

Feature: Health,Animals

## Malaysia is ground zero for the next malaria menace

*Deforestation brings monkeys and humans close enough to share an age-old disease*

By Yao-Hua Law 7:00am, November 4, 2018



**MONKEY MALARIA** People pick up malaria from mosquitoes. But in Southeast Asia, more of those biters are transmitting the parasites from monkeys, like macaques (one shown), to people.

Donald Walker/Shutterstock

Vinita Surukan knew the mosquitoes were trouble. They attacked her in swarms, biting through her clothes as she worked to collect rubber tree sap near her village in Sabah, the northern state of Malaysia. The 30-year-old woman described the situation as nearly unbearable. But she needed the job.

There were few alternatives in her village surrounded by fragments of forest reserves and larger swaths of farms, oil palm plantations and rubber tree estates. So she endured until a week of high fever and vomiting forced her to stop.

The night of July 23, Surukan was trying to sleep off her fever when the clinic she visited earlier in the day called with results: Her blood was teeming with malaria parasites, about a million in each drop. Her family rushed her to the town hospital where she received intravenous antimalarial drugs before being transferred to a city hospital equipped to treat severe malaria. The drugs cleared most of the parasites, and the lucky woman was smiling by morning.

Malaria has terrorized humans for millennia, its fevers carved into our earliest writing on ancient Sumerian clay tablets from Mesopotamia. In 2016, four species of human malaria parasites, which are spread by mosquito from person to person, infected more than 210 million people worldwide, killing almost 450,000. The deadliest species, *Plasmodium falciparum*, causes most of the infections.

But Surukan's malaria was different. Hers was not a human malaria parasite. She had *P. knowlesi*, which infects several monkey species. The same parasite had recently infected two other people in Surukan's village — a man who hunts in the forest and a teenager. Surukan suspects that her parasites came from the monkeys that live in the forest bordering the rubber tree estate where she worked. Some villagers quit working there after hearing of

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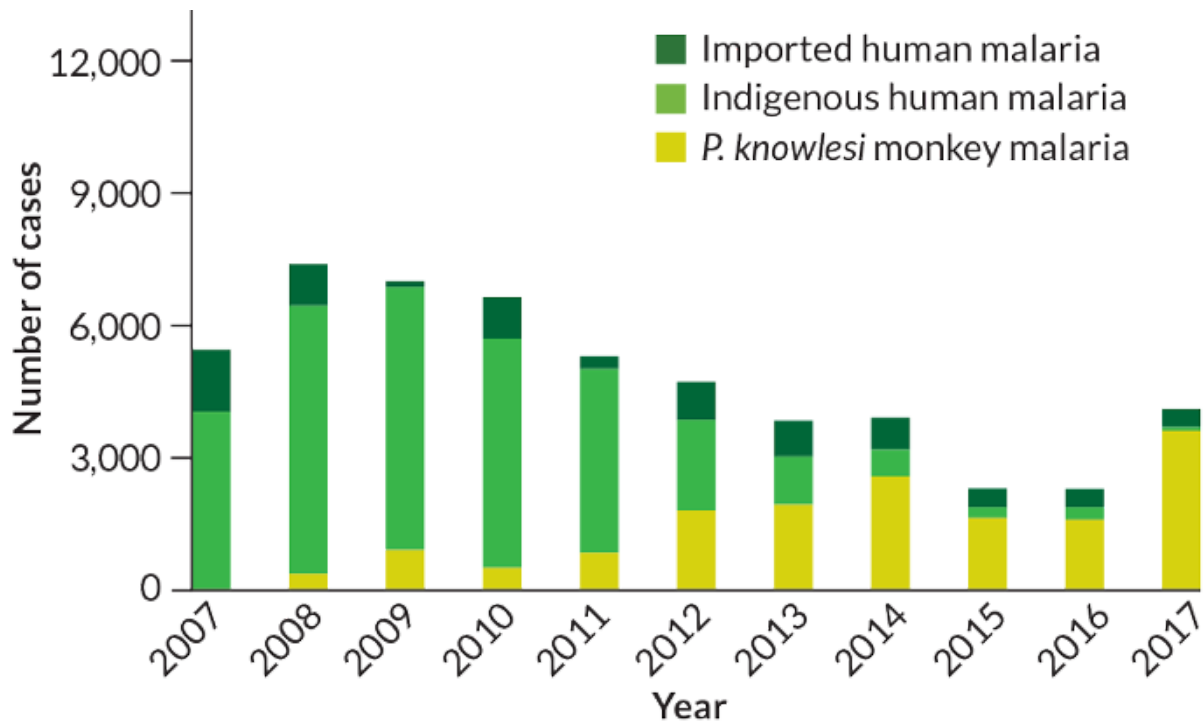
Monkey malaria, discovered in the early 1900s, became a public health concern only in the last 15 years. Before that, scientists thought it was extremely rare for monkey malaria parasites, of which there are at least 30 species, to infect humans.

Yet since 2008, Malaysia has reported more than 15,000 cases of *P. knowlesi* infection and about 50 deaths. Infections in 2017 alone hit 3,600.

### Emerging threat

Malaysia is close to eliminating human malaria. Yet cases of *P. knowlesi* malaria transmitted from monkeys are tenfold since 2008.

## Malaria cases in Malaysia, 2007-2017



C. Chang

Source: Ministry of Health Malaysia 2018

People infected with monkey malaria are found across Southeast Asia near forests with wild monkeys. In 2017, another species of monkey malaria parasite, *P. cynomolgi*, was found in five Malaysians and 13 Cambodians. And by 2018, at least 19 travelers to the region, mostly Europeans, had brought monkey malaria back to their home countries.

The rise of monkey malaria in Malaysia is closely tied to rapid deforestation, says Kimberly Fornace, an epidemiologist at the London School of Hygiene and Tropical Medicine. After testing blood samples of nearly 2,000 people from areas in Sabah with various levels of deforestation, she found that people staying or working near cut forests were more likely than people living away from forests to have *P. knowlesi* infections, she and colleagues reported in June in *PLOS Neglected Tropical Diseases*. Stepping over felled trees, humans move closer to the monkeys and the parasite-carrying mosquitoes that thrive in cleared forests.



**LOST LANDS** Several states in Malaysia, including Sabah, have lost large swaths of forest to oil palm and rubber tree plantations. *peacefoo/Shutterstock*

### It's out there

There's no feasible way to treat wild monkeys for an infection that they show no signs of. "That's the problem with *P. knowlesi*," says Singapore-based infectious disease specialist Fe Espino, a director of the Asia Pacific Malaria Elimination Network.

In 2015, the World Health Organization set a goal for 2030: to stop malaria transmission in at least 35 of the 91 malaria-endemic countries. WHO targets the four human malaria parasites: *P. falciparum*, *P. vivax*, *P. malariae* and *P. ovale*. Monkey malaria is excluded from the campaign because the agency regards it as an animal disease that has not been shown to transmit among humans.

But as countries reduce human malaria, they will eventually have to deal with monkey malaria, Espino says, echoing an opinion widely shared by monkey malaria scientists.

"Something nasty" could emerge from the pool of malaria parasites in monkeys, says malariologist Richard Culleton of Nagasaki University in Japan. Culleton studies the genetics of human and monkey malaria. Malaria parasites can mutate quickly — possibly into new types that can more easily infect humans (*SN*: 9/6/14, p. 9). To Culleton, the monkey malaria reservoir "is like a black box. Things come flying out of it occasionally and you don't know what's coming next."





**ON THE RISE** Researchers collect blood samples from local residents to check for malaria parasite DNA.  
Joshua Paul/London School of Hygiene and Tropical Medicine

Malaysia is very close to reaching the WHO target of human malaria elimination. In 2017, only 85 people there were infected with human malaria. But that success feels hollow as monkey malaria gains a foothold. And while monkey malaria has swelled into a public health threat only in Malaysia, the same could happen in other parts of Southeast Asia and beyond. Even in southeastern Brazil, where human malaria was eliminated 50 years ago, the *P. simium* malaria parasite that resides in howler monkeys caused outbreaks in humans in 2015 and 2016.

### From tool to threat

In the late 1800s, scientists discovered the *Plasmodium* parasite and its *Anopheles* mosquito carriers. Humans retaliated by draining marshes to stop mosquito breeding and spraying insecticides over whole communities. Governments and militaries pursued antimalarial drugs as the disease claimed countless soldiers during the two World Wars.

Scientists soon found malaria parasites in birds, rodents, apes and monkeys. To the researchers, the parasites found in monkeys were a tool for testing antimalarial drugs, not a threat. An accident, however, showed otherwise.

In 1960, biologist Don Eyles had been studying the monkey malaria *P. cynomolgi* at a National Institutes of Health lab in Memphis, Tenn., when he fell ill with malarial fevers. He had been infected with the parasites found in his research monkeys. His team quickly confirmed that the malaria parasites in his monkeys could be carried by mosquitoes to humans. Suddenly, monkey malaria was not just a tool; it was an animal disease that could naturally infect humans.

The news shook WHO, McWilson Warren said in a 2005 interview recorded by the Office of NIH History. Warren, a parasitologist, had been Eyles' colleague. Five years before Eyles became infected, WHO had launched the Global Malaria Eradication Programme. Banking on insecticides and antimalarial drugs, the agency had aimed to end all malaria transmissions outside of Africa. A monkey malaria that easily infects humans would sink the program because there would be no way to treat all the monkeys.

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A team of American scientists, including Eyles and Warren, traveled to Malaysia — then the Federation of Malaya — where the *P. cynomolgi* parasites that infected Eyles came from. Funded by NIH, the scientists worked with colleagues from the Institute of Medical Research in Kuala Lumpur, established in 1900 by the British to study tropical diseases.

From 1961 to 1965, the researchers discovered five new species of monkey malaria parasites and about two dozen mosquito species that carry the parasites. But the researchers did not find any human infections. Then, in 1965, an American surveyor became infected with *P. knowlesi* after spending several nights camping on a hill about 160 kilometers inland from Kuala Lumpur.

Warren surveyed the forested area where the infected American had camped. The hill sat beside a meandering river. Monkeys and gibbons, a type of ape, lived on the hill and in adjacent forests. The closest house was about two kilometers away. Warren sampled the blood of four monkeys and more than 1,100 villagers around the hill; he collected mosquitoes too.

He found *P. knowlesi* parasites in the monkeys, but none among the villagers. Only one mosquito species, *A. maculatus*, appeared capable of transmitting malaria between monkeys and humans, but Warren deemed its numbers too low to matter. He concluded that monkey malaria stayed in the forests and rarely ever spilled into humans.

With those results, NIH ended the monkey malaria project, Warren said, and the Institute of Medical Research in Kuala Lumpur returned to its primary focus: human malaria, dengue and other mosquito-borne diseases. Monkey malaria was struck off the list of public health concerns.

### Wake-up call

*P. knowlesi* landed back in the spotlight in 2004, with a report in the *Lancet* by malariologist Balbir Singh and his team. The group had found 120 people infected over two years in southern Malaysian Borneo. The patients were mostly indigenous people who lived near forests. Clinicians initially had checked the patients' blood samples under microscopes — the standard test — and diagnosed the parasites as human malaria. But when Singh, of Universiti Malaysia Sarawak, applied molecular tools that identify parasite species by their DNA, he revealed that all the samples were *P. knowlesi*. Monkey malaria was breaking out of the diminishing forests.

By 2018, *P. knowlesi* had infected humans in all Southeast Asian countries except for East Timor. Singapore, declared malaria free in 1982, reported that six soldiers were infected with *P. knowlesi* from wild monkeys in a forest reserve. The parasite also turned up in almost 380 out of 3,700 visitors to health clinics in North Sumatra, Indonesia, an area that is close to being deemed free of human malaria.



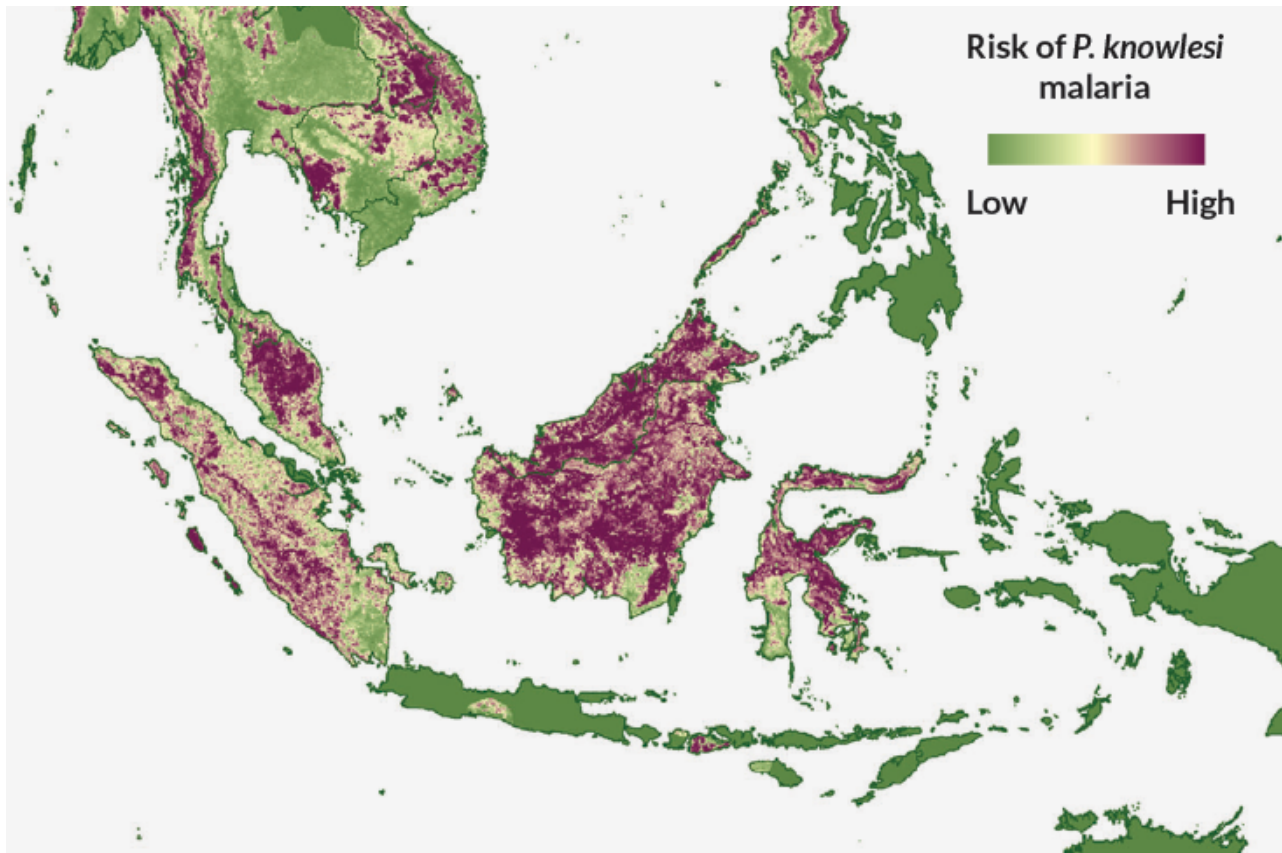
**INFECTED RESEARCHER** After becoming infected in 1960 with the malaria parasite found in his research monkeys, biologist Don Eyles took a team from the National Institutes of Health to Southeast Asia to study the parasites in nature. He is shown here with his pet gibbon, a type of ape, in Kuala Lumpur.

*Courtesy of Eyles Family*

## Expanded risk

Malaysia bears the brunt of *P. knowlesi* malaria infections. But this 2016 map shows high predicted risk of disease (maroon) in other parts of Southeast Asia as well, based on epidemiologic and environmental factors.

### Predicted risk of *P. knowlesi* infection in humans in Southeast Asia



F.M. Shearer et al/PLOS Neglected Tropical Diseases 2016 (CC BY 4.0)

Many scientists now recognize *P. knowlesi* as the fifth malaria parasite species that can naturally infect humans. It is also the only one to multiply in the blood every 24 hours, and it can kill if treatment is delayed. People pick up *P. knowlesi* parasites from long-tailed macaques, pig-tailed macaques and Mitred leaf monkeys. These monkeys range across Southeast Asia. So far, malaria parasites have been found in monkeys near or in forests, but rarely in monkeys in towns or cities.

Scientists propose several reasons for the recent rise in monkey malaria infections, but two stand out: improvement in malaria detection and forest loss.

Malaysia, for instance, finds more monkey malaria cases than other Southeast Asian countries because it added molecular diagnostic tools in 2009. Other countries use only microscopy for detection, says Rose Nani Mudin, who heads the vectorborne disease sector at Malaysia's Ministry of Health. Since 2008, annual monkey malaria cases in Malaysia have climbed tenfold, even as human malaria cases have plummeted. "Maybe there is a genuine increase in [monkey malaria] cases. But with strengthening of surveillance, of course you would detect more cases," she says.

Data collected by Malaysia's malaria surveillance system have also revealed strong links between infection risk and deforestation. Fornace, the epidemiologist, examined the underlying drivers of monkey malaria in Surukan's home state of Sabah. Fornace mapped monkey malaria cases in 405 villages, based on patient records from 2008 to 2012. Satellite data showed changes in forested areas around those villages. The villages most likely to report monkey malaria infections were those that had cut more than 8 percent of their surrounding forests within the last five years, she and colleagues reported in 2016 in *Emerging Infectious Diseases*.





**FIELD WORKERS** Kimberly Fornace (left) and collaborators at Universiti Malaysia Sabah collect blood samples from people in northern Sabah. The group checks blood for evidence of current and past malaria infections.  
Joshua Paul/London School of Hygiene and Tropical Medicine

Fornace's team went into the field for a follow-up study, published in June in *PLOS Neglected Tropical Diseases*. The team collected blood samples from almost 2,000 people in two areas in Sabah and checked for current and past malaria infection. People who farmed or worked in plantations near forests had at least a 63 percent higher risk of *P. knowlesi* infection, and — like in the 2016 study — forests and cleared areas escalated risk of infection.

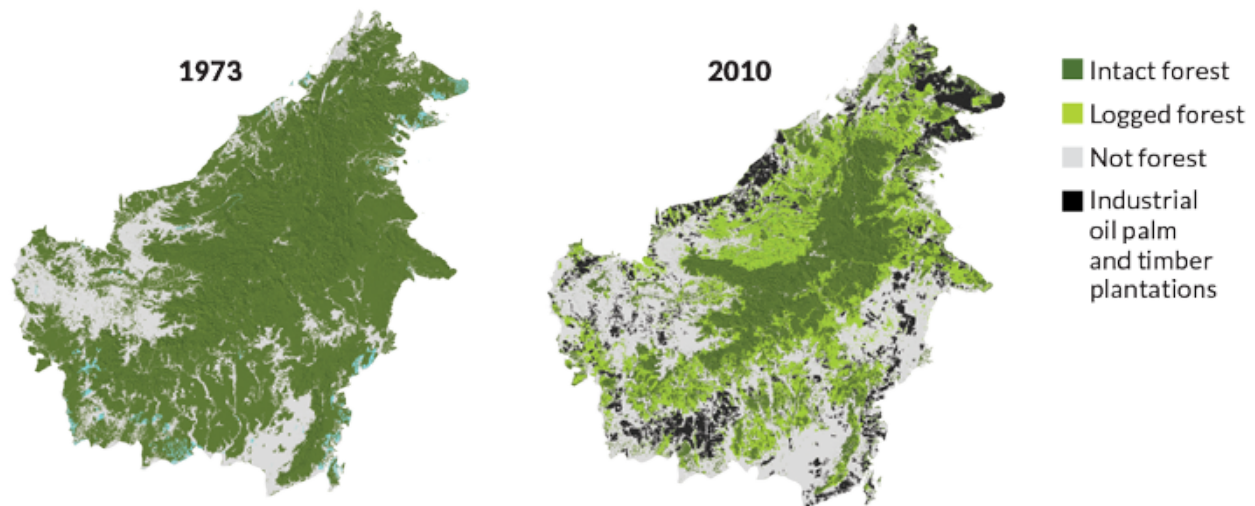
"It feels almost like *P. knowlesi* follows deforestation," Fornace says. Several years after a forest is cut back, nearby communities "get a peak of *P. knowlesi*."

Today, the hill where the American surveyor camped in 1965 is a small island in a sea of oil palm estates. From 2000 to 2012, Malaysia cleared a total amount of forest equaling 14.4 percent of its land area, more than any other country, according to a study published in 2013 in *Science*. A study in 2013 in *PLOS ONE* used satellite images to show that in 2009, only one-fifth of Malaysian Borneo was intact forest. Almost one-fourth of all forest there had been logged, regrown and logged many times over.

Since 2008, oil palm acreage in Malaysian Borneo has increased from 2.08 million hectares to 3.1 million, according to the Malaysian Palm Oil Board. In Malaysia, the four states hit hardest by deforestation — Sabah, Sarawak, Kelantan and Pahang — report 95 percent of the country's *P. knowlesi* cases.

## Forests to farms

From 1973 to 2010, Borneo's intact forests dwindled as farming and logging grew, satellite images show.



*D.L.A. Gaveau et al/PLOS One 2014 (CC BY 4.0)*

Fornace thinks deforestation and the ecological changes that come with it are the main drivers of monkey malaria's rise in Malaysia. She has seen long-tailed macaques spend more time in farms and near houses after their home forests were being logged. Macaques thrive near human communities where food is abundant and predators stay out. Parasite-carrying mosquitoes breed in puddles made by farming and logging vehicles.

Where monkeys go, mosquitoes follow. Indra Vythilingam, a parasitologist at University of Malaya in Kuala Lumpur, studied human malaria in indigenous communities in the early 1990s. Back then, she rarely found *A. cracens*, the mosquito species that carries monkey malaria in Peninsular Malaysia. But in 2007, that species made up over 60 percent of mosquitoes collected at forest edges and in orchards, she reported in 2012 in *Malaria Journal*. "It's so much easier to find them" now, she says.

As Fornace points out, "*P. knowlesi* is a really good example of how a disease can emerge and change" as land use changes. She recommends that when big projects are evaluated for their impact on the economy and the environment, human health should be considered as well.

## What to expect

While *P. knowlesi* cases are climbing in Malaysia, scientists have found no evidence that *P. knowlesi* transmits directly from human to mosquito to human (though many suspect it happens, albeit inefficiently).





**NEMESIS** Under a microscope, a dissected mosquito is checked for malaria parasites in Sabah, Malaysia.

Joshua Paul/London School of Hygiene and Tropical Medicine

Following [a review by experts in 2017](#), WHO continues to exclude *P. knowlesi* from its malaria elimination efforts. Rabindra Abeyasinghe, a tropical medicine specialist who coordinates WHO malaria control in the western Pacific region, says the agency will reconsider *P. knowlesi* as human malaria if there is new evidence to show that the parasite transmits within human communities.

In Malaysia last year, only one person died from human malaria, but *P. knowlesi* killed 11. “We don’t want that to happen, which is why [*P. knowlesi*] is our priority even though it is not in the elimination program,” says Rose Nani Mudin from the country’s Ministry of Health.

Unable to do much with the monkeys in the trees, Malaysian health officers focus on the people most likely to be infected with *P. knowlesi*. Programs raise awareness of monkey malaria and aim to reduce mosquitoes around houses. New mosquito-control methods are needed, however, because conventional methods like insecticide-treated bed nets do not work for monkey malaria mosquitoes that bite outdoors around dusk.

Fighting malaria is like playing chess against an opponent that counters every good move we make, says Culleton in Japan. Malaria parasites can mutate quickly and “go away and hide in places and come out again.” Against malaria, he says, “we can never let our guard down.”

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*This article appears in the November 10, 2018 Science News with the headline, "The Next Malaria Menace: Deforestation brings monkeys and humans close enough to share an age-old disease."*

*Editor’s note: This story was updated on November 6, 2018 to correct the WHO’s position on monkey malaria. The agency excludes monkey malaria parasites from its malaria eradication goals, not because those particular parasites rarely infect humans, but because the parasites have not been shown to transmit among humans.*

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## Further Reading

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