

UNIVERSITY OF LONDON
HEATH CLARK LECTURES 1953
delivered at
The London School of Hygiene and Tropical Medicine

Man's Mastery of Malaria

By

W

PAUL F. RUSSELL, M.D., M.P.H.

DIVISION OF MEDICINE AND PUBLIC HEALTH
ROCKEFELLER FOUNDATION



GEOFFREY CUMBERLEGE
OXFORD UNIVERSITY PRESS

London New York Toronto

1955

Oxford University Press, Amen House, London E.C.4

GLASGOW NEW YORK TORONTO MELBOURNE WELLINGTON

BOMBAY CALCUTTA MADRAS KARACHI CAPE TOWN IBADAN

Geoffrey Cumberlege, Publisher to the University

PRINTED IN GREAT BRITAIN

MAN'S MASTERY OF
MALARIA



Ague and Fever, by T. Rowlandson, London, 1792

From Holländer, 1905, Die Karikatur und Satire in der Medizin, published by F. Enke, Stuttgart

Respectfully dedicated to

JOHN DAVISON ROCKEFELLER

(1839-1937)

to his son

JOHN DAVISON ROCKEFELLER, JUNIOR

and to his grandson

JOHN DAVISON ROCKEFELLER, 3RD

who through their benefactions and

by their continued interest in the

well-being of mankind throughout the world

have assisted thousands of communities

to control disease-carrying mosquitoes

and to master

preventable afflictions

PREFACE

THE Heath-Clark Bequest was given in 1929 to make possible an annual series of lectures under the auspices of the University of London. It was stipulated in the Deed Trust that 'the general scope of the lectures to be given shall include the educational, cultural and humanistic aspects (as opposed to technical and manipulative training) of the History, Development and Progress of Preventive Medicine and Tropical Hygiene and their sanitary and social evolution both in temperate and tropical climates'. When the invitation came to me, I naturally thought first of the history of malaria because the disease has been of prime interest to me for many years. But I hesitated because the subject has already been so thoroughly publicized and I feared that what I might say would seem trite. Then I realized that the developments in malaria control in recent years have been so tremendous that it would be difficult to be dull in the telling of the story of how man has at last mastered malaria.

I hope that the title of these lectures is not misleading. One should remember that the verb 'to master' means 'to overcome, defeat, reduce to subjection'. So, to master malaria does not necessarily mean to eradicate it; nor should there be a connotation of freedom from further responsibility. On the contrary, malaria certainly remains for many people a harmful reality; it still does immense economic, social, and physical damage. Exactly how much malaria remains no one knows because the data reported are so inadequate, but on the basis of what I have seen and read, it seems to me safe to estimate that among the 2,500 millions of people in the world today, more than half live in potentially or actually malarious communities. While probably no fewer than 160 millions today are enjoying the protection of modern malaria control, an amazing achievement, yet it seems a fair guess that in 1954 some 250 million persons will suffer attacks of malaria and that very likely $2\frac{1}{2}$ million will die from its effects.

Malaria will continue to constitute a problem for health officials of international agencies and of certain countries for some time to come. No, the verb 'to master' does not imply an end to the matter: rather it suggests that having prevailed over an opposing force one has assumed moral responsibility for keeping it under control.

The point is that malaria, after centuries of effort, is now universally controllable. Techniques are available and for most communities, even those least developed, the cost of malaria control is not beyond local means. In several instances, countries once highly malarious have succeeded in stopping the transmission of this disease during the past decade. Malaria is retreating with spectacular acceleration. Man is indeed master at last. But can he overcome stubborn terminal opposition? Can he consolidate and maintain his mastery? I consider it entirely possible but not easy, especially in view of the increasing likelihood that the anopheles mosquitoes that transmit malaria will join the growing band of insects that are able to resist modern residual insecticides such as DDT.

While keeping in mind the realities one can nevertheless be confident that malaria is well on its way towards oblivion. Already as a malariologist, I feel premonitory twinges of lonesomeness, and in my own organization I am now a sort of 'last survivor'. So perhaps it is fitting that I should take this backward glance at the fascinating pages of malaria history.

I believe in the importance of historical studies. As Oliver Wendell Holmes once said: 'The debris of broken systems and exploded dogmas form a great mound, a Monte Testaccio of the shards and remnants of old vessels which once held human beliefs. If you take the trouble to climb to the top of it, you will widen your horizon, and in these days of specialized knowledge your horizon is not likely to be any too wide.'

But I do not present these lectures as more than a retrospect of the highway that has led, to quote the editor of *The Lancet*, 'from mystery to mastery'. Some idea of the fact that the following story is indeed only a brief survey,

not the whole account, may be had by consulting the first Index-Catalogue of the Library of the Surgeon General's Office, U.S. Army, dated 1883. Here, under the heading 'Fever—Malarial' in volume iv, were listed over 700 books and many hundreds of articles in journals, mostly nineteenth century. Add to these sources the hundreds of books and papers listed under 'Malaria and Malarial Diseases' in volume vii and one sees an astounding pile of untapped material already accumulated seventy years ago. Since then the literature has increased enormously. I fully realize that I have not been able to go far beyond the bare outlines of the subject.

Had I set out to write a definitive history of malaria, I would have ended it at or some time before the Second World War. It is, of course, too soon to evaluate with confidence the developments of the past fifteen years. But in this retrospect it seemed desirable to embrace the full length of the road, including that exciting part most recently travelled. I would be surprised as we go forward, if perspective did not indicate changed appearances in this area closest to us and reveal defects of interpretation and proportion in the following story.

But, limited though they are, these studies have repaid me for the effort. As the great medical historian Baas said so well, history offers to him who studies it a 'measure for the just and well-founded criticism of the doings of his own time, places in his hand the thread by which he unites past conditions and efforts with those of the present, and sets before him the mirror in which he may observe and compare the past and present, in order to draw therefrom well-grounded conclusions for the future'.

ACKNOWLEDGEMENTS

THE author is grateful to Dr. Andrew J. Warren, Director of the Division of Medicine and Public Health, Rockefeller Foundation, for permission to prepare and publish these lectures; to other colleagues in the Foundation—Drs. H. H. Smith, John Maier, and L. W. Hackett for helpful criticisms; to Sir Gordon Covell for inspiration over many years and for some difficult-to-find data; to General Vaucel and the Pasteur Institute of Paris for a photograph of Laveran's drawings of plasmodia; to Dr. E. J. Pampana of the Malaria Section of the World Health Organization for making available original documents and photographs, and for helpful suggestions; to the New York Public Library for permission to use Dr. Martin's letter; to Professor George Macdonald, Director of the Ross Institute, and to Mr. C. C. Barnard, Archivist and Librarian of the London School of Hygiene and Tropical Medicine, for access to original Ross letters and notebooks and for permission to publish one of the letters; to Dr. E. Ashworth Underwood, Director of the Wellcome Historical Medical Museum, and to Mr. W. J. Bishop and Mr. F. N. L. Poynter, Librarians at the Wellcome Historical Medical Library, for help in obtaining obscure references and rare photographs; to Dr. Emmet F. Horine for permission to use his copyrighted photograph of Daniel Drake; to the Maryland Historical Society for permission to consult the *Baltimore Observer and Repertory*; to the Armed Forces Library in Washington, and the Medical Library in Zürich, for facilities granted; to Dr. F. L. Soper, Director P.A.S.B./W.H.O. Office, and to the Secretariat of I.I.A.A., for information about their respective organizations; to Dr. J. A. Logan for an illustration from Sardinia; to Professors E. C. Faust, N. H. Swellengrebel, E. Mosna, G. Raffaele, E. G. Nauck, and C. Toumanoff, Drs. J. M. Andrews and F. C. Bishopp, and the Librarians of Columbia University, the Boston Athenaeum, the Rockefeller Foundation, the New York Academy of Medicine, and W.H.O. for data kindly supplied; to Miss

Amy Melville Anderson for secretarial help, especially with the indexes; and finally to Sir Roderic Hill, Vice-Chancellor, and to Dr. James Henderson, Academic Registrar, both of the University of London, and to Dr. Andrew Topping, Dean of the London School of Hygiene and Tropical Medicine, not only for making it possible for me to present and publish these lectures but also for their generous hospitality and consideration at the time the lectures were given.

PAUL F. RUSSELL
M.D., M.P.H.

GENEVA

July 1954

ILLUSTRATIONS

Ague and Fever (in colour)	<i>Frontispiece</i>
1. Daniel Drake	} <i>Between pages</i> <i>16 and 17</i>
2. Frerichs's pigment	
3. La Malaria	} <i>Between pages</i> <i>32 and 33</i>
4. Plasmodia as drawn by Laveran	
5. Jones's observation	
6. Lancisi's <i>De Noxiis Paludum</i>	
7. Pages from letter to Manson from Ross	<i>Between pages</i> <i>64 and 65</i>
8. Life-cycle of malaria parasite	} <i>Between pages</i> <i>80 and 81</i>
9. Coin commemorating recovery of Charles V	
10. Bloodletting	} <i>Between pages</i> <i>112 and 113</i>
11. <i>Cinchona succirubra</i>	
12. Cinchona bark	} <i>Between pages</i> <i>128 and 129</i>
13. Torti's <i>Therapeutice Specialis</i>	
14. Page from London Pharmacopoeia	} <i>Between pages</i> <i>160 and 161</i>
15. Coin commemorating Empedocles	
16. Title-page and frontispiece from Bauderon	<i>Between pages</i> <i>176 and 177</i>
17. Larviciding in Sardinia	} <i>Between pages</i> <i>208 and 209</i>
18. Spraying DDT in Taiwan	
19. Memorial to Darling and colleagues	} <i>Between pages</i> <i>224 and 225</i>
20. W.H.O./U.N.I.C.E.F. Malaria Control Squad in India	

CONTENTS

PREFACE	page vii
ACKNOWLEDGEMENTS	xi
LIST OF ILLUSTRATIONS	xv

SECTION I

THE UNFOLDING OF MALARIA AETIOLOGY

1. SPECULATIONS	2
2. THE PARASITE	30
3. THE MOSQUITO	37
4. HIDDEN PLASMODIA	67

SECTION II

THE UNRAVELLING OF MALARIA THERAPY

5. PRE-CINCHONA PERIOD	76
6. THE QUININE PERIOD	90
7. THE MODERN PERIOD	107

SECTION III

THE DEVELOPMENT OF MALARIA PROPHYLAXIS

8. DRAINAGE	125
9. MALARIA PREVENTION BY DRUGS	132
10. LARVICIDES	137
11. PROPHYLAXIS AGAINST ADULT MOSQUITOES	147
12. THE DDT ERA	160
13. MALARIA RECESSION	173
14. INSECT RESISTANCE TO TOXICANTS	187

SECTION IV

SOME INTERNATIONAL ASPECTS OF MALARIA

15. MULTILATERAL EFFORTS	195
--------------------------	-----

16. BILATERAL GOVERNMENTAL AGENCIES	<i>page</i> 219
17. MALARIA ACTIVITIES OF THE ROCKEFELLER FOUNDATION	229

SECTION V

MALARIA AND SOCIETY

18. MALARIA PROPHYLAXIS AND POPULATION PRESSURE	243
---	-----

REFERENCES	259
------------	-----

INDEXES

PERSONS	287
PLACES	299
GENERAL	303

SECTION I

THE UNFOLDING OF MALARIA AETIOLOGY

THIS is not a history of malaria. Here is simply a retrospect, a looking back at some facets, individuals, and ideas prominent in the long unfolding or opening up of what had been hidden from view. Somewhere it is written that the best history resembles Rembrandt's paintings: certain selected aspects vivid, the rest in shadow or unseen. One agrees and has tried to spot-light rather than to flood-light. So, too, the approach is optimistic and not in the spirit of Hegel's cynical remark that, 'The one thing one learns from history is that nobody ever learns anything from history.' It is true that some lessons come only through personal experience. Yet, historical study does add meaning and interest, it does dispel illusion. Ronald Ross used to say that 'an historical introduction is always necessary to give coherence to ideas'. Quoting Rowse of Oxford, 'History is part of the self-awareness of our environment.'

As one reads again various accounts of the long struggle against malaria, now flowing so dramatically in man's favour, it appears that there has been no steady triumphal march. Rather, as suggested by Conant's simile, the happenings resemble those of modern warfare: advance objectives wished for, reconnoitred, attacked, boldly seized, precariously held, and painstakingly consolidated.

SPECULATIONS

Prehistoric Beginnings

ONE must go far back into prehistoric time for the origins of malaria. Indeed, one might begin by crystal-gazing into a ball of translucent amber. Embedded in this fossil sphere is a mosquito caught by liquid resin in the Age of Reptiles, long before man existed. Or one might examine a flake of rock from the Insect Bed of the Isle of Wight, looking for a petrified mosquito, drowned and buried in the silt of its breeding-place, millions of years ago. These rare souvenirs include *Culex*, *Aedes*, and *Mansonia* mosquitoes and one may therefore assume that the malaria vector tribe of *Anophelini* was also present in those early days because, morphologically, it is an even more primitive stem than the specimens so far discovered.

Accordingly, we believe that when man appeared, mosquitoes were already an ancient form of life, with needles sharpened and adapted to the procurement of vertebrate blood. Very likely, too, the mosquito had already formed its close partnership with the protozoan that is the cause of malaria. In what vertebrate the plasmodia first existed as parasites we do not know, but it seems likely that they were not long, as time is measured, in adapting their metabolism to the chemistry of man's cells and fluids. One assumes, with Sigerist, that disease is as old as life.

Fossil bacteria are found in early rocks, in petrified fishes, and in the teeth and jaws of fossil vertebrates. In Egyptian mummies there are embalmed bacteria which seem to be those of tuberculosis and of plague. Calcified eggs of *Schistosoma haematobium*, the worm parasite that causes schistosomiasis, and enlarged spleens possibly of malaria, have also been found in mummies dating back 3,000 years. In fact, paleopathological studies seem to demonstrate

that disease has occurred during thousands of years in the same basic forms. Quoting Sigerist,

Whether the bones . . . were human or animal bones, whether they were neolithic or paleolithic, eocene or permian, we always found the same type of disease, disturbance of development and of metabolism, inflammation, and repair, new-growth, and true tumors, the same forms of disease that we can observe today.

Certain chimpanzees in Central Africa are naturally infected with what appears to be the identical *Plasmodium malariae* now found in man. This quartan parasite is perhaps the oldest species of plasmodium in the scale of evolution and may have been the first to invade man. Since parasitic infections abound in all the primates, it is not unreasonable to believe that early man suffered likewise.

Bone of our bone, and flesh of our flesh, are these half-brutish prehistoric brothers. Girdled about with the immense darkness of this mysterious universe even as we are, they were born and died, suffered and struggled.

William James—'Human Immortality'

No one can know how an infectious fever like malaria originated nor has any one witnessed the birth of a new protozoal disease. But one takes no great liberty with historical truth in assuming that prehistoric man, at least in some of the warmer regions, must have experienced malarial chills and fevers.

Pre-Grecian and Oriental Notions

Although references are relatively few and unsatisfactory, it seems reasonable to suppose that in pre-Grecian times malaria was not a serious problem in Egypt and the Near East but was highly prevalent in parts of Mesopotamia, India, and south China. The disease may have been rare in the Nile delta but more common in the upper valley. Egyptologists state that possibly the word AAT, found among the inscriptions of the temple of Denderah, meant malaria.

Allusions to fevers, some clearly intermittent in character, are fairly common in Babylo-Assyrian medical lore.