

# The Washington Post

## New form of malaria threatens Thai-Cambodia border

By MARGIE MASON and MARTHA MENDOZA  
The Associated Press

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PAILIN, Cambodia -- O'treng village doesn't look like the epicenter of anything.

Just off a muddy rutted-out road, it is nothing more than a handful of Khmer-style bamboo huts perched crookedly on stilts, tucked among a tangle of cornfields once littered with deadly land mines.

Yet this spot on the Thai-Cambodian border is home to a form of malaria that keeps rendering one powerful drug after another useless. This time, scientists have confirmed the first signs of resistance to the only affordable treatment left in the global medicine cabinet for malaria: Artemisinin.

If this drug stops working, there's no good replacement to combat a disease that kills 1 million annually. As a result, earlier this year international medical leaders declared resistant malaria here a health emergency.

"This is not business as usual. It's something really special and it needs a real concerted effort," said Dr. Nick White, a malaria expert at Mahidol University in Bangkok who has spent decades

trying to eradicate the disease from Southeast Asia. "We know that children have been dying in Africa - millions of children have died over the past three decades - and a lot of those deaths have been attributed to drug resistance. And we know that the drug resistance came from the same place."

Malaria is just one of the leading killer infectious diseases battling back in a new and more deadly form, the AP found in a six-month look at the soaring rates of drug resistance worldwide. After decades of the overuse and misuse of antibiotics, diseases like malaria, tuberculosis and staph have started to mutate. The result: The drugs are slowly dying.

Already, The Associated Press found, resistance to malaria has spread faster and wider than previously documented. Dr. White said virtually every case of malaria he sees in western Cambodia is now resistant to drugs. And in the Pailin area, patients

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given artemisinin take twice as long as those elsewhere to be clear of the parasite - 84 hours instead of the typical 48, and sometimes even 96.

Mosquitoes spread this resistant malaria quickly from shack to shack, village to village - and eventually, country to country.

And so O'treng, with its 45 poor families, naked kids, skinny dogs and boiling pots of rice, finds itself at the epicenter of an increasingly desperate worldwide effort to stop a dangerous new version of an old disease.

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Bundled in a threadbare batik sarong, 51-year-old Chhien Rern, one of O'treng's sick residents, sweats and shivers as a 103-degree fever rages against the malaria parasites in her bloodstream.

Three days ago Chhien Rern started feeling ill while looking for work in a neighboring district. So she did what most rural Cambodians do: She walked to a little shop and asked for malaria medicine. With no prescription, she was handed a packet of pills - she's unsure what they were.

"After I took the drugs, I felt better for a while," she says. "Then I got sick again."

The headaches, chills and fever, classic

symptoms of malaria, worsened. Chhien Rern's daughter persuaded her to take a motorbike taxi past washed out bridges and flooded culverts to the nearest hospital in Pailin, a dirty border town about 10 miles from O'treng.

Doctors say there's a good chance Chhien Rern was sold counterfeit drugs.

People generate drug resistant malaria when they take too little medicine, substandard medicine or - as is all too often the case around O'treng - counterfeit medicine with a pinch of the real stuff. Once established, the drug-resistant malaria is spread by mosquitoes. So one person's counterfeit medicine can eventually spawn widespread resistant disease.

Yet in most parts of the world, people routinely buy antimalarials over the counter

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at local pharmacies and treat themselves.

A recent study out of neighboring Laos found 88 percent of stores selling artemisinin-based drugs, the same ones scientists are desperately trying to preserve, were actually peddling fakes. Worse, nearly 15 percent of the counterfeits were laced with small hints of artemisinin, which could prompt resistance. The researchers found indications that some were made in China, feeding smugglers' routes that snake through Myanmar and into Laos, Thailand, Cambodia and Vietnam.

The counterfeits, along with outdated drugs, are jumping continents. In Africa, where malaria is endemic in 45 countries, the fake drug industry is thriving. A 2003 World Health Organization survey found between 20 percent and 90 percent of antimalarials randomly purchased in seven African countries failed quality testing, depending on the type of drug.

WHO and Interpol formed a task force three years ago to try to stop counterfeiters, seizing millions of fake malaria, tuberculosis, HIV and other pills in Southeast Asia and Africa. But officials say the work is only as good as the countries' legal systems.

"One of the problems is that there's not really any enforcement, so what happens when they find a drug that's counterfeit or

substandard?" says David Sintasath, a regional epidemiologist at the nonprofit Malaria Consortium in Bangkok. "The policy is to take it away from them. That's good until the next month when they get their next shipment, right?"

Countless unlicensed shops in Cambodia sell artesunate, a single-drug therapy that has been banned in the country. Artesunate, a modified version of artemisinin derived from a Chinese herb, has been hailed as miracle treatment worldwide because it works so well with so few side effects. But Cambodian surveys have shown that many patients take artesunate alone instead of mixing it with another antimalarial drug, making it easier for resistance to build.

"The drug has been around for a long time and misused for a long time and this is all encouraging the parasite to develop

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resistance," says Dr. Delia Bethell, of the U.S. Armed Forces Research Institute of Medical Science, whose research has been at the forefront of identifying emerging resistance on the border.

Back in western Cambodia a few miles from O'treng village, shopkeeper Nop Chen turns a flashlight on a glass case full of drugs he hawks from inside his cramped roadside house. He digs through the many boxes and produces two different types of artemisinin-based antimalarials. Both lack the full amount of a second required medication, mefloquine, necessary to treat the strain of malaria in the area and ward off more resistance.

But Nop Chen, a former Khmer Rouge medic, points to a small Cambodian seal on the boxes and says he feels confident the drugs are the real deal. Still, he acknowledges he is not licensed to sell the pills and he's unsure where they originated.

"I'm not concerned because it's got the sticker and the stamp," he says, squinting at the Khmer script on the labels. "Because of the logo, I trust it to not be fake - it was made in Cambodia."

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Walk past O'treng's cluster of sagging huts, cross another cornfield and hike a twisted mile on a dirt track to a wooden shack

where a string of smoke is curling through the wooden floor planks in a largely futile effort to keep mosquitoes away. It's here that skinny 13-year-old Hoeun Hong Da wakes up on the floor nauseous and burning with fever.

Hong Da recovered from malaria two months ago, but now the dizziness and headaches are back. He's been sickened by the disease six or seven times in his short life - too many to remember. He knows that if he doesn't get to a hospital soon, he could die.

With no new treatments in the pipeline, normally reserved scientists are quick to use words like "disaster" or "catastrophe" when asked what might happen if they don't contain the disease that's ravaging young Hong Da before it spreads to Africa. There, malaria already kills an estimated 2,000

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kids daily.

For the past 50,000 years the malaria parasite has been evolving, and migrating, alongside humans. It moves within the huts of O'treng, and into neighboring towns when men like Hong Da's father and older siblings float from job to job.

Some work is close enough for them to return home at night, but other jobs keep them away for stretches of time. They sleep in tight rows, sweating and weary, in disintegrating bamboo huts with workers who are also traveling, and possibly infected with malaria.

The concept of containing drug resistance has never been tried before. Scientists wonder: How do you control the spread of a resistant parasite transmitted by mosquitoes that bite people who live and work in infested jungle areas, then scatter in all directions, all the time?

This area, the former stronghold of the murderous Khmer Rouge, has a notorious history. Burmese migrant workers who once mined rubies and sapphires in these now deforested hills are believed to have helped transport strains resistant to the drug chloroquine back to Myanmar a half century ago. From there it spread to India and later over to Africa until the drug was useless worldwide.

A decade later, history repeated itself when resistance to the drug sulfadoxine-pyrimethamine followed the same path.

Now, in western Cambodia, scientists are concerned because the artemisinin-based drugs are taking longer than usual to kill the parasites. Earlier this year, an army of aid agencies and experts from the WHO began racing to this impoverished corner on the Thai-Cambodian border to divvy up a \$22.5 million grant from the Bill & Melinda Gates Foundation, aimed at stopping this virulent new strain.

But grants haven't stopped lines of Cambodians, sick or not, from queuing up every morning at Thailand's border, charging past the checkpoints in search of work or goods. Some may carry resistant strains in, others may bring them home.

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And grants haven't stopped the parasite from spreading in the O'treng area, despite widespread bednet distribution, awareness campaigns and enhanced surveillance systems. Some scientists say the only sure way to fix the problem is to eradicate malaria entirely from western Cambodia.

"It's really dangerous," says Dr. Rupam Tripura, who's conducting a study in Pailin for the Wellcome Trust-Mahidol University-Oxford Tropical Medicine Research Program. "What will happen to the mosquitoes? Can you kill those living in the jungle? No, so you cannot kill the strain."

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If O'treng is the epicenter of this emerging disease, Phoun Sokha is the point man aimed at controlling it.

At 47, Phoun Sokha is the village malaria worker who lives at the mouth of the hamlet and proudly displays an orange plastic kit that resembles a tackle box.

Phoun Sokha is serious about his packets of medicine and his rapid tests to prick blood from sick villagers' fingers to determine if they have malaria and if so, what type. He makes sure patients are taking their free medicines and checks to see if they're improving. If not, Phoun Sokha can even arrange transportation to the hospital.

But treating O'treng's malaria patients can be frustrating.

"Some of the patients, when they went to the hospital, after one month, maybe they get malaria again," he says.

Today Hong Da, the village boy who has fought malaria so many times before, heads home from the hospital after a few days of treatment. He clutches a new mosquito net he hopes will prevent yet another infection. Together, the recovering boy and his weathered mom shuffle past sick neighbor Chhien Rern's shack before disappearing among the tassels of the cornfield toward their home.

But all is not well.

Under a tattered quilt, Hong Da's 9-year-old sister Hoeun Chhay Meth is curled on a thin mattress atop the wooden floor inside

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the family's open-air home.

She had malaria alongside her brother two months ago. They share a mosquito net that she burned a hole in when she stayed up one night reading by the light of a makeshift candle. Her brother thinks that's how the mosquitoes infected them.

"Very afraid of dying," says Chhay Meth, who has started taking medicine provided by the village malaria worker. "I feel worse than before. I cannot walk myself or stand up by myself and cannot eat well."

Hong Da understands. He gently lifts his little sister's limp body, scooping her up, his strength returning. Chhay Meth reaches weakly for her mother.

Like her big brother, this child doesn't know about counterfeit drugs or antimalarials.

She only knows she's sick. And the medicines don't seem to work as well any more in this little village she calls home.

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Martha Mendoza is an AP national writer based in Mexico City. Margie Mason is an AP medical writer who reported from Cambodia while on a fellowship from The Nieman Foundation at Harvard University.

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