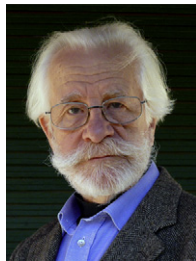




In memoriam

Robert Killick-Kendrick (1929–2011)



Much has been said about the brilliant scientific career of Robert Killick-Kendrick since he passed away. Many researchers have expressed their admiration and respect for this learned specialist and his humanistic qualities. We knew him well and confirm and illustrate this through the following brief review of some of his research in which we were also involved, especially on *Plasmodium* (with Irène Landau) and *Leishmania* (with Jean-Antoine Rioux).

Plasmodium research (I.L.)

In 1963, Bob became a member of the service headed by Professor P.C.C. Garnham at the London School of Hygiene and Tropical Medicine. At the time, this laboratory was teaming with young researchers, almost all of whom subsequently pursued a successful scientific career: J. Baker, R. Bray, R. Lainson, and J. Shaw. L. Canning of Imperial College and M. Wery of the School of Tropical Medicine in Antwerp could also be added to this list. Visitors from all parts of the world went there for training or to discuss their research. The activity was lively, rich, diverse and efficient: researchers contacted their colleagues as soon as they discovered a new element or when they needed technical assistance to perform a procedure requiring careful handling. Bob, for all of these reasons, embodied the soul of this small group. He was always available and fascinated by extraordinary and novel events, and readily provided useful information or help. The discussions often continued into the evening in the nearby pubs.

At that time, “biodiversity” was not yet a common buzzword, and was even looked down upon when used liberally by researchers lacking credits. Here it was the founding principle driving Garnham’s laboratory, where not only human and primate parasites were studied and taught from all angles, but also parasites of other mammals, birds, reptiles and insects. The approach was systematic, biological, immunological and epidemiological. Studies on parasites were facilitated by the abundance of available equipment and material (blood smears, sections, tissue blocks)—resources collected worldwide for examination by Garnham and his team.

Malaria was a key topic of research: Bob was actively involved in all experiments, especially those conducted by his mentor

Garnham on primate *Plasmodium*. Some of his personal contributions were:

- 1 Identification and description of the cycle of two rodent *Plasmodium* species (1966): *Plasmodium yoelii yoelii* and *P. chabaudi chabaudi*. These species are now standard experimental models used in many laboratories.
- 2 Description of *Plasmodium yoelii nigeriensis* (1973) and *P. vinckei brucechwatti* (1975) in *Thamnomys rutilans* in Nigeria.
- 3 The first detection (1967) of chloroquine resistance in *P. yoelii* (with D. Warhurst)
- 4 Production of *P. yoelii* gametocytes by pre-erythrocytic schizonts (with M. Warren, 1968).
- 5 Description of two new *Plasmodium* species in Anomaluridae in Côte d’Ivoire (1973).
- 6 The chapter “Taxonomy, Zoogeography and Evolution” in the still highly relevant book “Rodent Malaria” (co-edited with W. Peters, 1978).
- 7 Member of the Borneo Mission on “Research on Orangutan *Plasmodium*” led by Garnham and Peters: discovery and description of the new species *P. sylvaticum* and achievement of the experimental cycle.
- 8 Discovery, in *Plasmodium cynomolgi*, of a quiescent form, i.e. “hypnozoite”, by a team of eight researchers, including W.A. Krotoski, B. Bray and P.C. Garnham. This form was later also observed in *P. vivax* and *P. ovale* (1982). This major discovery clarified the origin of relapses in these two species. This latency phase, which was met with the disbelief of distinguished malariologists at the time, is now widely recognized.

In conclusion, Robert Killick-Kendrick was definitely one of the major players during this pivotal period for malariology—that of the epidemiology and fundamental biology of *Plasmodium*.

Leishmania research (J.A.R.)

We should now discuss a few of the highlights of Bob’s second life as a “leishmaniac”—an activity carried out, at the request of international organizations, in both developed and developing countries worldwide.

However, to limit the length of this discussion, we will simply focus on a few field studies conducted in a *Leishmania* outbreak area in the Cévennes region of Mediterranean France. In this way, we hope to illustrate the creative environment that prevailed for several years in our close and friendly collaboration.

Our first contacts with Robert Killick-Kendrick were in the 1960s. At that time, a major field survey was ending on the epidemiology of leishmaniasis in the South of France, commissioned by the French *Institut National de la Santé et de la Recherche Médicale* and conducted by the research team *Ecologie parasitaire* (CNRS

- *Faculté de Médecine*, Montpellier, France). In 1969, the results were published in the form of a *Monographie INSERM*, concerning which Professor P.C. Garnham, who was deeply attached to France, had published a highly complementary review. He then wished to visit the different studied sites. We were very flattered by his interest and decided to set up a team of parasitologists to accompany him on this visit, this team included Irène Landau, Alain Chabaud and Jean-Antoine Rioux. Of course, Robert Killick-Kendrick was also present. This tour took us as far as the Banyuls Oceanic Observatory (Pyrénées-Orientales region) where, right after the war, Garnham had ended a trip across France. In Banyuls, Prof. Garnham advised Bob to link up with the Montpellier group. This “suggestion” was the starting point for a productive and successful collaboration, and Garnham convinced several other British researchers to accompany him in the “*Midi méditerranéen*”.

The quality of this collaboration was confirmed a few years later (1974) during a conference on the Ecology of Leishmaniasis, organized by the *Université de Montpellier*, with the collaboration of CNRS. An impressive number of foreign specialists attended this conference, which was presided over by Garnham: N. Ansari, R.W. Ashford, A.E. Beliaev, R. Bray, M.L. Chance, J. Collado, A. Corradetti, P. De Raadt, J.M. Jadin, E. Jadavian, R. Lainson, D. Le Ray, D.J. Lewis, W.H. Lumsden, G. Lupascu, D.H. Molineux, A. Nadim, W. Peters, V.M. Safyanova, V.P. Sergiev, T. Simic, B.A. Southgate, O. Theodor, S. Yasarol, etc., and last-but-not-least, the Conference Secretary Bob Killick-Kendrick. Garnham’s opening speech was extremely innovative and modern for the time: “Global ecology of the leishmaniasis: introductory remarks”. This great thinker considered that “parasite ecology” should become a heuristic discipline—which it did, with “leishmaniasis ecology” becoming one of the major topics covered by several international teams.

But let us get back to the late lamented Bob. Granted, our friend loved “lab bench work”. He was highly skilled and technically efficient. However, these qualities were chiefly brandished *in natura*, when working on natural infection foci. In order to solve “scientific puzzles”, he would readily spend the night monitoring traps or dissecting captured insects. At this time, he was often involved in heated discussions on leishmaniasis pathogen complexes. In these cases he drew from his core disciplines, i.e. systematics, ethology, chorology and parasite-host development. Yes, Bob was an authentic “ecoepidemiologist”!

Our collaboration actually began in the lower Cévennes region of France, between Ganges and Le Vigan. In this area, several visceral leishmaniasis cases had been detected a few years previously. The town of Roquedur, located midway up the slope, was chosen as the base point for our team. A laboratory was set up in a traditional house, and included light traps, sticky traps, microscopes, dissection instruments, culture incubators, leishmaniasis test dogs. The “ecological study” was ready to start.

Several topics were investigated, but the four most significant were:

- 1 Experimental *L. infantum* infection of dogs and the vector *P. ariasi* was the first study. One trial was focused on two naive pups which were placed in contact (under mosquito netting) with pre-infected sandflies. After a few weeks, one died as a result of contracting an acute disseminated form of this disease. The second pup was clinically asymptomatic for over 1 year and then presented with anal secretion of red blood, a sign of a chronic form, which was successfully managed by antimonial treatment. This was clear evidence of leishmaniasis transmission to the dog via the *P. ariasi* vector.
- 2 The second topic concerned sandfly flight ranges. This research, like the previous, had major subsequent epidemiological impacts.

Until quite recently, apart from a few Russian studies on *P. papatasi*, it was generally considered that sandfly movements simply

involved jumps of a few centimetres. These vectors, which by nature do not move far from their home sites, could therefore not disseminate parasites over long distances—this could only be done via the canine reservoir.

However, in a study carried out a few years early in the Montagne Noire region (La Borie-Nouvelle), nocturnal flights of *P. ariasi* ♀ had been noted—on some hot and humid summer nights, abundant numbers these insects were observed flying over the holm oak forest.

At Roquedur, this phenomenon was confirmed by the findings of a capture–recapture study. This required a team of several dozens of people. Bob had convinced several English researchers to fulfil this task. In addition, thanks to them, we had access to fluorescent markers that enabled detection of tagged individuals. Without getting into a detailed description of the very complicated capture–tagging–recapture operation, we noted that some of the *P. ariasi* sandflies released in the vicinity of Roquedur (Hérault River valley, 250 m elevation) had travelled almost 5 km. In 3 days, several females (some blood gorged) had managed to get through the mountain pass located at 600 m elevation, and had then moved down the opposite slope (Arre Valley, 300 m elevation). This was quite an informative surprise: human (or canine) contaminations (but no leishmaniasis-infected dogs had been detected in the surrounding area) could be explained by the movement patterns of the infected vectors outside their home range.

Studies on *L. infantum* development in *P. ariasi* was a logical follow-up to the experimental vector infection study (see above).

3. Based on studies involving the infection of *Lutzomyia longipalpis* by *L. amazonensis*, which were conducted in Brazil with the team of Lainson (Bélem), Bob focused on cyclical promastigote transformations during their intestinal migration in the Cévennes vector *P. ariasi*. Spectacular results were obtained—the forms observed in Brazil were found in *L. infantum*, i.e. promastigotes in iterative division (middle intestine), infectious metapromastigotes (esophagous, oviduct), micro-, epi- and para-mastigote stages, free or fixed on digestive walls (sphincter, esophagous, oviduct). In addition, in some individuals, examination of the anterior intestine revealed the presence of hemidesmosomes, the puzzling structures that had been described in *L. longipalpis*.
4. In 1984, another conference was held in Montpellier, with the groundbreaking title: “Leishmania Taxonomy and Phylogeny. Ecoepidemiological applications”. W. Peters was the President and, again, Bob was the Conference Secretary. In 1987, he and Peters published a top-notch collaborative book, entitled “The Leishmaniasis in Biology and Medicine”.

Finally, it would be inappropriate to end this *in memoriam* without paying tribute to Mireille Killick-Kendrick. She was always involved in her husband’s research, even as early as the first studies in the Cévennes. She provided high technical and communications skills. In the laboratories of Imperial College (Ascot, G.B.) and Sumène (Fr.), she took care of establishing and maintaining many sandfly colonies. She recently participated in developing a pyrethroid-impregnated collar, which has been highly successful in the prevention of canine leishmaniasis.

Once more, we reiterate our steadfast attachment to Bob. By this tribute, we join all of the many colleagues and followers of Bob who expressed their admiration and recognition.

Jean-Antoine Rioux
Irène Landau