

# The Fever Trail: In Search of the Cure for Malaria

by Mark Honigsbaum

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At a time when the genomes of both *Plasmodium falciparum* and *Anopheles gambiae* have been deciphered, it is remarkable that the treatment of severe malaria still depends upon an extract of the bark of a South American tree first identified by Europeans as a cure for malaria nearly 400 years ago. The 'discovery' of quinine by Spanish colonialists in the first half of the seventeenth century and its subsequent introduction into Europe has been described several times before. In *The Fever Trail*, Honigsbaum passes over this part of the story fairly briskly in this very readable book that concentrates on the efforts of the European colonial powers to establish cinchona plantations in their expanding empires in South East Asia. This was considered of vital importance because of over-exploitation of natural stands of cinchona in South America, civil unrest among many of the newly independent South American republics, an increasing appreciation of the public health burden and economic costs of malaria in India as well as the high mortality from malaria among expatriates trading in parts of South East Asia and West Africa. The story of the establishment of cinchona trees outside their natural habitat is an exciting one involving enormous courage and fortitude from the cinchona tree hunters but also greed, deceit, official insensitivity and bungling and some good and bad science. Honigsbaum tells the story of the remarkable exploits of Charles-Marie de La Condamine, Richard Spruce, Charles Ledger, Sir Clements Markham and others especially well, perhaps in part because he has visited several of the sites that played important roles in their expeditions. His own experiences are never allowed to intrude on the main story but they must have given him an enhanced appreciation of what these explorers achieved.

The task that faced the cinchona tree hunters was a formidable one. By the be-

ginning of the nineteenth century, it was known that cinchona trees could be found, in relatively small numbers, over a wide area on the western side of the Andes and that their taxonomy was complex. Only a few species had bark with a high yield of quinine, but these were not easy to identify, as trees of the same species varied morphologically in different ecological conditions and hybrids were common. Furthermore, cinchona trees fruit irregularly so that even when suitable trees were found, it was at times necessary to watch them for months, or even years, before seeds and seedlings could be obtained. These then faced a perilous journey down steep trails and rivers to the coast followed by a long sea passage. Not surprisingly, early attempts at exportation failed when seedlings were lost to natural disasters or to deliberate damage by local collectors who, justifiably, feared losing their livelihood. The problem of shipment was overcome only with the development by Nathaniel Ward of sealed boxes with glass walls and tops that allowed seedlings to survive adverse conditions over periods of several months.

The first seedlings established successfully in Batavia were collected by Justus Hasskarl. Unfortunately, as a result of either bad luck or bad science, these trees (*Cinchona pahudiana*) were poor quinine producers and were subsequently replaced by *C. ledgeri*, which produced bark with a much higher quinine content. These trees were grown from seeds collected in Bolivia by Manuel Mamani, a Bolivian Indian, for Ledger, an English trader and explorer who had spent most of his life in South America. Ledger's brother had tried to sell his seeds to the authorities in London but had been rebuffed. Seeds of another species, *C. succirubra*, collected by Richard Spruce, a professional plant collector and colleague of Alfred Russell Wallace, were established successfully in the Nilgiri Hills in India. These trees were also poor quinine producers but their bark contained other effective anti-malarial alkaloids. With the exception of Markham, who became a distinguished President of the Royal Geographical Society, the contributions of the cinchona tree hunters received little official recognition during their life-

times. Spruce and Ledger died in relative poverty and Mamani died from a beating he received from the Bolivian police when they tried, unsuccessfully, to make him disclose for whom he was collecting cinchona seeds.

In the latter part of the book, Honigsbaum describes briefly the discovery of the malaria parasite and its vector and the development of the synthetic anti-malarials such as chloroquine and the extraction by Chinese scientists of highly effective anti-malarials from the plant *Artemisia annua*. It would be interesting to know more about how this was accomplished but this would require access to Chinese sources. The last chapter of the book describes the quest for a malaria vaccine with an emphasis on the work of the Colombian scientist Manuel Patarroyo, thus providing a link back to South America. However, this chapter seems out of place in the book.

As the international community begins once again to grapple with the problem of malaria in poor countries, there are many relevant lessons to be learnt from the quinine story and Honigsbaum highlights these well. Quinine was initially very expensive, as may be the case for some of the new antimalarials under development, and this led Cardinal Lugo to introduce a tiered pricing system for Jesuit bark in Rome in the mid-seventeenth century through

which the rich subsidized the poor. The transfer of cinchona seedlings from South America to South East Asia by the colonial powers, often by underhanded means, can be viewed as a typical example of exploitation of the resources of poor developing countries by the rich. Markham, however, did not see it this way. His objective, which seemed to be genuine, was to make an effective anti-malarial available in every small shop in India at a price (one farthing) that the poor could afford, a very contemporary objective. For a while, he succeeded only to run into the problem of cartels (the Kina Bureaus in Amsterdam) and various other restrictive practices.

*The Fever Trail* is very well written, informative and entertaining and should appeal to a wide audience interested in the history of medicine, exploration or international health.

