



THE BIG STING

At a village community in the Solomon Islands, an international team of researchers is discovering the secrets of a malaria-transmitting mosquito that harbours a deadly secret weapon.

STORY BY ASHLEY HAY PHOTOGRAPHY BY RALPH ALPHONSO

Anopheles aglow. A mosquito adjusts to its coat of fluorescent powder, which has been applied as part of a classic mark-release-recapture experiment involving these important malarial insects.

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THE ISLAND OF Nggele Sule, or Big Nggele, in the Solomon Islands' Central Province, pushes out of the ocean with picture-book lushness. Beyond the prow of the banana boat I'm in, it looms as a rugged and vertical landscape, impossibly green. There are palm trees along the shore and stretches of pale sand, hewn from coral.

It's a place of all sorts of beauty: flying fish, fireflies and dragonflies that look as if they're cut from thick maroon velvet. But what's brought me here is tom of insect, furry brown and spotted with white. It's *Anopheles farauti*, the mosquito that transmits malaria in this part of the world, where attack rates are some of the highest after those in Africa.

For 12 years I've cohabited with malaria. I live with its language: words such as "Anopheles", "geneflow", "vectors" and "cryptic species". My scientist husband Dr Nigel Beebe works in this field through the University of Queensland and CSIRO. The vectors he speaks of are nothing to do with maths or geometry, but rather the mosquitoes that transmit disease. And his cryptics are nothing to do with crosswords — they're insects with the same external appearance that are, genetically, completely different species.

I'm heading for Haleta, a small village on the north-western flank of Nggele Sule, to learn some of the complexities of their particular mosquitoes: how they do what they do, and when, and how some of the latest scientific research hopes to defeat them. I'm here to see something of what Neil Lobo, scientific director of the Malaria Transmission Consortium (MTC) calls rather drily, "real malaria".

Malaria is the kind of global health issue many people now feel familiar with, thanks, in part, to high-profile philanthropists such as Bill and Melinda Gates, who finance the MTC through their foundation.

"Twenty years ago, you met people who'd say, 'Is there still malaria? Didn't you get rid of that?'" recalls Professor Tom Burkot, from James Cook University (JCU). There have been many attempts, and the World Health Organization ran a global eradication campaign for 14 years before abandoning it in 1969. Malaria was eliminated from Europe, North America, parts of South and Central America, parts of Asia and Australia. In the Solomons, the campaign wiped out two of the three mosquitoes that transmitted the disease — but the third, *A. farauti*, had a secret weapon.

In the one-size-fits-all design of that campaign, the insides of houses were sprayed with the insecticide DDT. Most malaria mosquitoes bite people late at night, when they're inside their houses, after which

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Ralph Alphonso's last photography commission for AUSTRALIAN GEOGRAPHIC was our *Hives* for humanity story (AG 112).



the insects rest on nearby walls, encountering the insecticide. *A. farauti's* advantage was subtle: a section of its population bit people earlier in the evening, when they were outside. "Because some *farauti* bit earlier, they avoided the insecticide, survived and reproduced, passing on this behavioural trait," Nigel explains. "In this way, the species could shift most of the population to this early biting behaviour."

It's a dazzling display of what Tom describes as mosquitoes' "nimbleness", and of the mechanics of evolution. It also poses a serious problem for a disease now mainly addressed with a single tool: insecticide-treated bed nets. Although these are an important weapon in the arsenal, Tom says "we need to do more". Bed nets are of much less use where mosquitoes are biting outdoors, Neil points out.

HALETA IS TYPICAL of many villages in the Solomon Islands: rural-coastal, with a subsistence lifestyle. There's no plumbing or sanitation, just one tap for its 428 inhabitants. There's no electricity, although some houses have a small solar panel. There are no roads, transportation is by boat or on foot. There's a school, a church, a soccer field and a swamp — from which crocodiles occasionally emerge.

Four times a year, researchers come to run several weeks of intense investigations into *A. farauti* and the mechanics of malaria transmission: When do these mosquitoes bite? What or who do they bite? Where do they lay the eggs they generate after they've taken that blood-meal? How long after a meal do they want to feed again? And, how flexible are these events?

"We've been studying these vectors for the last 60 years for the purpose of control and eradication, but it's amazing how little we really know about their behaviour and biology," says Bob Cooper, a retired Army Lieutenant-Colonel from the Australian Army Malaria Institute (AMI). "One of the reasons is that until 20 years ago, people thought

Continued page 55 >



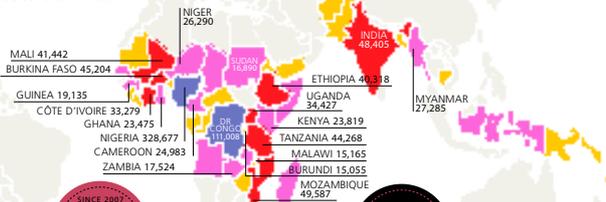
In the field. The village of Haleta (above), in the Solomons' Central Province, is home to huts, vegetation and a swamp where mosquitoes lay their eggs, creating what researchers call "a very simple microcosm of the world". While Tom Burkot (right) samples the swamp's water for mosquito larvae, Neil Lobo (left and below) prepares larval pans in which the insects can lay eggs.



THE TERRIBLE TOLL OF MALARIA

Malaria is still a major cause of death worldwide, particularly in sub-Saharan Africa.

Estimated malaria mortalities in 2010, according to the Institute for Health Metrics and Evaluation.



SINCE 2007
MALARIA
DEATHS HAVE
DECLINED BY
7%
A YEAR

91%
OF MALARIA
DEATHS IN 2010
WERE IN THE
AFRICAN
REGION

3.3 BILLION
people live in areas at risk of malaria transmission, in 106 countries and territories.

Since 2009, malaria health efforts have been funded to the tune of more than
\$1.9 BILLION
annually.

1 MILLION
people died from malaria worldwide in 2010.

Malaria is the world's
NO.3
most deadly infectious disease in children under five.

ONCE BITTEN

The life cycle of malaria

- 1 A mosquito infected with malaria bites a human.
- 2 The malaria parasite – at a worm-like stage called a sporozoite – travels to the liver via the bloodstream. It moves into a liver cell and replicates.
- 3 These liver cells burst, releasing parasites into the bloodstream where they invade the human's red blood cells and replicate. This cycle of rupture and replication is what causes illness in people.
- 4 Some of the parasites that rupture out of the blood cells become male and female cells.
- 5 When an *Anopheles* mosquito bites this human they will ingest these cells.
- 6 Inside a mosquito's midgut, these male and female cells mate to form a single cell that can move out of the midgut before it is digested. These cells generate new sporozoites outside the midgut, and they invade the mosquito's salivary glands.
- 7 When this mosquito bites a human, sporozoites are transferred from its salivary gland into the bloodstream, infecting the human and continuing the cycle.

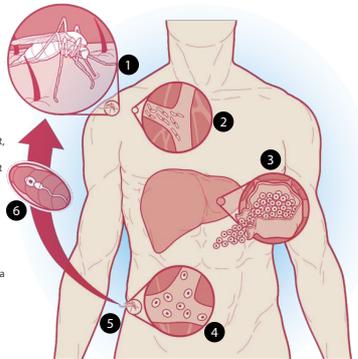


ILLUSTRATION: JACQUES-ANTOINE LAFITE/ISTOCKPHOTO.COM; PHOTO: JACQUES-ANTOINE LAFITE/ISTOCKPHOTO.COM



Mobile lab. In an ad-hoc workspace in their Tulagi hotel, researchers Neil Lobo and Nigel Beebe identify mosquitoes collected in Haleta.

Research is often stereotyped by high-tech gadgets in antiseptic labs, but it's much more low-tech here.

they were dealing with a single species of mosquito. Now we know that we're looking at different species – called cryptic species – that look exactly the same but have their own behaviour and ecology."

The first eradication campaign thought it was dealing with a single *farauti* mosquito; researchers now know that there are eight separate species in the *farauti* group. Although malaria is a global problem, "one of the clearest things that's come out of MTC's research worldwide is that transmission is so specific to site," says Neil.

"Haleta, as a site, is ideal," adds Tom. "It's a very simple microcosm of the world: the houses are together and most animals are penned. These are the raw materials for a mosquito to take the blood-meal it needs to make its eggs. And here there's just one big swamp where it's going to lay those eggs. With such a nice clean system, you can get some very precise estimates of mosquito behaviour." Unravel which aspects of mosquitoes' biology or behaviour might be vulnerable to intervention, and it will be easier to design one that can have an effect.

Just by Haleta's swamp, villagers have built the researchers a two-room hut. "The Haleta

Entomological Research Station; that's 'HERS,'" jokes JCU researcher Tanya Russell. Inside are rudimentary shelves along bamboo walls, a couple of camp stretchers and three decorative plywood mosquitoes. Scientific research is often stereotyped by high-tech gadgets in antiseptic labs, but it's much more low-tech here.

The pans to catch larvae laid by mosquitoes are cut-down plastic measuring cups set in white foam Christmas wreaths – Neil bought the components from craft and homeware stores before he flew out from Indiana, USA, where he works at the University of Notre Dame's Eck Institute for Global Health. And the dozens of cups sent out for each night's collections are bright-pink gelato containers.

"AMI had been using these cups for more than 30 years," Bob says. "They're strong, they're a good size, and they're waterproof." In the early 1990s, the company that made them went out of business. "So we went to the warehouse and bought all the stock they had. They had no idea what we were using them for. They thought we were ice-cream makers." Now the supply is nearly exhausted and no satisfactory alternative has been found.

Continued page 59 >



TO WATCH THE research team at work in Haleta, download the **viewa** app, select the AG channel and hold your smartphone over this page.

Village life. The research team prepare for the evening's collections in front of the hut built for them by the villagers, while Haleta's children play nearby.



Tropical medicine. Catherine Kikoa, left, and Jeffrey Vili, centre, discuss their work with writer Ashley Hay. Their laboratory is located within Tulagi Hospital (pictured below).

THE SCOURGE OF THE POOR

As they work to treat and prevent malaria, scientists suggest that small changes might make a big impact.

THINKING ABOUT malaria means thinking in extremes: 10mm worth of individual mosquito against the 3.3 billion people estimated to be at risk from malaria worldwide.

"We infect the mosquitoes, they infect us. We invent new interventions to control them, they adapt and we have to invent more. Researcher Neil Lobo calls it an arms race. "When the mosquito changes, we've got to have the next control tool ready," adds Professor Tom Burkot.

While laboratories around the world continue to search for vaccines, new drug treatments and insecticides, visitors to the 109 countries deemed malarious mostly carry preventative medicine. But, locals can't live on this permanently. "For them, malaria is...



like the common cold," says Tanya Russell. "Except this cold can kill you," adds Tom.

Contract the disease and a clinic might be hours away. "Then there has to be treatment available," says Neil. "And, most people don't go to the clinic until someone's really sick."

Working in the malaria lab of the Tulagi Hospital in Central Province, Solomon Islands, Catherine Kikoa and Jeffrey Vili see blood samples from perhaps 15 potential cases each day, three of which may test positive. It

takes 15 minutes to make, stain, dry and read each blood slide. Although their clinic has electricity, some health posts use mirrors and the sun to illuminate their microscopes.

Science, however, is not the only weapon. "Poor people suffer from malaria," says Neil, simply. "On a daily basis, wealthy people don't. If we had enough money, we could impact malaria greatly. Give everyone a TV, an air-conditioner and a house that they could close up...and malaria would contract."



The perfect cup. Captured mosquitoes are placed into collection cups and covered with a fine mesh before scientists begin processing and recording.

This is not the science of eureka moments; it's painstakingly laborious...mosquitoes are processed, counted and recorded.

Just before 6pm, the light dips to a quick, golden twilight and the fireflies begin to emerge. Meals are cooking, games are ending, and children are being led to and from the places they use as a toilet and the streams in which they wash. The 24 local mosquito collectors assemble their cups, head torches and aspirators. For six hours, each will sit in his designated space, catching any mosquito that lands on his bare feet and legs by sucking them into an aspirator – a clear tube attached to a narrow rubber pipe – and blowing them into a mesh-covered cup.

At the end of each hour, the cups will be brought in by a team of overseers, headed by John Lodo from the Solomon's Vector Borne Disease Control Program. Besides his involvement with MTC, John's main workload lies with an ongoing program of indoor spraying and the distribution of bed nets – 12,000 across the province in 2010, with top-ups of several thousand in subsequent years. "We distribute the top-up nets when we find them damaged or broken, or someone has taken the net away, or people are not using them properly," he explains. Improper uses include covering fruit trees, protecting chickens and catching fish – someone jokes that the

nets were coloured blue to stop them from being appropriated for weddings. Someone else points out how impossible it is to actually sleep under one in a tropical climate: they cut off any available breeze.

At 7pm, the first hour's collections come in. Tom Burkot calls "incoming", and jokes that this could be the mosquito version of the TV show MASH. This is not the science of eureka moments; it's painstakingly laborious. The mosquitoes are processed, counted, recorded, identified by genus (anophelines versus other non-malarious species) and by their most recent meal (blood; sugar). Some samples are separated for later genetic analysis. They also have to be checked under UV light for fluorescent dust – the glamour dust of dance parties – because batches of the insects caught each night in this trip have been dusted with particular colours and released again. It's a classic mark-release-recapture experiment. Not particularly novel, explains Tom, but it's revealing a very short turnaround between blood-meals.

On the Sunday I arrive, the first batch delivers two pink-dusted mosquitoes released the Friday previous – they have already dropped a batch of eggs and are seeking their next feed.

"They're going through that cycle of taking blood, laying eggs and coming back to take blood very quickly," Tom notes. This might prove important.

Mosquitoes are not born with malaria; they are infected when they bite a human who is carrying malaria parasites. Those parasites then need to develop within the insects for 10–14 days before the mosquitoes become malarial. This provides a significant window in which to put that mosquito in harm's way of some intervention – whether insecticide-based or environmental-based. If they feed every two days "we've got more opportunities to kill that mosquito," says Tom. It may prove a crucial vulnerability in a highly adaptable foe.

IT'S WELL AFTER MIDNIGHT, the final collections have been processed and the prized gelato cups returned. Tanya carefully dusts a posse of the night's mosquitoes with white powder; they'll join the yellow, pink and blue insects already on the fly.

Between them these researchers represent an array of expertise – from ecological to genetic – and about one century's worth of time spent considering malaria

underway around the world in the quest to eradicate malaria – can be incorporated into mathematical modelling that tries to match particular treatments to specific situations.

"The days of one intervention being globally implemented, like DDT, like bed nets, that may be pretty much over," says Tom. "We're going to be targeting individual species with 'boutique' interventions – maybe what's good for the Solomon Islands will be no good for Indonesia. So we need good quality data that we can feed into the models and make projections of what the impact of an intervention might be – and there are big gaps in the data that's available around the world." In the Solomons, for example, even the mosquitoes' seasonality – when numbers are high and low – was unknown. "Filling those gaps is critical," says Tom.

We track the incandescent mosquitoes for a while – some rubbing at themselves with cartoon-like determination to brush away the alien white dust – and then we pile into the boat and head out. But when the research team leaves, the work goes on. Monthly collections are co-ordinated by Allen

"We're not just looking at bugs... We're trying to make an impact on people's lives."

in the south-west Pacific. Tom and Bob have each been in the game for three decades, while Captain Weng Chow is a freshly minted Australian Army Malaria Institute scientist, making his first trip into the field. "In two weeks here I've learnt more than I've learnt in the lab in a year," he says. "You see the people in their environment. In a lab you can't really picture the issues you might come up against."

"Australia as a country has always punched above its weight in terms of malaria research and control – at least in the 30 years that I've been involved," says Tom, an American who first came to Queensland in 1988. "It's not about protecting Australians who go out on holiday. It's about being a good neighbour and doing the right thing."

We shine UV torches at the cup in Tanya's hands and the mosquitoes shimmer and glow. At the village edge, Tanya slowly peels the gauze away and the insects sit for a second or so, a perfect constellation. Then they flicker and rise like tiny flares, darting back into the night. Our torch beams trail in their wake, picking up a mosquito on a leaf, another on a branch. One perches on photographer Ralph Alphonso's shirt as he leans forward to focus his camera.

How many go out, how many come back and when: this, like all the other data collected here – and so much more generated by countless other experiments

Apairamo, a technician with the National Malaria Control Program who works closely with John Lodo, before the data is sent on to Dr Hugo Bugoro in the capital Honiara (who oversees the field team in-country) and to James Cook University.

"Now, we're starting to see that seasonality," says Bob. Higher mosquito numbers usually correlate with higher rainfall, but Haela's mosquitoes reach their highest numbers at the end of the dry season.

"In this game, answers often generate more questions," he adds.

Above the boat, a half-moon's light obscures the bright track of the Milky Way. The water looks like silver glass shaped perfectly to the Earth's curve. It's serenely beautiful. Soon, I'll travel from the third world to the first in just seven hours – by banana boat, taxi, aeroplane and train. In my yard, I'll brush at a suburban mozzie – an annoyance, not a threat.

"We're not just characterising discrete parts of the mosquito life cycle so we can decide what to do next," says Neil of the research project. "From what we've already found, we can actually start trialling some interventions. We're not just looking at bugs... We're trying to make an impact on people's lives."

Find more of Ralph Alphonso's photos online at: www.australangeographic.com.au/journal/issue14



Sunset on paradise. Haela (above) is an island at risk – 14.5 per cent of residents test positive for malaria. From 6pm, collectors (left) capture mosquitoes, some of which are dusted with fluorescent powder and released later that night (right). When Tanya Russel and Weng Chow (below) find the dusted mosquitoes, they can begin quantifying the feeding-and-breeding cycle.

