the past 10,000 years “and probably more recent than that,” Besansky says.

*A. gambiae*’s golden opportunity occurred when *Homo sapiens* made the transformation from wandering about as small nomadic tribes to settling into large agrarian societies. “Humans not only obliged *Anopheles gambiae* by creating dense populations, but we also created perfect habitats for them as well,” Besansky says.

Besansky is focusing her study on a relatively new phenomenon: the breeding of *A. gambiae* in an altogether new site: rice fields.

“It turns out that there is a different race of *Anopheles gambiae* that has exploited the rice field breeding sites of West Africa,” she adds.

The damming of rivers and the creation of extensive networks of irrigation channels to raise this new cash crop, not to mention the scale of rice cropping itself, presents *A. gambiae* with new opportunities to exploit, and presents us with important public health consequences. Irrigation of normally dry regions, and irrigation during the dry season, bring *A. gambiae*—and therefore malaria—into new territory.



Besansky and her graduate students are conducting a study funded by a five-year grant from the National Institutes of Health to examine the situation from the ecological and genetic points of view. “The question is: What are the genes that are conferring adaptation to this new habitat?” she asks.

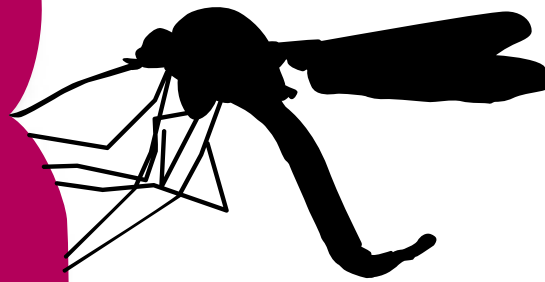
Besansky is convinced that ecological specialization leads to reproductive isolation and eventually speciation, since races that are adapted to different types of larval habitats rarely interbreed. By using molecular markers, she and her crew are trying to uncover the tell-tale signatures that may clarify what gene or genes are involved in these new adaptations and in reproductive isolation.

Ultimately she is hoping to uncover what it is that makes *A. gambiae* so successful. If the secret is found, ultimately we may find ways to block or interfere with the traits that make our tormenter such a good vector.

“Maybe,” she says, “one day we can bite back.”

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*Nora Besansky was elected AAAS Fellow in October, 2005.*



My name is Meagan Fitzpatrick, and I am a senior biology major. Since sophomore year, I have been working in the lab of Dr. Nora Besansky, part of Notre Dame’s Center for Tropical Disease Research and Training (CTDRT). I have been studying population genetics and speciation within *Anopheles gambiae*, the mosquito that is the primary vector of malaria in sub-Saharan Africa.

Malaria is a devastating disease that kills between 1.5 and 2.7 million people every year, with over 90 percent of the deaths occurring in sub-Saharan Africa. Over one million of these victims are children under the age of five. These statistics are shocking and sobering. For most of my time working in the CTDRT, however, the statistics were just numbers, describing a reality far from the one I knew. That all changed this past summer, when I had the opportunity to travel to Bamako, Mali, and work at the Malaria Research and Training Center (MRTC) at the University of Bamako.

The MRTC is a high-tech facility, providing first-world training to doctors and scientists in a third-world country. At first, that contradiction was the most shocking thing. Equipment and research tools that rival those at Notre Dame stood in labs where the water does not always run clear. I was inspired by the perseverance and the optimism that I found in the researchers, and not just in Bamako. On the way to a collection site, we stopped in Bandiagara, a small village with yellow brick walls and corrugated tin rooftops. Unbelievably, the village was the center of high-profile research into Hemoglobin C and the protection from malaria it confers. PCR machines and computers ran on generators. Out of a hot, muddy field comes new diagnostics and a wealth of information. What motivates these people to accomplish so much?

Let’s go back to that statistic. Over one million children each year die from malarial infection in sub-Saharan Africa. The statistic takes on new meaning when you’re standing outside of a two-room mud hut, filthy inside and out, where twelve to fourteen beggar boys spent the night with 250 of their closest Anopheline friends. Can’t picture that many mosquitoes? Neither could I, until the night I ate dinner in a room with mosquitoes so thick on the walls and windows that they looked like part of a slightly fluttering wallpaper pattern.

In Mali, the reality of those statistics took the forefront, and the motivation of the researchers became clear. These are not just numbers, they are people, they are friends and children of friends falling victim to a curable disease. That is the driving force.

For me, the statistics will never be just numbers again. My experience in Mali opened my eyes, allowing me to see exactly what I am working against, and who stands to benefit. I went to Mali to study speciation, and ended up learning far more about culture, language, and the effects of disease than any book could have taught me. I also learned one more valuable lesson—about the resiliency of the human spirit, and the ability we have to overcome seemingly insurmountable obstacles. It has made me realize how much we have here at Notre Dame, and how many possibilities lie within our reach. If researchers in rural Mali can make such huge strides toward conquering malaria, we can surely do so much more. And that, for me, was the most amazing realization of all.

*Meagan Fitzpatrick’s visit to Mali was made possible by a generous grant from the Kellogg Institute at Notre Dame.*