



PROFILE: FRANÇOIS NOSTEN

## The Dour Frenchman on Malaria's Frontier

When he arrived at the dangerous Thai-Burmese border in 1984, François Nosten barely knew what research was. Today, he's one of the world's top malaria scientists

**MAE SOT, THAILAND**—You'd think that a malaria scientist in François Nosten's position would need lots of charm and excellent diplomatic skills. He's a foreigner working in Thailand, a country where smiling seems a prerequisite for getting anything done. His work straddles the politically sensitive and occasionally violent border with Myanmar, formerly Burma, and he manages a health care system primarily for illegal immigrants from that country—people the Thai government largely ignores.

But as it happens, Nosten, 53, doesn't exude much charm, he rarely smiles, and one colleague calls him "famously undiplomatic." When *Science* came to visit him in this border town, a 7-hour drive from Bangkok, Nosten's long face bore a scowl. "I'm often grumpy," he confessed.

Yet despite his frequent sourness, Nosten has built an unmatched international resume in malaria. The Shoklo Malaria Research Unit (SMRU), which he founded 25 years ago, not only provides basic health services to tens of thousands of poor people, but it's also one of the most respected and prolific clinical malaria research centers in the world. With more than 230 published papers, including co-authorship of a report on page 1175 of this issue of *Science*, Nosten ranks as one of the 10 most-cited researchers in his field.

It was at SMRU that the so-called artemisi-

nin-based combination therapies (ACTs), a class of new drugs that has become the standard worldwide, were pioneered. Most of the clinical trials of malaria treatment for pregnant women—who are especially vulnerable to dying from the disease—were done here. Epidemiologist Philippe Guérin, who worked with Nosten for 3 years in the late 1990s, calls his contribution "somewhere between enormous and critical." As to his demeanor, "people either love or hate François," says Guérin.

Those in the former category say you just have to get used to him. And indeed, Nosten seemed to thaw when, after a quick stop to pick up some cold beers, he invited this reporter to his wooden Thai house, set in a huge, private, fenced garden. "Welcome to Mae Sot," he said after popping open the first two cans. And as the evening went on, Nosten



**True to his roots.** After 25 years in Thailand, Nosten still feels "completely French."

**A doctor first.** François Nosten treating a sick child at the Mae La refugee camp.

talked passionately about his unusual career. He even managed a smile or two.

### Arms and legs

Nosten, who grew up in Toulouse, France, arrived in Thailand in the early 1980s as a long-haired doctor for Médecins Sans Frontières (MSF), the French charity. He knew next to nothing about malaria, and he wasn't trained as a scientist. It was his curiosity as a doctor that drove him to research. He quickly noticed that the standard malaria drugs weren't doing their job because the parasite had developed resistance, and he wondered whether mefloquine, a new drug developed by the U.S. Army, would do any better. So he embarked on his first clinical studies.

In 1985, he met Nicholas White, a British malariologist who had just set up shop in Bangkok, funded by the Wellcome Trust, and had a professorship at the University of Oxford. White was scouting for malaria research locations; Nosten was running a jungle hospital just across the border in Myanmar. "It was made out of wood and leaves, but it was a very good hospital," White recalls. Impressed, he convinced Nosten to leave MSF and do studies for him.

A quarter-century later, SMRU has five clinics serving an area roughly 200 kilometers long on the Thai-Burmese border, along with a research unit in the center of Mae Sot, a town of some 30,000 inhabitants. Nosten employs more than 350 people, 20 of them ex-pats from various Western countries. White, still in Bangkok, remains "the brain" behind this operation, he says. "I'm the arms and the legs. But I don't care. I'm very happy with him, and I'm his disciple." Guérin calls that false modesty, as Nosten has become an opinion leader himself.

To his staff members, Nosten is "like a demanding, old-fashioned father," says Marcus Rijken, a Dutch physician who came here 3 years ago to study the effects of malaria on unborn babies. Don't expect praise from him just for agreeing to come live in this dull, remote town, Rijken says: "He puts the bar very high, for himself and everybody else." Although some have left in frustration, those who stayed say Nosten is also a very helpful and witty mentor and an inspiration in his own peculiar way.

### Porous border

When it comes to public health, border areas are often chaotic. Differing policies, language barriers, and human movement create messy

circumstances where infectious diseases thrive. The Thai-Burmese border is a prime example, says Nosten, as he provides a tour in his Land Rover the next morning. Burma, just across the river, is dirt-poor and has a dismal health system. Tens of thousands of refugees have lived in semipermanent refugee camps on the Thai side for decades—most of them members of the Karen, an ethnic minority fighting for autonomy.

In addition, migrants from Myanmar continually cross the border looking for a better life. On any given day, dozens of people wade or raft across the Moei River. The Thai government is “in denial” about the influx, Nosten says, and the Thai health system is neither equipped nor financed to help people from Burma. “That’s why we do it,” he says. While the Wellcome Trust funds his research, Nosten is continuously hunting for funds

Nosten says he’s careful to stay out of politics. “If I started criticizing the Burmese generals or the Thai politicians, I couldn’t survive here,” he says. Nosten identifies strongly with the Karen and is well-known and beloved by them, says staff manager Honey Moon, who’s been with SMRU for 25 years and is Karen herself. He married a Karen woman in 1989, and although he speaks Karen, his Thai is rudimentary. White, who’s fluent in Thai, handles most of the bureaucratic and political hurdles, while Mahidol University in Bangkok—on whose faculty both Nosten and White serve—provides important backing.

Nosten says he’s never tried that hard to integrate. “I was very happy to remain completely French,” he says. So French, indeed, that he taught his housekeeper how to make baguettes, and he keeps an apartment near the Place de la Bastille in Paris, where he travels

the first clinical trial of a combination of artesunate and mefloquine; by 1994 they were convinced that it was safe and effective.

SMRU has helped test every other ACT to come to the market since. But Nosten is frustrated that it took so long for combination therapies to become universally adopted. In Africa, in particular, ACTs weren’t introduced broadly until about 5 years ago, despite evidence that older drugs were useless. “It’s something strange about the malaria community,” he says. “There are a lot of preconceived ideas, a lot of things preventing people from changing their minds.” He says he’s tried his best to change them—sometimes in not-so-subtle ways. “At meetings, I can be a bully,” he admits.

### Monstrosity

Nosten attributes SMRU’s success to its hybrid nature: part humanitarian, part scientific. “We’re not coming in big white vans, taking samples, and disappearing,” he says. “We’re embedded within the communities, so we have much better access to patients. And if treatment A works better than B, we can immediately implement that.” Malaria rates, for instance, have plummeted in recent years in the border area.

But over a plate of spicy noodles at a roadside restaurant, he acknowledges that the model may not be sustainable. It’s hard to attract people of international stature to the middle of nowhere for the long term. He says things might be easier if SMRU were split into a medical NGO, perhaps run by locals, and a research center where scientists could spend shorter amounts of time. “But if you do that the wrong way, then you break the link, and the research dies,” he says.

“I guess I’ve created a monstrosity. I don’t know what will happen with it after I’m gone,” he concludes, as he musters another one of his rare smiles.

—MARTIN ENSERINK



**Hybrid.** SMRU is a research center as well as a health-care service for Karen refugees and migrants.

for the health service, which has gradually expanded and now includes maternal care and treatment for HIV and tuberculosis.

The conditions have long been harsh. For about a decade, the team lived in Shoklo, one of the camps, under primitive conditions and with little contact with the outside world. Massive floods almost swept away the hospital several times in the early 1990s, and Nosten nearly drowned while rescuing a Karen nurse. “Get the files! Get the files!” former SMRU researcher Christine Luxemburger recalls yelling during one such episode; the data from a malaria vaccine study were among the few items saved from the water. The camp also came under attack from the Burmese army, and in 1997, the Thai government decided that SMRU staff members could no longer stay there overnight. They had to move to Mae Sot.

several times a year. He received an important recognition from his home country when he won the prestigious \$400,000 Christophe Mérioux award in 2008.

Part of Nosten’s appeal is that he has remained an MSF doctor at heart; his scientific curiosity is driven by the people he lives among, says Jean-René Kiechel of the Drugs for Neglected Diseases Initiative, a nonprofit in Geneva, Switzerland, with which Nosten has collaborated. It’s also what led Nosten to explore the potential of ACTs. When mefloquine started failing soon after it was introduced, Nosten and White decided to try a new family of drugs called the artemisinin derivatives, isolated in China from a plant named *Artemisia annua*. To preempt resistance, they proposed combining a derivative called artesunate with another drug, a novel concept in malaria. In 1991, they started

