

## Book Reviews

MALARIA: GENETIC AND EVOLUTIONARY ASPECTS. By Krishna R. Dronamraju and Paolo Arese. New York: Springer. 2006. 190 pp. ISBN 0-387-28294-7. \$129.00 (hardcover).

In his book *The Red Queen*, Matt Ridley ponders the fact that host and parasite are locked in a close evolutionary embrace. This embrace is the essence of this magnificent book coedited by Krishna Dronamraju and Paolo Arese. *Malaria* focuses on genetic and evolutionary insights into a parasite blamed for the death of a child every 30 s worldwide.

The link between thalassemia and malaria was noticed decades ago. The book opens with Dronamraju's introduction to J. B. S. Haldane's malaria hypothesis and provides an abundance of geographical and epidemiological evidence supporting the idea that malaria shaped the frequency and distribution of several hereditary hemoglobinopathies. This theory raises fascinating questions about the consequences of malaria eradication; chiefly, how would eradication impact the distribution of the hemoglobinopathy genes? In this context, the hypothesis put forward by Robin Bannerman that the fluctuation of environmental factors around the world can impact microcytic foci and lead, over centuries, to their appearance or regression is thought provoking.

The mechanisms responsible for the less severe malaria symptoms exhibited in heterozygotes are incompletely understood and controversial. A chapter by Arese et al. critically reviews studies suggesting that red blood cells affected by certain hemoglobinopathies are not favorable for parasite development as well as reports arguing that this proposed mechanism does not satisfactorily address malaria resistance in certain people. The authors reveal the existence of methodological bias at several levels and propose an alternative mechanism to which the enhanced phagocytosis of ring forms developing inside mutant red blood cells is fundamental. Pathogenesis, in their opinion, is best explained by the increased production of reactive oxygen species, which they view as the common denominator among all hemoglobinopathies, genetic and clinical differences notwithstanding. Heterozygote advantage is not limited to malaria. Carriers of the cystic fibrosis trait have a lower incidence of tuberculosis. The frequency of the CCR5-Δ32 mutation, which confers resistance to HIV-1 infection, is thought to have increased under selective pressure exerted by an unknown infectious disease, bubonic plague and smallpox being the most likely candidates. Insights into the molecular mechanisms by which hemoglobinopathies confer protection against malaria will therefore improve our general perspective on host-parasite interaction.

*Plasmodium falciparum* genetic polymorphisms have proved a powerful tool to examine parasite population structure and history. Rich and Ayala review evidence for and against their malaria's Eve hypothesis, which posits that all existing parasite populations derive from a recent (several thousand years) common ancestral strain. Their data and arguments are fascinating and controversial at the same time. While malaria's Eve hypothesis is backed by some authors, such as Conway, who provide supportive evidence emerging from mito-

chondrial genome analyses, other groups favor the idea that the parasite is much older and much more diverse. Phylogenetic trees based on the cytochrome *b* and circumsporozoite proteins show that the four human parasites are very remotely related to each other and that *P. falciparum* is more closely related to the chimpanzee parasite *P. reichenowi* than to any other *Plasmodium* species. Based on the absence of differences in the *csp* gene between *P. malariae* and *P. brasilianum* and between *P. vivax* and *P. simium*, it was concluded that lateral transfer between humans and monkeys occurred in recent times. Rich and Ayala present captivating arguments to support the lateral transfer of parasites between humans and monkeys; even more engaging are the debates concerning its direction.

The emergence of drug-resistant parasite strains is one of the causes for the recent increase in malaria mortality and morbidity, and host and genetic factors involved in malaria resistance constitute a cardinal theme of the book. A chapter by Mehlotra and Zimmerman examines human enzymes involved in drug metabolism, a topic so far underexplored. Their analysis implicates human metabolic enzyme polymorphisms in the selection for drug-resistant strains and in the variability noticed in antimalarial drug effectiveness. The authors underscore the urgent need to develop an integrative approach for assessing treatment response. Such an approach would take into consideration not only the drug sensitivity of a parasite strain but also the variability in host metabolic drug response. Sharma underscores the importance of vector genetics in malaria control in India. His chapter illustrates how genetics solved one of the paradoxes related to the differential vector potential of *Anopheles culicifacies*, the major vector of malaria in India, in regions that are similar geographically and improved our understanding of parasite transmission dynamics.

Two classic papers authored by Haldane in 1949 conclude the book. "The Rate of Mutations of Human Genes" emphasizes the importance of human gene mutation rates for understanding evolutionary theory and for solving practical problems. "Disease and Evolution," the publication that introduced the malaria hypothesis into the scientific literature, examines the evolutionary significance of the struggle against infectious diseases. This article suggests that, from an evolutionary perspective, the struggle against infections differs significantly from the struggle against other agents such as natural forces or predators. Several intriguing questions emerge from this section, such as whether disease serves a purpose or is a disadvantage in the interaction between species, and what advantages genetic and biochemical diversity impart to a species.

*Malaria: Genetic and Evolutionary Aspects* will benefit a broad range of medical, scientific, and public health professionals. Besides strengthening our understanding of the evolutionary origins of malaria, the text opens new perspectives into infectious diseases. Understanding the evolutionary origin of pathogens has important implications for the prevention and treatment of infectious diseases, vaccine design, and clarification of the relationship between hosts and pathogens over time.

The evolutionary biology of microorganisms lies at the core of our ability to understand, prevent, and treat infectious diseases. Some of the most urgent topics in infectious disease research are the emergence of new diseases and the reemergence of old ones; the appearance of drug-resistant microorganisms; the involvement of previously known microorganisms in the pathogenesis of new diseases; and the ability of some pathogens to cross species barriers. An evolutionary perspective is fundamental to comprehending how virulence, drug resistance, and host–pathogen relationships have evolved through history. Ultimately, this

approach will unveil the complex and dynamic interaction between microorganisms, host, and environment.

RICHARD A. STEIN  
*New York University School of Medicine,  
New York, New York*

---

DOI 10.1002/ajpa.20591  
Published online in Wiley InterScience  
([www.interscience.wiley.com](http://www.interscience.wiley.com)).