In 1965, Ralph Lainson left London for Brazil with a three-year Wellcome Trust grant. He never came back. What was it about tropical Brazil that appealed to the young man? The parasites, of course.

Ralph Lainson, like many, loves Brazil, but not for the reasons you might expect. "The Amazon region is a veritable mine of parasitological information, yet very, very few people work in this field here," says the 84-year-old scientist, enthusiastically. "I've always said to young Brazilian students what a wonderful place they're in. If you turn over a stone you are likely to find four new species underneath it."

It was this passion for the microscopic world that drew him away from his native England to the tropics some 50 years ago. It has also resulted in Professor Ralph Lainson now holding the titles of Fellow of the Royal Society and Officer of the Order of the British Empire, and being the Wellcome Trust's longest-serving grantholder - a record 47 years and
counting. Such a background might not seem to fit with his strange-but-true stories of the anaconda that swallowed a visiting dentist, and the angler attacked by piranhas while clearing his boat's propeller. Yet Ralph is a leading authority on parasites, particularly protozoan (single-celled) parasites. The clues to this are his sand-fly-patterned tie and the smile on his face when I ask about his specialism, the neotropical Leishmania.

Ralph's long relationship with the parasite began in 1959 in Belize (then British Honduras). At the time, no one in the country was sure of the origin of 'Chiclero ulcer' (cutaneous leishmaniasis). Ralph says: "We had the parasite isolated from human beings and we knew that most of the people who acquired the disease worked in the forest, often for long periods. It was reasonable to assume, therefore, that there were some reservoir hosts of the parasite among the forest animals." For two years they tracked all manner of creatures, with little success until a natural disaster lent a helping hand.

"Hurricane Hattie I'll always remember," says Ralph. "It was a terrible experience, levelled flat a lot of the forest, but the result was the wild animals found it difficult to find food. We had no problem capturing a large number of rodents, opossums and other animals in our baited traps." Among them was a rodent with lesions on its tail, lesions that turned out to be full of the parasite. Ralph identified three different species of rodent frequently carrying the parasite.

He and his team also captured hundreds of phlebotomine sand flies (using themselves as bait!) and offered them hamsters experimentally infected with Leishmania from patients. Dissection of the sand flies several days after their hamster blood meal revealed the parasite inside. This left Ralph and his entomologist, John Strangways-Dixon, in no doubt that the same species of insect that transmitted Leishmania in the Old World did it in the New World.
It only remained to prove the sand fly's role in the transmission of the causative parasite to humans.

"Now was the time to obtain a volunteer and feed these infected insects on him," says Ralph. "Strangways-Dixon was keen to be this person. He said that as the entomologist he was the correct person to do this. He said, they're my sand flies so if they're going to feed on anything or anyone it's going to be me. I'm their boss!"

"We fed the flies on Strangways-Dixon's belly, and a few weeks later a tiny lesion appeared, containing the parasites. It was most exciting: the first experimental proof of transmission to man of a neotropical Leishmania species by the bite of a phlebotomine sand fly! The moment we worked that out was, I suppose, when I realised that I was a real scientist."

**New World order**

Ralph soon returned to the UK, but pined for the tropics and the opportunity to continue his research in the New World. So, in 1963, he toured Latin America collecting strains of Leishmania and sizing up different research institutes. He went through Central America, down to Colombia, Venezuela and elsewhere, until his final stop, the Instituto Evandro Chagas in Belém, part of the Amazon delta of north Brazil.

There, he showed the researchers his photographs of rodent lesions in Belize. One of them, Dr Otis Causey, said he had seen very similar lesions on the Oryzomys capito rodents common to the region, but thought they were simply bacterial or fungal infections growing on damaged tails. Two weeks later in Rio de Janeiro, he approached Ralph with a slide made from a rodent in Belém. It was teeming with Leishmania parasites. They had for the first time found the reservoir host of at least one Leishmania species infecting humans in Brazil.
Although cutaneous leishmaniasis manifested itself in different forms in Central and South America, many clinicians thought the disease was due to the same parasite, Leishmania braziliensis, and that this was the same as L. tropica, the strain that caused leishmaniasis in the Old World. Ralph was among those certain that different leishmanial parasites were involved in the disease in different parts of the continent. Arriving in Brazil with a three-year Wellcome Trust grant, his team collected parasite samples from all sorts of animals: armadillos, opossums, foxes, porcupines, monkeys and more, as well as human patients with different forms of leishmaniasis.

Their findings were striking: the parasites found in Oryzomys were clearly much larger than those of L. braziliensis - the human parasite was tiny, only about 2-3 micrometres in diameter, whereas those that Otis Causey found were nearly twice the size. Furthermore, when they inoculated the Oryzomys-derived parasite into hamsters it produced huge tumour-like lesions in the skin very quickly, whereas L. braziliensis took six months or more for one tiny lesion to appear.

Ralph's team found a small number of the parasites that were the same as those from Oryzomys (which they named L. mexicana amazonensis). In the following years they identified a (still-increasing) number of different Leishmania species, often with specific or closely related sand fly vectors and different wild animal reservoirs. By 1979, so many different Leishmania species had been discovered - at the time, 13 from the Americas, eight of which infected humans - that the researchers proposed a new classification of them. Ralph has speculated that, "considering the remarkable number of Leishmania species that have now been recorded in the neotropics, and particularly in the Amazon region, this area might well be the birthplace of this genus".

These findings have helped to define outbreaks of the disease in the region, with considerable public health implications. People infected
with L. amazonensis may develop diffuse, anergic cutaneous leishmaniasis (affecting patients whose immune systems are incomplete, a condition incurable at the time), and those infected with L. braziliensis stand the risk of developing mucocutaneous leishmaniasis, which can be very disfiguring. Such patients require prompt and particularly intensive treatment. Moreover, people immune to one species of the parasite are usually vulnerable to others, complicating vaccine production. And Brazil's increasing urbanisation and population movement has meant that groups are often exposed to different species - and the different sand flies that transmit them - as their environment changes.

"One by one, we've shown that there is not a single parasite causing neotropical human cutaneous leishmaniasis, but six or seven," says Ralph. "These are now known, identified and recognisable such that people can tell which one a man is infected with. Every bit of knowledge gained regarding the ecology, epidemiology and distribution of the different species is of help in control of the diseases they cause."

Ralph's three years in Brazil turned into 30 and firmly established the research group that became the Wellcome Parasitology Unit. Under his directorship, the Unit made a string of important discoveries, in leishmaniasis and other parasitic diseases. In 1969, they published the first record of Chagas' disease in the Amazon region of Brazil, demonstrating that the disease could spread easily through food contaminated with faeces from species of blood-sucking triatomine bugs. In 1977 they published in 'Nature', describing the first experimental evidence that the bite of sand fly Lutzomyia longipalpis transmits Leishmaniasis chagai (the cause of American visceral leishmaniasis) to vertebrates. And in 1981, the Unit discovered a new sand fly transmitting L. braziliensis in Amazonian Brazil, which they named Lutzomyia (Psychodopygus) wellcomei (says Ralph: "We have an expression in Portuguese: pucha saco, which means that by giving it this name, we might persuade the Trust to continue our grant!").
Although the Unit closed in 1992, its legacy continues at the Instituto Evandro Chagas, now a hub for visiting scientists researching all aspects of Leishmania and other parasites, from ecology to epidemiology, immunology and the genetics of host responses to infection. It also boasts a significant resource in its collection of cryopreserved parasite material and records, amassed during the Wellcome Unit's life.

Ralph has helped to discover nearly 100 new parasite species and even had one named after him: L. (Viannia) lainsoni, discovered in 1987. His efforts have earned him a string of awards. He tells me of his pride on becoming a Fellow of the Royal Society ("the finest appreciation that anybody can give a scientist") and receiving the OBE from the Queen in the name of science ("you get footballers who are knighted, probably because they're very useful economically - a scientist is usually underpaid and usually not very much appreciated by the majority of the population"). And though he 'retired' in 1996, Ralph never got out of the lab. Fourteen years later he spends his spare time staring down a microscope, addicted to filling in a jigsaw puzzle that will never be complete: an ever-fuller picture of the parasites.

"What I love about my work is the opportunity to discover and enjoy the extraordinary beauty of structure and complicated life cycles of these little organisms. It's not work, more of a very interesting hobby. Because these parasites are rather beautiful little creatures."

More information: References


Lainson R et al. Experimental transmission of Leishmania chagasi, causative agent of neotropical visceral leishmaniasis, by the sandfly...


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