

BITTEN BY THE BUG: 50 YEARS OF NEW WORLD PARASITOLOGY

Background

Leishmaniasis is a disease caused by a single-celled (protozoan) parasite (*Leishmania*) whose life cycle is completed in different mammalian hosts, for example many wild animals, dogs and humans. It is transmitted between its two hosts by a tiny (2 to 3mm long) blood-sucking sandfly. Of the human diseases caused by a parasitic protozoan, leishmaniasis is second only to malaria in its impact on public health around the world. In cutaneous leishmaniasis, the disease causes multiple ulcerated sores on the skin, which can be very disfiguring. In visceral leishmaniasis, the parasite attacks internal organs, leading to severe anaemia, bouts of fever, swelling of the liver and spleen and, frequently, death within two years of infection if the disease is not adequately treated. There are about 1.5 million new cases of leishmaniasis and 60 000 deaths from the disease every year.

There has been disproportionately little research on leishmaniasis given the scale of suffering and the economic impact it causes in many low-income countries of the world. For many years, the Wellcome Trust has supported a coordinated group of scientists working on leishmaniasis in Brazil. Ralph Lainson has spent his career at the centre of these efforts and has received 42 years of Trust funding for his lead in the field.

Professor Lainson trained as an entomologist and parasitologist and then worked as a junior lecturer at the London School of Hygiene and Tropical Medicine. In 1964 he was funded by the Trust to carry out a field study on the ecology and epidemiology of leishmaniasis in Amazonian Brazil. His original grant and field trip were for three years; he has ended up staying for over 40 years.

Advance

In 1965, Professor Lainson established the Wellcome Unit of Parasitology at the Instituto Evandro Chagas, Belém, Brazil and he directed it until his official retirement in 1992. Over the years the Unit published a large volume of research on the ecology and epidemiology of leishmaniasis and other parasitic diseases and hosted many visiting scientists. In addition to their work on leishmaniasis, the Unit published on the first record of autochthonous cases of Chagas' Disease in the Amazon Region, suggested that transmission was by the oral route following contamination of foodstuffs by the faeces of infected sylvatic species of triatomid bugs, and demonstrated the ease with which oral transmission can be achieved in laboratory animals fed with a variety of kitchen foods contaminated by *Trypanosoma cruzi*.

A study by Professor Lainson and colleagues in *Nature*, in 1977, described the first experimental transmission of the parasite causing American visceral leishmaniasis to a vertebrate by the bite of the sandfly *Lutzomyia longipalpis* – long suspected to be the vector of the disease. In 1981, the Unit described an important new sandfly vector of Amazonian cutaneous leishmaniasis and named it *Lutzomyia (Psychodopygus) wellcomei*, in honour of Henry Wellcome. They also discovered and named six new species of *Leishmania*, five of which are known to cause human cutaneous leishmaniasis, and identified wild mammalian hosts and sandfly vectors of these parasites.



A common site for a focus of Amazonian visceral leishmaniasis: a disorganised shanty town with a high density of the sandfly vector and an abundance of dogs.

With each of these discoveries, Professor Lainson and his colleagues pieced together an understanding of the many host–vector–parasite complexes involved in the ecology and epidemiology of leishmaniasis in Brazil. In 1993 and 1994, when there was a marked resurgence of visceral and cutaneous leishmaniasis in Brazil, Professor Lainson's work helped define outbreaks of the visceral disease in the Amazon Region. These factors included an increased urbanisation and movement of people to areas where they were exposed to different species of *Leishmania* and their vectors.

Professor Lainson has also worked more broadly in the field of parasitology. He started his research career with an important study on the development of resistant cystic stages of *Toxoplasma*, which are now known to serve as a common, alternative mode of transmission of the parasite to man following his ingestion of raw or undercooked meat. Together with Dr Irène Landau and Jeffrey Shaw, he indicated the presence of a new family of malarial parasites, the Garniidae, in lizards.

How it's making a difference

Professor Lainson's studies on neotropical *Leishmania* species, their natural hosts, and the sandfly vectors have helped to define the nature and extent of this disease and the threat it poses to public health. His work has revealed a highly complex group of interactions between parasite and hosts involving numerous species of the parasite and its vector. His colleagues and he have also identified four distinct clinical diseases in humans caused by infection with the protozoan. This research has firmly established the ecology, epidemiology and taxonomy of neotropical *Leishmania* species, it has contributed to the control of the disease in humans and has also been a useful model for the study of other parasitic protozoa.

Professor Lainson's work has shown policy makers that as a result of changing human demography people who were naturally immunised against one species of *Leishmania* are then at risk. A clear implication of their work for public health policy makers is that disruption of the parasite–host relationships in leishmaniasis and other diseases can have huge impacts on human health.

The Unit in Belém created a significant resource with the collection, over many years, of cryo-preserved parasite material and associated records. It was also a centre for visiting scientists researching all aspects of leishmaniasis from the ecology and epidemiology of the disease to the immunology and genetics of host responses to infection.

Next steps

The leishmaniasis programme at the Instituto Evandro Chagas, Belém, is now run by Brazilian scientists Professor Fernando Silveira and Dr Adelson Souza. Professor Lainson is currently the recipient of a Trust project grant, and is collaborating with scientists at the Institute to continue his work in parasitology. He has maintained his interest in leishmaniasis and has broadened his research to include other protozoal parasites of the Amazonian fauna that he has encountered over the years. In this work Professor Lainson is following the advice of his mentor, the late Professor PCC Garnham FRS, who once told him: "You can only regard yourself as a true parasitologist when you have some knowledge of parasites within all the different parasitic groups."

References

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Table of achievements

Inputs

- Wellcome Trust grant for three-year field study (1964)
- Wellcome Trust Parasitology Unit opened (1965)
- Professor Lainson's research and the Leishmaniasis Unit at Belém receive continuous funding from the Wellcome Trust from 1964 until Lainson's retirement in 1992
- Wellcome Trust research grants (2002, 2005)

Key activities/outputs

- Discovers the cause of *Toxoplasma* transmission from the ingestion of infected meat
- Defines many host–vector–parasite complexes around Brazil
- First experimental proof that sandflies are the vector of visceral *Leishmaniasis*
- Defines 13 species and many subspecies of *Leishmaniasis*
- Discover species of sandfly vector including *Lutzomyia (Psychodopygus) wellcomei* and identifies vertebrate hosts of the parasite

Outcomes

- Ralph Lainson and his lifelong collaborator Jeffrey Shaw are leading authorities on New World Leishmaniasis – a collaboration that has firmly established the science of Leishmaniasis
- Director of the Wellcome Unit of Parasitology, Belém, Brazil, from its opening in 1965 until its closure in 1992
- Received many awards including the Royal Society's Chalmer's Medal and made an OBE for his services to parasitology
- Made fellow and honorary fellow at the Royal Society, Third World Academy of Sciences, London School of Hygiene and Tropical Medicine, British Society of Parasitology, Royal Society of Tropical Medicine and Hygiene, Society of Protozoologists

Timeline of Professor Ralph Lainson

