NEWS RELEASE

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Nov. 9, 2012

INSECTICIDE RESEARCH

During World War II, U.S. Army General Douglas MacArthur was quoted as saying, "It's going to be a very long war if for every division I have facing the enemy, I have one sick in the hospital and another recovering from this dreadful disease"—meaning malaria. Today, the battle against insects that cause disease is still being fought to help protect deployed U.S. troops and enable them to accomplish their mission.

Mosquitoes, sand flies, ticks, mites, and other biting arthropods transmit pathogens that cause some of the most devastating diseases. Malaria, dengue fever, yellow fever, Japanese encephalitis—all transmitted by mosquitoes—and a host of other diseases affect people around the globe and are a particular problem for militaries that send men and women to places where such illnesses are endemic.

For example, "In 2003, 80 out of 225 U.S. marines deployed on a mission to Liberia came down with malaria, but no deaths were associated with that incident," says U.S. Air Force Lieutenant Colonel Douglas Burkett, research liaison officer with the Armed Forces Pest Management Board (AFPMB). "The trouble with most widely used insecticides is that we have fewer available active ingredients for public-health pest control and at the same time, we have a global increase in insecticide resistance to our best chemical tools."

The mission of the U.S. Department of Agriculture is critical to the U.S> Department of Defense (DOD), Burkett says. The Agricultural Research Service, USDA's in-house research arm, has excellent research capabilities and is good at developing and test pesticides and developing application technologies that support public health.

A strong alliance has long existed between USDA and DOD—as far back as 1932, when an entomological research laboratory was established in Orlando, Florida, to combat mosquitoes, filth flies, and disease-transmitting arthropods like fleas and mites.

"It was important to have a laboratory in an area where there were a lot of malaria vectors at that time," says Ken Linthicum, director of the ARS Center for Medical, Agricultural, and Veterinary Entomology (CMAVE) in Gainesville, Florida. "During World War II, one of the laboratory's objectives was to determine how to interrupt malaria transmission in the South Pacific to protect soldiers stationed there."

Today, a new battle plan is under way. The Deployed War-Fighter Protection (DWFP) research program was implemented in 2004 to prevent or defend against insect attacks on troops. USDA receives $3 million of the $5 million allotted to the AFPMB by the U.S. Congress each year for research that focuses on developing public-health insecticides, improving personal protection for troops, and devising improved application technologies to kill insects. Remaining funds are distributed through competitive grants to universities, military laboratories, and private industry.

"Across DWFP, we have build a real strong network not only with the U.S. Department of Defense and the USDA, which is what this partnership is all about, but with universities, industry, and others," says U.S. Navy Captain Stanton Cope, former AFPMB director and DWFP manager. "When you consider this program has only been in existence for a short period of time, its outreach and productivity are phenomenal."

In the 1940s, USDA scientists at the Orlando lab, which was later moved to Gainesville and eventually became a part of CMAVE, developed delousing techniques that prevented millions of cases of louse-borne typhus, a disease with a high death rate and no effective treatment at that time. They also created the aerosol spray canister. Other achievements included the discovery of DEET by scientists at the Henry A. Wallace Beltsville Agricultural Research Center in Beltsville, Maryland. Today, DEET remains a primary defense against biting insects.

"DEET is still the best topical repellent we've got," Burkett says. "It has a long safety track record, but some soldiers don't like the odor and feel, and they prefer to have other options."

Initially, DWFP funds were to be used to bring together the skills of scientists at different ARS laboratories—starting with basic ideas that would end with registered products. This goal was mostly achieved, says Dan Strickman, ARS national program leader for Veterinary, Medical, and Urban Entomology. The research team includes 15 scientists at 5 ARS laboratories located in Florida, Maryland, Mississippi, and Texas.

We're strongest in discovery and have developed entirely new classes of insecticides out of the DWFP program," Strickman says.

Unlocking the Chemistries of Folk Remedies

Some of those discoveries have come from plants gathered in the wild and from traditional folk remedies—two methods used by scientists at the Natural Products Utilization Research Unit in Oxford, Mississippi, to find plant-derived compounds to deter insects.

A story about a farmer in the 1930s crushing leaves of the American beautyberry plant and putting them under the harnesses of stock animals to keep pests away led to the discovery, in that plant, of the compound callicarpenal, which has significant repellency against mosquitoes and ticks. (See "Learning From Our Elders: Folk Remedy Yields Mosquito-Thwarting Compound," *Agricultural Research*, September 2006.)

Working closely with scientists at the ARS Mosquito and Fly Research Unit in Gainesville, Florida, and with Abbas Ali and others at the National Center for Natural Products Research at the University of Mississippi, chemist Charles Cantrell, plant pathologist David Wedge, and research leader Stephen Duke are exploring additional promising compounds from the American beautyberry and other plants to find natural alternatives that are as effective as or better than DEET at repelling arthropods.

Recently, Cantrell examined mosquito-deterrent effects of callicarpenal and looked at an efficient synthetic approach for commercial companies interested in producing it as an insect repellent.

Following up on a tip about people in Africa and India who burn *Jatropha curcas* seed oil in lamps to keep insects out of their homes and other areas, researchers identified which of the oil's components are responsible for mosquito repellency.

In the lab, smoke was extracted from burning *J. curcas* oil and analyzed. A number of active compounds—free fatty acids and triglycerides—were found to be effective at preventing mosquitoes from biting.

"Fatty acids are well known to have insect repellence," Cantrell says. "We identified the triglycerides as also having repellent activity, the first such report, to my knowledge."

Another possible source of repellents is breadfruit, which contains compounds similar to those in *Jatropha* sp. Cantrell hopes to combine the two sources into a more effective product.

One novel discovery is being kept under wraps for now. Chemist Kumudini Meepagala at the Oxford lab, collaborating with chemist Ulrich Bernier at Gainesville, has developed a natural-product-based mosquito repellent that is more active and lasts three times longer than DEET. A patent application has been filed on this undisclosed compound.

An additional benefit from the advanced research are new, naturally occurring insecticides discovered that will have agricultural benefits as well.

SOURCE: *Agricultural Research,* November-December 2012, Vol. 60. No. 10. ISSN 0002-161X

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