INDIAN JOURNAL OF MALARIOLOGY

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FOREWORD

In this explosive age of science, the starting of a new journal is a common phenomenon and need not attract special comment. One often hears scientists desperately trying to catch up with published information exclaim : "Oh ! yet another Journal !"

In the case of the Indian Journal of Malariology, the position is somewhat different. It is not in fact a new journal, it is an old journal being revived to meet a need. The Journal was started in 1929 by the Indian Research Fund Association (now the Indian Council of Medical Research) as the Records of the Malaria Survey of India at the time the Malaria Survey of India was formed. In 1938, the name of the Journal was changed to that of Journal of the Malaria Institute of India, in conformity with the change in the name of the Institute. Later in 1947, as the scope of the Journal widened and articles were published not only from workers at the Institute but also from other parts of India and abroad, the name of the Journal was changed to the Indian Journal of Malariology. This Journal was an important medium for publication of results dealing with malaria in all its aspects. It played an important role in the historic fight against malaria. It provided a window to the researches on malaria being carried out in India on parasitology, vector biology, chemotherapy, prophylaxis, etc. The Indian experiences published through the medium of this Journal played an important role in launching National Malaria Control/Eradication Programmes not only in India but in many countries in the world in the 50's of this century.

It is now common knowledge that malaria control programmes based on residual insecticide spray proved to be an instant success generating hopes that at long last, this ancient scourge of man-kind could be eliminated from our planet. The Saga of malaria control is too well-known to need repetition here. As malaria became less and less frequent, interest in malariology began to decline and the publication of the Indian Journal of Malariology ceased altogether in 1963.

Now with malaria back and with renewed efforts being made by scientists all over the world to overcome biological resistance of parasites and vectors through the development of alternative approaches, malariology has once again moved to the centre of the stage. The

chances of this field of research attracting able men and women are heightened by the fascinating possibilities that exist in the application of molecular biology to the resolution of tropical health problems such as malaria

The Indian Journal of Malariology is reborn and it is our hope that through its pages, results of researches in basic and applied aspects of malaria would be disseminated speedily, far and wide and that this would be helpful in our fight against malaria. The greatest need for a journal is to be needed. I would like to express my sincere good wishes on the occasion of relaunching of the Indian Journal of Malariology with the efforts of the Malaria Research Centre of the Indian Council of Medical Research.

V. Ramalingaswami

May 22, 1981

(V. Ramalingaswami)
Director-General
Indian Council of Medical Research
New Delhi

Messages

Central Drug Research Institute
Lucknow (India)

India's contribution to Malaria research are very well-known. It started with the discovery by Ross of the Vector for malaria infection and the cycle of transmission towards the end of the ninteenth century. Subsequent research work covered different aspects of malaria, including epidemiology, vector control, development of experimental models for the infection and chemotherapy. The often quoted contribution of scientists like Dr T. R. Rao, Dr A. P. Ray, Col. Jaswant Singh and Dr S. P. Ramakrishnan are a source of inspiration to young workers in this field. It is gratifying that with the resurgence of malaria, there is a sharp focus of interest to revive research in this important field in the country, which would naturally need a suitable medium for publications. I am very happy that Indian Journal of Malariology is being revived and I am sure, it will soon regain its old prestigious place in the field of malaria publications. I wish this journal great success.

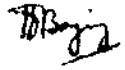
Nitya Anand

(Nitya Anand)
Director

March 26, 1981

Directorate of Health Services
Nirman Bhavan
New Delhi (India)

I am happy to learn that Indian Council of Medical Research has revived the publication of Indian Journal of Malariology. This Journal had served well in the past and I hope the Scientific Workers in the field of Malaria both in the country and outside will be greatly helped with the revival of this Journal.

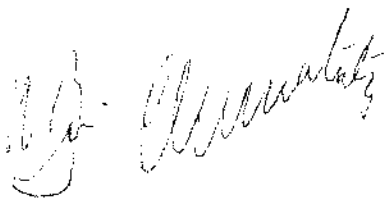


H. D. Bajaj
Director General of Health Services

April 22, 1981

Wellcome Museum of Medical Sciences
London (UK)

Your letter of 11th March 1981 brought me the good news that the Indian Journal of Malariology is being revived after 17 years since it ceased its publication. Much has changed during this time and the over-optimistic hopes that I had and shared with my two USA colleagues, Dr Martin Young and Mr Jack Henderson, as members of the 1951 US AID Advisory Team on Malaria Eradication in India, had not been fulfilled. But the fight against malaria, that old scourge of the tropics, has not been given up. We might have changed our time schedule and instead of looking for some early and spectacular successes, the new strategy of the campaign demands prolonged, persistent and dedicated efforts directed against the malaria parasites and, against its Anopheles vectors, with the full cooperation of an enlightened community. The role of Indian science in this great task has been proved in the past and is now greater than ever before. I welcome the reappearance of the Indian Journal of Malariology and all my colleagues in the United Kingdom, and particularly the Fellows of the Royal Society of Tropical Medicine and Hygiene, send you and your staff our best wishes for the future.



(L. J. Bruce-Chwatt)
Emeritus Professor of Tropical Hygiene
University of London

March 30, 1981

77, Jodhpur Park
Calcutta (India)

While cherishing the reminiscence of the Indian Journal of Malariology I welcome its revival like a phoenix. The setbacks in our anti-malaria campaign showed that mosquitoes were more cunning than we imagined. The campaign has again become a health priority. Available measures need be reviewed taking into account past experiences to shape the future policy. The Journal will help malariologists in tackling the right problems in the right way for publication.

(R. N. Chaudhuri)
Formerly Professor of Tropical Medicine
and Director, School of Tropical Medicine,
Calcutta

April 2, 1981

Calcutta School of Tropical Medicine
Calcutta (India)

I am delighted to know about the most welcome decision for the resurrection of the Indian Journal of Malariology after an interval of 17 years. Needless to mention, the journal with its glorious past will remain as an eloquent testimony to the historic fight against malaria, exacting a devastating toll in our country. What is more, it has played a crucial role for the development of malariology in its proper perspective, essential for the containment of this menacing health problem. With this proud heritage, I am sure, the journal will continue to inspire generations of scientific workers, current and yet unborn.

(A. B. Chowdhury)
Director

March 12, 1981

World Health Organisation
South East Asia Region
New Delhi (India)

Specialized medical journals have occasionally been discontinued because the disease with which they deal appears to be suffering a similar fate. Actions in this respect concerning malaria have unfortunately been shown to be premature. The resurgence of this disease in many parts of the world including south-east Asia, and the revitalization of the research and control operations essential to combat it, make it eminently desirable that so respected a publication as the Indian Journal of Malariology should once again appear bringing articles and information of world-wide as well as of local significance to those fighting the disease.

David F. Clyde

(David F. Clyde)
Senior Malaria Adviser

March 11 1981

Imperial College at Silwood Park
London (UK)

During the recent celebrations at the Central Drug Research Institute, Lucknow, it was with the greatest pleasure that I heard from Dr V P. Sharma that the famous Indian Journal of Malariolgy is to be resuscitated; it had been with an equal degree of grief that I had learnt in 1963 of what was then thought to have been its last number As long as malaria—this terrible affliction of mankind—remains undefeated, specialist publications on the subject are desirable, and that is why we welcome our old friend back from the dead.

Many classical researches have been described in the pages of this Journal and its various predecessors of different names, but under the same band of Indian and British Editors. The "Records of the Malaria Survey of India" which first appeared over 50 years ago were avidly awaited every three months by malariologists all over the tropics, because we had little literature on the subject beyond the Rivista di Malariologia, whose publication ceased in 1967.

As long ago as 1909, the Government of India agreed to a proposal that a permanent organisation should be formed to enquire systematically into the practical and scientific problems of malaria and that a Journal should be published quarterly under the editorship of Major S.P. James (later Colonel and F.R.S.). Thus began in 1910 the original ancestor of the Indian Journal of Malariology under the name of "Paludism".

I have had the privilege of contributing several articles to the Journal and hope that other will be accepted in the future. I wish it all success!

P. C. C. Garnham

(P. C. C. Garnham)
Emeritus Professor of Medical Protozoology
of the University of London

April 6, 1981

Indian Council of Medical Research
New Delhi (India)

Indian Journal of Malariology served the scientific community with distinction for 34 years. Near eradication of malaria in early 1960's resulted in the closure of this important medium of scientific communication. Malaria is once again a major public health problem. Research on malaria is being strengthened. There is an urgent need of a specialised journal for establishing close linkages between the malariologists working in this country and abroad. The decision to revive the Indian Journal of Malariology is indeed most appropriate. I congratulate the Centre for undertaking this responsibility and wish the journal all success.

(N. P. Gupta)
Senior Deputy Director-General

May 18, 1981

World Health Organisation
South East Asia Region
New Delhi (India)

Revival of the Indian Journal of Malariology is indeed a welcome event. There is a manifest need in this Region for a journal which will present the latest developments in malaria research and control in the varied epidemiological context of India, and the high standards that made the original journal of universal significance may confidently be expected to be maintained in the present publication

(U. Ko Ko)
Regional Director

May 1, 1981

Liverpool School of Tropical Medicine
England

The decision to revive the Indian Journal of Malariology is a wise one Through its pages past generations of workers benefited from the experience of others, and with the resurgence of malaria both in India and elsewhere it is more than ever essential that malaria workers communicate their finding to one another I wish the Journal every success in meeting its objectives.

(W. W Macdonald)
Professor, Department of
Medical Entomology

March 30, 1981

World Health Organisation
Geneva (Switzerland)

Welcome back to the Indian Journal of Malariology.

Under the able editorship of the late Sir Gordon Covell and the late Colonel Jaswant Singh, the Journal played a significant role in bringing to the attention of malariologists vast quantities of epidemiological and other scientific observations, and truly reflected the Indian school of thought on malaria between 1947 and 1963.

At a time when malaria control in the world is facing considerable technical, operational, administrative and financial difficulties, you have my heartfelt good wishes for the success of your enterprise: I do hope the new Journal will regain an important role — even beyond the borders of India — and that within the subcontinent it will be of support to the malaria control programme as an essential part of the national strategy of health for All by the Year 2000.

(H. Mahler)
Director-General

March 25, 1981

5 Thorngrove Road, Wilmslow
Chashire, SK91DD, England

I was immensely pleased to learn of the rebirth of the Indian Journal of Malariology after a lapse of 17 years. I feel confident that the Journal will again achieve international fame as a means of disseminating new knowledge of malaria and I send my very best wishes for a successful future

(H. W. Mulligan)
Formerly Director
Malaria Institute of India

March 19, 1981

Institute of Medical
Parasitology & Tropical Medicine
Martsinovsky (USSR)

With great satisfaction I have learned that with this issue scientists and public health workers in India will see a revival of a very famous publication the Indian Journal of Malariology. In fact, I take it as an indication of a revival of the Indian School of Malariology. the school without which the world would known much less about malaria than it does at present. It is hard to start anything but you have already started again a long a steady walk towards understanding malaria problem as it stands today.

I wish to assure you that the numerous colleagues of yours in the USSR wish you all the success.

(V. S. Orlov)
Dy. Director

May 13, 1981

38, Ch. du. Pont Ceard
Ch-1290 Versoix
Geneva (Switzerland)

I am so glad to know that the Indian Journal of Malariology is being revived after 17 years of being discontinued In fact, I was personally opposed to its discontinuation at that time. It was obvious that as we progress in achieving our mastery over malaria we would have to face difficult problems. Results of further investigations on problems such as resistance of mosquitoes to insecticides, resistance of malarial parasites to drugs, discovery of new drugs and development of vaccines would require a forum for wide dissemination. The Indian Journal of Malariolgy would ideally fill this need as it was regarded as one of the most prestigious journals all over the world. I wish the journal and its editors success and fulfilment.

R. Pal

(R. Pal)
Formerly Chief, Vector Genetics
and Bionomics (WHO)

April 27, 1981

National Malaria Eradication Programme
Delhi (India)

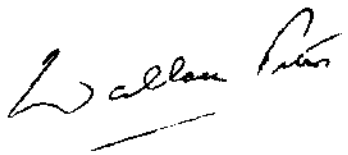
It is indeed a great pleasure for me to learn about the revival of the Indian Journal of Malariology by the Malaria Research Centre. The lead taken in this regard is commendable and I am sure that the publication of articles in the journal will give lot of encouragement to the entire scientific community in India and abroad.

(S. Pattanayak)
Director

April 30, 1981

London School of Hygiene and
Tropical Medicine
London (UK)

The Indian Journal of Malariology was one of the leading journals in this field and its temporary demise was regarded by malariologists around the world with dismay. At a time when India is once again facing a major resurgence of malaria, it is most appropriate that this excellent journal should once again see the light of day. I wish you every success and look forward to the journal being once again on my shelves.



(W. Peters)
Professor of Protozoology and
Director of Department

March 13, 1981

5th, Eighth Main Road
Malleswaram, Bangalore
(India)

It will gladden the heart of every public health worker in the country to know that the Indian Journal of Malariology will start appearing again. Not only can it be expected to be the medium for publication of the results of the greatly expanded research but also to stimulate many more workers than at present to take interest in Malariology, a subject which had recently ceased to attract creative minds. I express the hope that the Journal will maintain the highest standards and even better its previous record which had given it a unique place in the malaria literature of the world.

(T. Ramachandra Rao)
Retd. Director (NIV, Pune)

May 1, 1981

P. falciparum Containment Programme
National Malaria Eradication Programme
Delhi (India)

The first attempt at disseminating knowledge of Malariology in India was made in 1910 with the publication of "Paludism" which lasted for three years.

However, the Records of Malaria Survey of India, published in 1929 and its successors, the Journal of Malaria Institute of India (1938-46) and the Indian Journal of Malariology (1947-1963) provided the medium for continuous dissemination of newer knowledge that had been accumulating from observations made in various fields by scores of workers, on an unprecedent scale! It can be said without fear of contradiction that it was the single most important factor that had brought India in the malaria academic world of yester years.

The first noticeable impact of the professional journal was the stimulation of research, initially confined to Kasauli Complex but later it did not remain monopoly of one institution. The field also covered observations on parasitology, entomology, epidemiology, immunology and not of the least importance laid the foundation of the modern chemotherapy of malaria.

On account of continuous relay of information on observations made in varied fields in different parts of India, the journal had served in the past, as still it will do today, as one of the most important sources of reference for guidance in the field of research, survey and control of the disease. It also brought to the notice of the workers and administrators alike the manifold problems which had to be overcome.

Obviously therefore, the revival of the journal of Malariology is most opportune to serve as an important medium for the guidance.

(A. P. Ray)
Chief Coordinator

May 8, 1981

1900 Lauderdale Drive, D309
Richmond, Virginia 23233
(USA)

I am delighted that the Indian Journal of Malariology is being revived, and that you will be its Editor. It is a pity that its publication was ever suspended. This was an important Journal and I am sure that under your direction it will again become very useful; and that it will assume leadership in the campaign against malaria in India and elsewhere.

I wish you success in your Editorship.

(Paul F. Russell)
Formerly Staff Member Emeritus
The Rockefeller Foundation
New York

May 8, 1981

The Rockefeller University
New York (USA)

Those of us old enough to know the old Indian Journal of Malariology will remember how we looked forward to each issue. There were many excellent and interesting papers, and a number of outstanding ones.

With the renewed recognition of the continuing importance of malaria, and with the surge of exciting new work in the field, I look forward to a better than ever Indian Journal of Malariology and I congratulate you, Dr Sharma on being the Editor of this important enterprise.

Wm Trager

(William Trager)
Professor of Parasitology

March 17, 1981

Editorial

With the release of this issue we announce the revival of the Indian Journal of Malariology after 17 years of its discontinuation. The Journal was started in 1929 by the Indian Research Fund Association (now ICMR) as the Records of the Malaria Survey of India, at about the same time as the Malaria Survey of India was formed. The name of the journal was changed to the Journal of the Malaria Institute of India in 1938 in conformity with the change in the name of the institute. In 1947 the scope of the journal was widened and the name was once again changed to the Indian Journal of Malariology.

The success of malaria control on global basis began with the availability of DDT for use in public health after the World War II. In 1953 Government of India launched National Malaria Control Programme (NMCP). Initial success in the control of malaria was so spectacular that the objective of the programme was changed from control to eradication and National Malaria Eradication Programme (NMEP) was launched in the entire country in 1958. The strategy of NMEP to break the chain of malaria transmission by spraying DDT as residual insecticide appeared to have nearly eradicated malaria from the country. Malaria incidence was greatly reduced in the mid 1960s, and about 0.1 million cases were recorded in 1965 in the entire country with no deaths. In those days of euphoria malaria it was no longer considered a public health problem. As a direct consequence of this, research on malaria received a setback and it was restricted to a few workers. There was therefore a great paucity of papers submitted to the journal. Also it was felt that research in malariology had diversified and refined so that the few papers that may be emanating may be more appropriately accommodated in a variety of specialised journals. The Indian Council of Medical Research therefore announced the retirement of the Indian Journal of Malariology with the publication of the December 1963 issue (Vol. XVII, No. 4).

Resurgence of malaria compounded with the twin problems of insecticide resistance and drug resistance are formidable challenges to the present day scientists and public health administrators. A more disturbing fact is that more vectors are showing resistance to one or more groups of insecticides in more geographical areas. Similarly the drug resistant strain of *P. falciparum* is spreading to hitherto chloroquine susceptible areas. There are also problems both at the cellular level and in the field that needs to be resolved with sustained research. Realising this situation, the Indian Council of Medical Research convened a meeting of experts on malaria in 1977. This group reviewed the status of research on malaria and prepared a document "Research on Malaria—an Outline" which served as a blue print for future research-cum-action programme for the country. In the same year ICMR established the Malaria Research Centre, Delhi, strengthened the Vector Control Research Centre, Pondicherry, and also sanctioned research projects on malaria to different institutions. In the Ministry of Health and Family Welfare, Government of India, a high powered Board on malaria was created. This Board sanctioned a number of fundamental and field operational research projects to the research institutes, medical colleges, and universities, etc. The Government of India also revised the classical phasing of NMEP's eradication strategy and implemented the Modified Plan of Operation in 1977. In a recent meeting of the scientific working group on malaria held in the ICMR Headquarter's office in October 1980, it was revealed that in about 3 years, since these major decisions to strengthen our capability to fight against malaria were taken, considerable progress had been made in different areas of research in malariology. It is also heartening to state that during this period, India hosted three international conferences on malaria, the first one in 1977 on the "Recent Advances in Malaria Research" sponsored by the organisation of Pharmaceutical Producers of India with the technical guidance and support of ICMR at Delhi, the second was held to celebrate the birth centenary of Alphonse Leveran "Hundred Years of Malaria Research" held under the auspices of the Institute of Postgraduate Medical Education and Research, Calcutta, and the third on "Chemotherapy and Immunology in the Control of Malaria, Filariasis and Leishmaniasis" held under the auspices of the Central Drug Research Institute, Lucknow. Early this year a monograph "The Anophelines of India" by Dr T. Ramachandra Rao was released by the Council.

The increasing momentum of research and our capability to accept the challenges were reflected in the need of a specialised journal that could take up the role played by the Indian Journal of Malariology and establish close linkages between malariologists working in different disciplines. The Council therefore decided to revive the Indian Journal of Malariology and entrusted the publication of this journal to the Malaria Research Centre. The scope of the journal is broad based to cover fundamental, applied and field research on all aspects of malariology. The journal would also publish letters to the editor inviting frank scientific opinion on the papers published in the Indian Journal of Malariology. The journal would also review papers submitted for publication from an ethical point of view before approving such papers for publication in conformity with the policy of the Council.

This generation of malariologists is passing through an age full of major breakthroughs, such as discovery of crown ethers for the synthesis of enzymes, hybridoma technology for monoclonal antibodies, gene cloning, recombinant DNA technology, ultrastructural studies and alike, and we hope that in not too distant a future, we would be able to apply these newer technologies in the fight against malaria. It is a matter of great satisfaction to us that malaria research in the country has been organised on sound footing. A beginning has been made in the right direction. We are optimistic that in near future researches would provide practicable answers to the most complex and vexing problems of the field and we would be soon back on the road to victory, and contribute in our own way in realising the Alma Ata declaration "Health for all by the year 2000".

May 5, 1981 V. P. Sharma

Indian Journal of Malariology
Vol. 18, June 1981, pp. 4-11

Problems in Malaria Research

T. Ramachandra Rao[1]

The last few years have seen a strong and welcome spurt in research on malaria, as a result of the recognition that the presently available knowledge on the cure, prevention and control of the disease, good as some of it is, is not adequate to meet the present situation. Though the world has slightly lowered its sights and seems to be content at the moment to aim at an effective control rather than eradication of the disease, all progressive minded scientists still believe in the need for eradication as the ultimate target. We, of the previous generation, are all too familiar with the ravages of malaria to accept the thought that malaria should be allowed to continue to have a foothold, even if under control. However, realism has demanded and won the point that malaria should be immediately brought again under effective control and every endeavour be made to forge new weapons to permit another attempt towards eradication.

The strategy then is first to do everything possible to keep malaria under complete control and secondly to devise ways and means to give the final punch to knock it out once and for all.

Many experienced and eminent malariologists have expressed their views and opinions as to why the world failed in its massive effort to eradicate the disease. There have been divergent opinions as what went awry; some believe that all facets of the problem had not been well understood before eradication was attempted, while on the other side are those who feel that the failure was as a result of poor management. In between are many who hold various intermediate points of view. But all believe that the remedy to the ills lies in mounting research of a high quality to understand more about the disease and methods of control so that our future actions are dictated by sound knowledge of the enemy.

Several seminars, symposia and workshops have been held under national and international auspices and the lines of research which should be pursued have been reasonably well identified. The Indian Council of Medical Research has taken a positive step in reviving its Expert Advisory Committee on Malaria and in 1977 organised several task forces which listed all important lines of research needed. Based on that broad review, several projects have been initiated. A recent review of these projects revealed that considerable progress had been made and the country was now in a position to go ahead with more expanded research activities. There is no gainsaying that a solid foundation for research has once again been laid. Parasitology, immunology, epidemiology, entomology and even experimental control have all been included in the studies and have yielded useful results. The establishment of the Malaria Research Centre at Delhi and of the Vector Control Research Centre

Accepted for Publication : 5 *May* 1981.

[1] Retd. Director, National Institute of Virology (formerly Virus Research Centre), Pune.

Present Address: 5, Eighth Main Road, Malleswaram, Bangalore 560 033.

at Pondicherry has revitalised research in this field, which, for unfortunate reasons, was dwindling towards extinction. The revival of the Indian Journal of Malariology to become the forum for publishing the results of the greatly expanded research activity is a logical and progressive step which is bound to elicit an energetic response from our young scientists. The prospects of intensive research are indeed very bright, though there is still the bottleneck due to shortage of research manpower but already there are signs of improvement. The Government and the Indian Council of Medical Research could do no better than make heavy investments in this regard.

Short and Long Range Problems

It would be unnecessary to make even a partial list of the problems in malaria on which research has to be mounted immediately. Almost every branch of malariology, ranging from simple studies on local epidemiology to sophisticated technology needed for subjects like immunology, present features which need a better understanding. So also are the innovative investigations needed for the development of vaccines, immunological techniques, parasite behaviour in the human and mosquito hosts, development of newer and better insecticides and drugs, genetics both of insecticide resistance and of the poor response of the parasites to chemotherapeutic drugs, newer methods of vector management control, methods of environmental improvement, etc. The behaviour of vectors is among the foremost fields of study having a very practical bearing in the application of control methods. Most of these problems in research are so obvious and imperative that to dwell on them at any length would be superfluous. They will undoubtedly receive the utmost attention from those organising research programmes. More appropriate would be to dwell on this occasion upon a few fundamental problems relating to malaria which are not so immediately obvious but are nevertheless very important in the long range objectives of malaria control or eradication.

Environment, the fourth factor — Epidemiology, perhaps, is the most important field which needs urgent attention. The basic factors of epidemiology, *viz.* the vectors and their habits, the parasites and their vagaries and the human element and its idiosyncrasies present numerous aspects in which there are still lacunae in our knowledge. Added to these, there is the fourth factor, the environment, which plays a very vital role in determining the quantum and quality of the three other factors. Environment has long been neglected by malariologists, because there was not much to ponder over it. All that was considered necessary was to break any one of three links (Fig. 1).

It is the environment which regulates the abundance of the vectors and the control of the links. It is the environment that shapes human ecology and determines the degree of receptivity and vulnerability of a locality. It

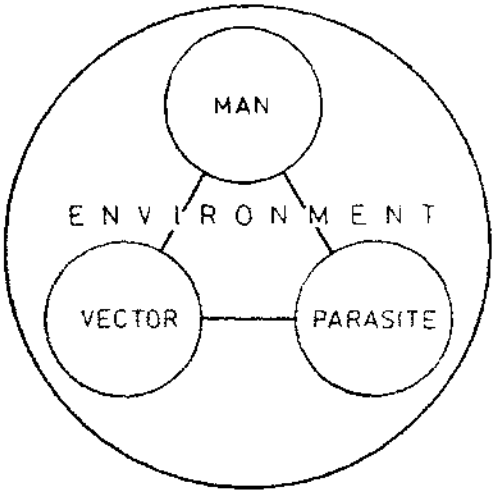


Fig. 1—All Pervading Nature of the Environment

is a deep understanding of the environment and making improvements in it, that will ultimately help in reducing malaria to levels of unimportance. The role of the environment has to be better recognised.

Epidemiology of persistent malaria — Another epidemiological factor that demands serious thought is the manner in which malaria persists in certain localities. It is a serious problem to reckon within the final phases of any eradication programme in large countries like ours. It occurs in a subtle way over wide areas. In our country several areas both in the east and west had been identified as problem areas with persistent transmission. The effort needed to trace and treat the few remaining cases is several folds that needed for control in earlier phases. Few administrators would countenance expenditure of large sums on only a few cases of malaria. The consequence is that the efforts required get diluted at a time when the greatest concentration is needed. Even from the technical point of view the problems posed by persistent malaria are very different both in kind and degree from those presented by normal malaria. A question which often arises is whether the epidemiology of low grade persistent malaria is not very different from that of the endemic or epidemic malaria. Do the elegant mathematical models developed to measure and quantify disease transmission really hold good for the persistent malaria also? Do the terms Reproduction rate, Vectorial capacity, etc. have the same applicability when the disease smoulders in an area? Is there a 'critical density' of the vector in such situation?

Self preservation is one of the characteristics of biological entities. Nature fights against extinction, though numerous animal and plant species have disappeared from the world in the past aeons, but it is indeed remarkable that so many others like malaria parasites and malaria mosquitoes have survived for a long time. In their cases it is not merely food, shelter, or reproduction for which facilities were necessary. In the case of parasites adaptation to two kinds of hosts, man and the vector, had to be evolved. Their survival depends on combinations of several factors to occur at the appropriate time in an environment so diverse and complex. The long survival in nature would not have been possible unless there was great biological resilence, adaptive abilities and reproductive potentials, all favourably compounded. It would appear that it is not massive numbers of the vectors, the parasites or the host, that make transmission possible in low grade persistent malaria but some subtle biological processes which keep it going.

The factors which help self preservation are not easily analysable. Their existence may be even unknown. Who for instance could have dreamt that insects already had in their genetic constitution a gene which would regulate the detoxification of DDT, even before the use of DDT was known to man? It may be that this gene had some other function but became adapted to the development of resistance to DDT. There are also other genes for resistance to other insecticides, some dominant, some recessive. Who could have foreseen that some vector mosquitoes would circumvent the effect of insecticides by increasingly staying out of doors? This seems to have happened with several species, such as *A. philippinensis*. Outdoor resting is a more ancient habit than resting indoors and it seems that reversion to an older habit has occurred. How can we explain the survival in nature of very rare species like *A. sintoni* or *A. culiciformis*? They are so uncommon (it seems to us) that the wonder is how they find their mates in a vast forest environment to mate and reproduce? It may be that there are ecological niches where they tend to congregate. *Plasmodium malariae* can survive for long

periods and relapses have occurred after decades. Recently an outbreak of malaria occurred in the island of Granada, 16 years after 'eradication', because one individual was believed to have sheltered the parasite for that period. These examples would indicate the ability of the vectors and the parasites to develop methods of survival in subtle and unexpected ways. Biological phenomena in their basic aspects may not always act in a precise manner conforming to mathematical formulae.

Probably many instances of persistent malaria in the recent past were due solely to, operational causes such as inadequacies in insecticide coverage, insecticide resistance, incomplete or ineffective chemotherapy, etc., but such deficiencies which were common even in the "easy" areas were multiplied several folds in forests, hills and inaccessible regions. These features of geography and terrain coupled with such factors as tribal behaviour and customs, scatter of housing, mosquito bionomics including exophily and exophagy, etc., have also played a part in the persistence of the disease. Moreover, no major region of the country, probably no district, was completely free of malaria parasites even at the peak of the success of our efforts in 1965-1966. What prevented their complete elimination? Movement of nomads? Symptomless carriers? Aggregation of labour? Unsuspected vectors? Subtle features in the biology of the vectors and the parasites? Active transmission in undetected closed circuits in isolated pockets? One could postulate several such possibilities for persistent malaria. Unless such factors are intensely studied and remedial measures devised no programme of malaria eradication can succeed.

In any event the liquidation of a focus of persistent malaria is likely to become a serious problem when the present efforts to control the disease reach a critical stage. Malariologists should begin to think from now itself as to how the situation can be met and what procedures should be built in into the programmes. Even as an academic subject, it poses challenges to our biologists to study and understand the complexities of persistent malaria. One may call this a study of the 'Epidemiology of Persistent Malaria' just as a decade or two ago we were using the term 'Epidemiology of Disappearing Malaria'.

Role of chemotherapy as a public health measure—Serious thought is necessary to the question whether massive chemotherapy would help in the elimination of malaria parasites in a community and how much reliance can be placed on it. It would be natural to expect that if a thorough programme of drug administration could be organised, the parasites would be automatically eliminated by a process of progressive depletion. No one has claimed that it does actually happen, but in a nation-wide programme of malaria control the effect of massive drug administration should be accurately assessed. As an expedient measure to minimise morbidity and prevent mortality, drug distribution takes the pride of the place and has rightly been adopted in the NMEP, but the question is whether as a public health measure, it has any lasting value as a means to the reduction of the potential of transmission and to gradually eliminate the parasite. A critical evaluation of chemotherapy as a public health measure, its advantages and limitations, seems to be an urgent necessity. This is so because a major tool we seem to be employing today is the widespread use of antimalarial drugs, in conjunction with insecticidal spraying to a certain extent in selected areas. Even the ambitious programme of the "falciparum containment" in eastern India has chemotherapy as the main plank. If

chemotherapy does provide a suitable answer, it should be used more extensively, with better combination of drugs and a revitalised organisation. If it does not provide the answer, too much reliance on it would be unjustified. The gradual reduction in the number of malaria cases now being detected and recorded may give an unbalanced sense of security. It would be wise and expedient to undertake intense studies on the effect of widespread chemotherapy on all the three species of parasites, their prevalence and behaviour.

Long term effects on vector populations—The long term effects of the use of insecticides on mosquito populations, their abundance, prevalence and behaviour also hold many pointers as to what may happen in future. Whether reliance will continue to be placed on insecticidal spraying or recourse will be taken to measures directed against the larva, or even if environmental improvement will become the order of the day, the status of the vector population would have to be properly appreciated to obtain maximum benefits. Nature reacts to our attempt to control it in many ways. Undoubtedly changes have taken place in the prevalence, distribution and habits of some of the major vectors during the last two decades. For instance, the anthropophilic *A fluviatilis* seems to have become very scarce all over the Western Ghats. What are the possibilities of its reappearance? *A. culicifacies* populations have dwindled in the Pattukottai area of Tamil Nadu, but seem to have gained a wider prevalence in Thana district of Maharashtra and Surat district of Gujarat. What are the probable reasons for these changes and how much of the persistent malaria in the latter area is due to the increased prevalence? *A. philippinensis* is reported to have become almost extinct in Bengal, but is still quite common in the "Assam" area though it is rarely found in houses during day time. It can be collected in the latter region in good numbers biting man and animals both outdoors and indoors at night. Apparently it has become predominantly an outdoor rester. Are the environmental conditions in Bengal very different or are there inadequacies in technology of collections which fail to detect the adults of the species? The notorious *A. minimus*, once so widely prevalent, is being reported to be totally absent in the whole of the Himalayan belt and Assam and to have dwindled even in parts of China, but seems to be thriving in Thailand. The case of *A. sundaicus* is well known. It has withdrawn from coastal Andhra Pradesh and Orissa and has become restricted to a small area in the Sunderbans of Bengal. What has taken the place of *A. sundaicus*? Has any other species occupied the ecological niche left by it? Even *A. stephensi* which used to form about a quarter of the total adult anopheles population in the Deccan is now reported to be very difficult to be collected. How have these changes come about and what is their impact on the prevalence of malaria? Are there natural long range changes in mosquito populations? It would be of utmost importance if these changes are studied to help in organising better programmes of control at present and planning for eradication in the future. They are warnings of the likely types of changes which may take place in the biological environment, some of which may be beneficial to man but others may be dangerous.

Some Immediate Problems

Vaccines—Reverting to the more immediate problems of research, immunology and chemotherapy hold promise of early breakthroughs. Not only would immunological techniques help in developing methods of assessment of the intensity of malaria transmission, but also will help in the development of an immuno-

prophylactic methods. Already very remarkable success has been obtained (including in India) on the cultivation of malaria parasite, an essential preliminary needed for large scale production of vaccines. It may be expected that experimental vaccines, either produced from the blood parasites or sporozoites, will be available sooner than we expect. It is essential to make a proper assessment of the role and utility of the vaccine now itself and its advantages and limitations evaluated. Firstly vaccines, whether killed or live, have to have an immunological effect better than that of a natural infection to be successful in nature. We are all familiar with the frequency of malaria reinfections and the very transitory nature of immunity after a natural infection. The vaccine has to provide a more lasting effect to stimulate immunity against all the three species of the parasites, each of which seems to be immunologically different. Let us hope that immunologists will produce such a vaccine. However, the prospects of using vaccines on a large scale seem to be slight. Moreover, the organisation required to immunise millions of people each year is itself a formidable task, and needs production and logistic facilities far in excess of what we were accustomed to even at the height of the NMEP. The protective inoculation is not a one-time affair like smallpox vaccination. Multiple vaccinations every year would be needed. But there are undoubtedly situations such as those found in organised civilian and defence personnel, limited populations facing a serious epidemic and perhaps even school children, where vaccines would be useful, but repeated vaccinations of millions of people every year may pose problems. Obviously, as viewed at present, vaccines have an important place for personal protection, but whether they can be of that quality or effectiveness to prevent persistence of transmission or to be useful as an extensive public health measure is a matter which needs careful evaluation before the country embarks upon a programme of mass immunisation against malaria.

Assessment of malaria incidence — The question of the assessment of the incidence of malaria demands also urgent attention. Governments have the right to know what has been the effect of the programmes on which large funds are being expended. Malariologists are also interested in knowing the manner in which malaria incidence is being affected so that they can make suitable projections of the probable future needs. It is imperative that accurate and reliable data are available. Since NMEP was started in 1958, sole reliance is being placed on the data collected by the surveillance organisations. The data consist of the number of parasite positive malaria cases detected in the total population. The data are further analysed in terms of API (Annual Parasite Incidence), ABER (Annual Blood Examination Rate), etc., for every region or district. Very valuable as these data were at one time, their present accuracy and validity have been questioned as parameters for measuring malaria incidence. The pre-1977 data were based on the collection of blood smears in untreated populations, but with the introduction of the modified plan and the widespread use of chemotherapeutic drugs, a question arises whether the sample now being examined is comparable. Do they not largely consist of treated populations? While chloroquine was administered prior to 1977 as a presumptive treatment after taking the blood smear, in post-1977 period chloroquine is being freely distributed and every encouragement given through the press, radio and even through postal stationery, for self-medication even before blood smears are collected. Therefore, a critical and unbiased evaluation of the methods should be undertaken immediately and also attention given to the development of alternate methods of malaria assessment. Much innovative research is needed demanding utmost objectivity. Sero-

logy may provide one of the possible solutions, but it has also certain limitations and organisational obstacles which rather militate against its widespread use. Malariologists have to bestir themselves very soon to settle this matter and start collection of data comparable year after year.

Environmental improvement — The discovery of DDT and its role in public health was perhaps the greatest factor which stimulated and made possible a global attack on malaria. Will such an event occur again? Will human ingenuity provide an alternative? However, such an event does not seem to be in sight at present. Various types of chemical compounds are being developed (unfortunately not in our country yet) and tested. Almost every new insecticide synthesised seems to be able to induce resistance in some insect or another sooner or later. While we may wait and look for better insecticides comparable in effectiveness, safety and cost with DDT, it would be prudent to explore methods to control the vectors without too much reliance on insecticides. A better understanding of the physiology and genetics of resistance may help us temporarily to overcome the difficulties, but in the long run, it is the elimination of the sources of production of the vectors that is likely to be the answer to the problem of many vector-borne diseases. As already stated, it is the environment which determines the degree of vector prevalence and distribution. The improvement of the environment in villages and towns to eliminate the vectors at source would be an ideal permanent method of disease control. Even if a fraction of the Rs 80 crores being annually expended on malaria in this country could be diverted to improving the environment, long lasting benefits will accrue. In vast parts of the country such improvements can be brought about by a concerted programme extending from 5 to 10 years. There are other places, however, in which the breeding places of vector are so extensive that environmental improvement as a means to vector control would not be feasible at present. But even if malaria can be got rid of in vast areas of the country by simple methods of minor engineering, it would be a solid achievement. While all other methods tend to reduce malaria incidence temporarily, the environmental improvement acts by actually reducing the malaria potential permanently. Unfortunately the idea does not look much enthusiasm among the workers who would rather prefer easier and more spectacular methods but which may fail in the long run. This subject has been discussed elsewhere and need not be discussed in detail here.

Research methodology—Finally, the methodology of research itself requires careful attention and much revamping. Research should be organised in such a manner that each project has definite objectives and is time bound. Specific questions should be posed and answers to it obtained. The plan of work should be discussed and decided before the studies actually commence and assessment made on pre-determined parameters. In the past, all too often, research projects have been commenced with well meaning, broad but vague objectives leading to much waste of effort on unessentials. However, scientists are not automatons and a few who wish to take part in exploratory research should also be encouraged if their rationale is supported by sound reasoning.

The above brief account reflecting the author's personal thoughts emphasises if nothing else, the existence of a multitude of problems which still remain unsolved in malariology. Perhaps another

author would have given a different set of topics needing urgent attention. Differences of opinion are inevitable based on each person's background and degree of commitment to the problem. Discussions and debates are an essential requisite to sort them out and to plan research for the future. What is needed is a constructive and positive approach with a determination to get results. All research has one objective, the final liquidation of malaria at a not distant future. It can be achieved only if a scientific attitude is maintained all the time.

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Some Aspects of the Socio-Economic Impact of Malaria and its Control

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Preamble

Discussing on the subject of malaria and its devastating effects on the socio-economic aspects of a community, as well as measures required to control the disease, many a worker in the field, such as Ross (1926) had observed in the past, that while it is true that control measures cost money, but the disease itself is a source of expense. Even if the cost of protecting the community is as much as malaria itself, which is seldom the case, it is worthwhile. All were in agreement that in countries afflicted with malaria, specially in the tropics, economic and industrial efficiency is materially retarded (Hehir, 1927; Bentley, 1925; Christophers, 1930).

A treatise written by Sinton (1935) on "What malaria costs India" recorded that the problem of the very existence in many parts of India was the problem of malaria. It constituted one of the most important causes of economic misfortune, engendering poverty, lowering the physical and intellectual standards of the nation and hampering prosperity and economic progress in every way. A review of the literature indicates that if such was the case in India it was true for most of them alarious countries specially in the tropics.

At the same time there was consensus, that quantification in terms of economic gains by affording protection through health projects is problematical. The situation becomes more complex because of competitions for the limited funds not only amongst different departments but also from programmes within the same department.

In view of these conflicts there were some who advocated that the solution might lie, first in estimating the economic loss caused by malaria (Rao, 1928). Some of the pioneers in the field tried precisely to do that by analysing the effect of the disease in terms of deaths, disability (thus absenteeism from schools or work) during acute illness as well as debility as a result of repeated attacks on account of relapses and reinfections, and the adverse effects in terms of output, whether in the field of agriculture, industry, mining construction, engineering, railway and other projects, so vital to developing countries.

Having presented these quite systematically, some made attempts to show the benefits (though indirectly), which would accrue by controlling the disease. To some extent a few of them were able to substantiate their claims on the effects of organised control programmes in areas with economic potentials, especially in certain types of agricultural industries like tea, coffee, rubber and oil palm.

But it would seem that these exercises were not convincing enough for the planners and

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economists. But their attention was soon to be focussed with the publication in 1951 of an article on the "Cost of Sickness and the Price of Health" (Winslow, 1951). This appeared to be timely as, because of national economic planning in many developing countries, people were evincing more and more interest in the economic benefits of health programmes which have all along been considered as a non-productive expenditure. The subject received further recognition when the University of Michigan sponsored a conference in 1962 on the Economics of Health and Medical care. In this context mention should be made of two papers on "Malaria Eradication and Population Growth" (Newman, 1965) and "The Economic Effects of Malaria Eradication" (Barlow, 1968). A further reference will be made on these issues at a later stage.

Meanwhile it should be stressed that the main asset of developing countries is the people. It is a poor asset, if the population is crippled with diseases like malaria and the vast majority of the people remain ignorant. Socio-economic development requires a healthy alert population with hope and belief that something can be done, not one which is depressed and ill convinced of the hopelessness and inevitability of it all. In this context Myrdal (1968) focussed attention to the enormous difficulties experienced in the measurement in monetary terms, of the benefits of education and health.

Considering the complicated nature of the task of evaluation of health programmes, in recent years economists prefer to use some yardsticks like "input" and "output" as they are accustomed to apply in other fields. The "input" connotes resources invested, "output" refers to reduced mortality and morbidity, improved labour efficiency and its impact on productivity, and thus on the economic scene. Some advocates the inclusion of other areas like the effect of improved attendance in school, tourism and such matters, however trivial it may sound.

Because of a number of falacies, as yet it has not been possible to determine output in terms of money, that is, if 'X' is invested, how the output such as 'Y' should come up to within a given time, after successful run of a health programme like malaria control.

Malaria, Mortality and the Impact

Human suffering, be it due to malaria or any other disease cannot be measured. But the number of deaths, in a certain percentage of cases can be counted. Malaria has all along been known as one of the most important factors responsible directly and indirectly for infant and child mortality in areas where the disease is highly prevalent. The toll is much higher during epidemics which in undivided India were responsible for an estimated two million deaths against one million in normal years. This was the picture in respect of a population of about 300 million. Even in the recent years it is noted that where there is no organised programme for the control of malaria, such as in African countries South of the Saharas, the mortality amongst infants and children below 14 years is estimated at one million a year (WHO, 1974).

Almost half a century ago, in his Presidential address at the Fifth Indian Science Congress, Christophers (1924), one of the vanguards in the field of malariology, had remarked that "All men must die, but it is to be hoped that each will have a run for his money, so to speak, and live to a reasonable age, say 50 years". Interpreted in the correct perspective this would connote that the average man should live long enough, not only to have a fruitful life, but also to contribute sub-

stantially towards the economic well-being of the community.

In recent years the same view has been expressed by Bryant (1969) indicating that a child is an asset to yield future return. Thus, if the mortality at an early age is of sufficient magnitude, expectation of life in the community is shortened and the work force is relatively small. If, however, the control activities are effective, there should be reduction in deaths specially amongst infants and toddlers. This is indeed promising from many points of view.

But many may argue that such as ituation could be interpreted as a positive pressure on population growth, thereby exerting a downward trend in the economic field. This might appear to confuse the issue about the socio-economic benefits of controlling a disease; and therefore, this aspect has been elaborated somewhat at a later stage.

Malaria Morbidity and the Influence on Socio-Economic Sector

In the absence of more specific and reliable data on diseases in many developing countries, understandably, health administrators and economists had to lay emphasis on mortality statistics in determining the effects of health activities. Mortality is a simpler method of measurement. It can provide information on the prevalence of diseases that can be fatal and the extent to which these cannot be prevented from being fatal. But it does not provide other information like number of sick days, physical weakness, incipient illness, malnutrition and many other conditions.

Hence, the importance of morbidity, study of its prevalence, the degree and duration of disability (sickness) as well as debility, that is incapacitation for full participation in relation to national productive activities in various fields such as in agriculture, industry and many developing projects. Some indications have already been given earlier about the crippling effects of malaria in a community in respect of agricultural countries, especially in the tropics. It may also be added that in such countries often the malaria transmission season spans across the sowing to harvesting seasons, thus affecting both the activities. Often enough there is gross under-production. Besides, the quality is also affected. Understandably, therefore, the cost of production is high and the market value is low.

Against this background, attempts had been made by a number of workers to compute the likely financial losses directly attributable to malaria. Estimates made in early thirties by the Malaria Commission of League of Nations indicated that third of the global population suffered from the disease every year, that is about 650 million. Obviously the financial loss must have been quite enormous. One of the most pragmatic exercises undertaken in 1935/36 was related to India.

Some of the estimates were based on the evidence that 100 million people suffered from malaria annually (Chopra, 1933) and of this a third (33 million) were adults of productive age group earning about Rs 7.5 per month (Christophers, 1930). Further, on various considerations it was calculated that the actual working days lost per man, per year was about 15 days because of disability during primary attacks, relapses and reinfections. This was an extremely modest estimate as in hyper and mesoendemic areas the number of sick days used to be many more.

However, on the basis of these, the financial loss in the community in terms of lost wages, Sinton (1935) calculated the amount to a

level of Rs 1237 lakhs or Rs 12.3 crores (£ 10 million at the than prevailing exchange rates).

Debility, arising out of frequent attacks of malaria and lack of adequate treatment facilities, is known to result in loss of efficiency. The problem is compounded on account of economic stress and as a result malnutrition, because of loss of wages during the period of actual sickness and thereafter inability to work on full time basis. Some had estimated that such a loss of efficiency could vary from 10 to 25 per cent. Even at 10 per cent level and on the same adult wage scale indicated earlier, the loss of productive power equivalent could be computed at Rs 2 975 lakhs or Rs 29.7 crores (£ 22 million).

Thus without taking into account issues like the cost of medical attendance, loss to agriculture, mining, industry and in other fields, the financial loss on account of disability and debility alone due to malaria, amounted to Rs 42 crores (£ 32 million). One might argue that, had there been no efforts to control malaria and the situation was allowed to continue today at the same intensity, the economic loss to the community on account of loss of wages alone at the present level of population in India and the wage scale could have reached a staggering level of Rs 735 crores a year.

Control of Malaria and its Impact on the Economic Scene

Agriculture — Agriculture is the life line of developing countries. Since industrial countries are dependent on the developing ones for raw materials, there is some interdependence between the two groups. Because of this, health should be a matter of concern to both.

In this context attention is invited to some of the points raised at Alma Ata Conference in 1978 indicating about the existing gross inequality in health status of developing and industrial countries and that efforts be made to reduce the gap. It is also reiterated that promotion and protection of the health of the people is essential to sustained economic and social development.

There are, however, those who argue that improved 'health' will no doubt yield more, but because of ever increasing population growth, there will be more mouths to feed and, therefore, the gains achieved by the control of a disease, say malaria, will be nullified in the economic sense. But this appears to be an over simplification of the issue. Perhaps the concept is based on the assumption that the traditional methods of agriculture will be pursued while the labour force will continue to grow. It seems unlikely that due cognizance has been taken of the fact that better physical capacity helps in the acceptance of the improved and modern technology by the farmer. The spread of the high yielding variety programme and also the increase in the intensity of cropping as in Indian agriculture, is due not in small measure to the control of diseases including malaria (P. K. Mukherji, personal communication). A new agricultural technology requires more man-days of labour and greater physical efforts in terms of intensive cultivation through larger use of modern imputs such as fertiliser, pesticides, improved seeds and better irrigation. It should also be borne in mind that development of irrigation project itself needs healthy and hard working people.

One may also bring up the issue of small and marginal farmers, whose income from land, even if intensely cropped, is not sufficient to make both ends meet. The alternatives for them are either to look for some temporary work, away from home obviously as labourers, or to go in for ancillary occupations such

as animal husbandry, fisheries and such others along with farming. But again freedom from diseases is a prerequisite for the project to be successful.

Agricultural Industry – The story of malaria and its control in rubber plantations in Malaysia is too well-known for repetition except to point out that in the past, the breaking of new ground for expansion of plantation brought in its wake much malaria and less production. This may seem to be a paradox because such opening of new areas was aimed at greater production because of the earlier good harvest and better market value, which is always uncertain. But at present sickness due to malaria is no longer a problem in view of the launching of the malaria eradication programme from 1969. This has led to a considerable extention not only of rubber plantation but also of oil palm industry.

The economic scene in the tea industry is also familiar. There are volumes of reports pointing out that the loss in production could be directly attributable to malaria (MacDonald & Chowdhury, 1931; Manson & Ramsay, 1933; Gupta *et al.*, 1933), and the excellent results achieved after control of the disease (Strickland & Murphy, 1932).

In this context it may be added that in 1947, prior to the large scale use of residual insecticide like DDT, studies were carried out in the notoriously malarious areas like the Duars of West Bengal. Ray (1948) demonstrated that when the working population of a tea garden was placed on suppressive treatment with antimalarials for the entire tea plucking season, not only the normal output increased considerably as compared to the average of previous years, but the labour force was able to work over time during the entire season. In an identical neighbouring tea garden, which was kept as a comparison area and where neither antimalarial drugs nor any kind of antimalaria measures were taken up by the management, the incidence was so high that during major part of the season, plucking had to be abandoned or considerably slowed down thus affecting both quantity and quality.

Mining — Mining promotes export trades and as such the industry is an important source of income especially in terms of hard currencies. It is, therefore, in the national interest that the work should continue without any breakdown on account of sickness. In many countries there is general awareness of the problem of malaria and the expenditure incurred is considered as sound investment (Coulbourne & Stevenson, 1970).

Forestry — This is another source of substantial revenue. But most of the forest areas in very many countries in the tropics are malarious, and often under the influence of very efficient malaria vectors. Because of the high intensity of the disease the population density is low and the people are sick major part of the year. It is, therefore, necessary to import labour. But unless malaria is controlled the turnover is usually high and the expenses are so enormous that the enterprises ceases to be a commercial venture.

Power, irrigation, railway constructions and other engineering projects — In developing countries the activities of the type mentioned above are common. But it is not often clearly realised that closely associated with these projects there are invariably two major problems, the first being the creation of mosquitogenic conditions which is likely to increase receptivity of an area from malaria transmission point of view. The second is the 'tropical aggregation of labour' (Clyde, 1913) which results in the increased

vulnerability of the area on account of importation of malaria carriers. Experience would show that these factors could create explosive situations resulting in the slowing up of the activities. Moreover the turnover of labour often enough is so high as to increase the cost of construction to an unexpected level.

The "Victory in Panama Canal" can be cited as an example. The construction was hunted by malaria and yellow fever for years at the turn of the century. But effective control of the two diseases led to the completion of one of the world's greatest engineering feats (Harrison, 1978). In India there are many examples of delays and even temporary abandonment in the parts of projects like embankments, dams, irrigation, railways to name only a few.

Recent experience also clear that lack of an in-built system of control of some of the preventable diseases during construction and other projects, is often responsible for enormous financial loss, subsequent increased cost of operation besides delay in fulfilment of the target.

Malaria Control and Population Growth

It is an well accepted fact that in an effective malaria control programme, the first and immediate impact is noticed in the rapid reduction in the infant parasite rate and consequently in deaths. In stages the same is expected to happen in respect of toddlers and older children. As a consequence rise in population is to be expected.

Using population growth as an yardstick in measuring the effect of malaria control, Newman (1965) reported that the rise in the rate of growth increased upto 60 per cent in Sri Lanka since the inception of the control programme. This certainly resulted in a larger and more effective labour force. However, according to Barlow (1968), the gains attained was short-lived because the rise in population exerted a negative economic pressure.

On this issue some have raised the question whether decline in deaths after control of malaria is primarily responsible for increase in population. Although the present paper does not provide much scope for detailed discussions, it may be pointed out that there are other factors responsible for saving millions of lives such as antibiotics, the ever improving system of medical and health care, development of MCH facilities, to name only a few. In this context an earlier report by Frederickson (1960) regarding malaria situation in Sri Lanka and the population growth, indicates that three-fifths of the population of the country lived in the essentially non-malarious fifth of the parts of the country in the south west corner and the northern tip of the island. Against this background, the high population growth rate attributable to the control of malaria does not appear to be valid.

But, to say that control of malaria has no impact in the demographic field at all, would be quite unrealistic as it is well-known that any effective public health measures will undoubtedly reduce mortality and thus cause an increase in population growth. Thus, some have taken a balanced view that malaria control or eradication like other successful public health measures is bound to reduce mortality in young people and lengthen life span thus increasing the population pressure (Bruce-Chwatt & Meade, 1965). But are also some economists who believe that though improvement in health is accompanied by demographic changes, this does not justify leaving the health factor out of the economic development growth model. Furthermore, it has been empirically demonstrated through the evaluation of family welfare programme that the reduction

of infant mortality due to diseases has led to a larger acceptance of the family welfare programme. This implication is too obvious for elaboration.

Summing Up

It is not that there had not been a general awareness in the past about the socio-economic impact of malaria in a community, and the benefits accrued from control of the disease. Many had observed that in developing countries specially in the tropics the disease is all pervasive and contributed an important factor for economic misfortune, engendering poverty, diminishing the quality of food supply, lowering physical standard and hampering prosperity and economic progress. The magnitude of the problem had been so great that even as early as in 1916, the Second Pan American Sanitary Bureau Conference resolved that 'malaria must be eradicated whether it took one generation or ten.'

Many had tried to estimate the economic loss on account of malaria and the financial gains attained by controlling the disease, but at the same time recognised the difficulties in demonstrating convincingly either the loss or gain, in terms of money. Of these exercises, the one undertaken in India is worth noting. Without taking into account the expenses incurred for treatment of malaria cases, it was estimated in 1935 that on account of disability and debility alone, caused by malaria, the financial loss amounted to Rs 42 crores. Based on the same pattern of calculation today, and had there been no attempt to control the disease, the loss to the country would have reached a staggering level of Rs 735 crores.

Likewise in a number of countries attempts had been made to demonstrate the economic gains in the fields of agriculture, mining, construction projects and others through control of malaria. Although there have been general agreement in many quarters that the progress of development depended much on the effective measures for the control of diseases, particularly where malaria poses a serious problem, it has always been a sisyphean task to convince the planners and the economists about these benefits.

In retrospect one can see some lost opportunities in the recent past, when pilot projects were undertaken for the control of malaria in many countries, as a prelude to the launching of nation-wide control/eradication campaigns. It would seem that the preoccupation then was on feasibility studies, oriented primarily to technical issues. Sociological, health economics and management aspects under various political and administrative set-up did not receive due importance. Furthermore, in view of the initial success of the programme when eradication of the disease seemed to be attainable in near future, little attention was focussed to these vital issues. Perhaps the planners and health administrators, like many others, believed that once the disease was eliminated no further expenses were to be incurred and that funds could be diverted to other fields. Obviously this was an over-optimistic approach, as maintenance of the gains achieved needed full attention and due financial support.

Soon enough there arose other problems. In the more successful programmes, where malaria was brought down to an all time low level, the law of diminishing return began to be operative eventhough eradication of the disease had yet to be achieved. There were also some who argued that since malaria had reached almost to a vanishing point whether the expenses were still justifiable. As a result while some projects began to stagnate there was resurgence of the disease in others, because of downgrading of priorities and

thus funding. In one of such programmes the loss in terms of daily wages alone, as a result of resurgence of malaria, has recently been estimated to be quite considerable. This is even without taking into account the loss of productivity in many fields, nor the amounts that are now being spent first to contain the epidemic and later to undertake long term control of activities (Viswalingam *et al.*, 1972).

Disillusion came in respect of some other programmes, where after initial success there were varying degrees of set-back for one reason or other. Although there was an enormous reduction in malaria, the fact that eradication was not achieved as per target, hardened the attitude of the planners, economists and the administrators, who began to have second thoughts about investments in projects without any apparent return.

Against the above background, the dilemma becomes more acute when one realises the growing expectations of people of developing countries for better health and living standards, at a time when many have to face ever increasing financial constraints and competition for the limited funds between different departments and even programmes within the department.

Therefore, it becomes quite obvious that health plans specially in respect of preventable diseases should include socio-economic aspects. But at the same time it is felt that there is also the need for further development of a comprehensive system of economic evaluation techniques, besides those already recommended like opportunity cost, quantity/quality conflict, cost/benefit analysis to name a few (WHO, 1975). In the present context its increasing importance should be apparent, specially in the field of malariology when newer strategies are being conceived with a multidisciplinary approach and targets defined according to tactical variants (WHO, 1979). Assessment of the expected costs and benefits can be a useful tool (Cohen, 1972) in arriving at a correct decision about the wisdom of selecting strategies under different situations.

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Urban Malaria Scheme of the National Malaria Eradication Programme of India

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A phased urban malaria control scheme was introduced from 1971-72, which now operates in 125 towns covering 43 million people. Basically, it is an antilarval operation for mosquito control with special emphasis on malaria vectors, thus supplementing the general pattern of National Malaria Eradication Programme. The genesis and the role of this scheme have been outlined in this article. Emphasis has been laid to the fruitful implementation of the scheme considering the alarming rise of malaria cases in urban localities and its impact on the rural malaria control programme. Considering its similarity in operational aspects with that of the National Filaria Control Programme, the scheme has been proposed to be integrated with the latter.

Introduction

In the National Malaria Control Programme, NMCP (1953-58), only hyper meso-endemic areas covering 160 million population in the rural areas were taken up for the control work. In 1958, the NMCP was converted to National Malaria Eradication Programme (NMEP) where the main strategy of attack was on the coverage with residual insecticidal spray throughout the country. However, urban areas having a population of 40 000 and above were left out of this generalised indoor spray operation, and in them, only the peripheral belt was sprayed. Under special circumstances some areas with aggregates of labourers as well as riverine and receptive areas were also covered (e.g., Jumna belt). In these bigger urban areas antilarval operations by local bodies were recommended. While the incidence of malaria in the rural areas went down considerably due to NMEP operations, the disease incidence in towns remained a major problem. This was due to inadequate and uncertain and unsatisfactory operations by the local bodies as the plea of lack of resources which were expected to be supplemented by the State Government if necessary. As a result, the old slogan that "malaria is a rural disease" was reversed in many areas and cases were exported to the rural areas where the incidence used to be extremely low.

Realising the importance of urban malaria programme in the overall strategy and implementation of the NMEP in the country and also taking into account the financial difficulties experienced by the local bodies, a new scheme to deal with the problem was proposed, which emerged as Urban malaria scheme (UMS) during 1971-72.

The present paper discusses the magnitude of the urban malaria problem and the outlines of the activities of the urban malaria scheme.

The Problem

Incidence--In the early part of the century

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malaria problem was very acute in Bombay city. This was studied in depth by Bentley (1911) and Covell (1928, 1930) and the solution recommended by the latter and implemented by the municipality has remained a classic in the public health history of India. The confident note with which Covell (1928, 1930) declared that eradication (in those days) of this man-made disease could be achieved from Bombay was very inspiring. Even today, this much expanded city enjoys freedom from indigenous malaria.

Localised outbreaks of malaria were reported in the pre-eradication are (i.e., before 1958) from Lucknow, Calcutta, Bangalore and Ahmedabad (NMEP Directorate Manual, 1960). Localised focal out-breaks of malaria also occurred in Bombay city in 1963 and 1965, when many of the closed wells were opened up as war emergency measure, leading to prolific breeding of *A. stephensi*. Transmission stopped soon after the wells were closed and sealed again. Later on there were large scale transmission in many towns and cities of Andhra Pradesh, Madras and Mysore specially in Salem, Guntur, Vijayawada and some other smaller towns.

Active and Passive case detection (ACD & PCD) of malaria cases was started from 1960. ACD was however, not taken up in the cities of Bombay and Calcutta due to operational reasons. Active case detection ACD in qualitative terms was not as good in the urban area as the rural areas; nevertheless, this gave quantitative numerical figures about the number of cases and it became possible to compare the figures with the rural situation.

Roy *et al.* (1976) studied the urban malaria problem of Tamil Nadu from 1961-72 and observed that in 1963, 95 per cent of the cases came from urban areas. Between 1964-67, it constituted 80 per cent of the problem. Even today, Madras city contributes about 40-50 per cent of the total malaria cases in the state. The problem was reported to be quite serious, not only in big towns but also in many small towns. This problem was acute also in Andhra Pradesh, Gujarat, Rajasthan, and later on, Delhi and Chandigarh also showed large number of cases.

It is interesting to note that the states of Kerala, Sikkim, Nagaland, Mizoram and Meghalaya did not have urban malaria problem.

The extent of damage that the urban malaria was causing to the rural health was referred to by the "In Depth Evaluation Committee Report (1970)" where it was estimated that 25 per cent of the malaria cases detected in the urban areas were exported to rural areas before drug treatment could be completed.

The reverse was also true in some towns, i.e., the disease got introduced into the towns from the endemic rural areas through migration of people as well as through influx of seasonal labourers. Thus rural and urban malaria got mutually supported.

The number of cases in the ten major cities of India for the period 1975 to 1979 is given in Table 1 for general information.

Vectors—*A. stephensi* and *A. culicifacies* play important role in the transmission of urban malaria in India, the former in the central part of the town and the latter in the peri-urban areas. *A. stephensi* prefers small breeding places, like wells, cisterns, overhead tanks and generally breeds profusely in clean potable water. This mosquito can however tolerate some salinity and some organic contamination also. N. L. Sitaraman (personal communication) found *A. stephensi* breeding in the drains with heavily polluted

Table 1– Malaria Positive Cases in Ten Major Cites of India (1975-79)

Name of cities	Population in million	1975	1976	1977	1978	1979
Ahmedabad	1.67	41 799	37 500	21 372	26 705	30 506
Bombay*	4.98	2 713	4 231	3 180	2 635	1 605
Baroda	0.47	52 507	60 239	30 557	29 866	14 424
Bangalore	1.65	85	365	627	952	820
Bhopal	0.39	6 264	5 215	3 577	2 656	2 339
Chandigarh	0.23	4 238	16 294	61 253	34 748	32 283
Calcutta	5.64	2 692	3 099	1 894	1 244	2 342
Delhi	3.52	11 165	19 204	1 11 089	3 32 683	75 625
Hyderabad	1.27	3 493	4 663	3 339	2 559	1 288
Madras	2.17	36 207	40 631	28 437	24 953	33 463
Total	21.99	1 61 193	1 91 441	2 65 325	4 59 001	1 94 695

*All imported cases.

water in Vijayawada, Guntur, etc. of Andhra Pradesh and noted that *A. stephensi* could thrive side by side with culicine breeding. This finding was a decisive factor in taking up culicine control activity also under the UMS.

A. culicifacies plays a very important role in the peri-urban areas. Some towns have agricultural plots inside or very close to the urban areas and the vector freely infiltrates into the urban areas. Amongst urban areas, Delhi city showed the largest number of malaria cases in the country in the recent years and Pattanayak *et al.* (1977) noted a changed pattern of malaria transmission in the city. Though the overall sporozoite rate of *A. stephensi* and *A. culicifacies* for the period of study was estimated at 0.39 and 0.18 respectively, the area under the influence of *A. stephensi* only, had shrunken very much and the extended city had the *A. culicifacies* influence. These findings are of great importance in streamlining the urban malaria control strategy. There is a strong need to evolve a methodology which would not only help to eliminate breeding foci of *A. stephensi* but also a diverse range of *A. culicifacies* breeding which is responsible for the bulk of malaria in urban Delhi.

Before the reclamation of the Salt Lake near Calcutta, *A sundaicus* was an important vector in the peripheral part of that city but its importance for malaria transmission is now lost. In some of the coastal towns falling within the influence of the erstwhile distribution of *A. sundaicus*, this vector may again play important role if it can re-establish itself. As a result of indoor residual spray, this vector is nearly extinct and is having a very low density, if at all found. *A. annularis* may also play some role in some towns in coastal Orissa, which are under the influence of this vector. No detailed studies have however, been carried out in the recent years and its precise role in this regard is not known.

Urban Malaria Scheme and Criteria for the Selection of Towns

As a result of greater realisation about the importance of the urban malaria, it was decided that control operations should be started in the urban areas. The first reaction was to cover all the left out towns with a population over 40 000. But on closer scrutiny, it was noted that all towns were not malarious and only those with the problem should be identified. One-hundred-thirtytwo such towns were identified but due to financial constraints it was decided to take up the towns in a phased manner. The criteria for selection of towns under UMS is followed as:

1. The town should have population above 40 000. In some exceptional cases, an agglomeration of small towns has been included in this scheme.

2. The higher the incidence of malaria the greater was the priority attached. The minimum Annual Parasite Incidence (API) should be two or above.

3. Towns adjoining highly malarious areas would be given preference.

4. Towns already under the National Filaria Control Programme (NFCP) would not be selected for UMS to avoid duplication of work.

5. Some towns with bad past reputation of urban malaria control were included under the scheme to prevent the re-establishment of the disease. The lack of ACD and poor PCD in these towns did not provide accurate API figures and therefore, this precaution had to be taken.

During 1971-72, the initial selection was restricted to 22 towns. Six more towns were added during 1972-73 and till 1976-77 only 28 towns continued to be uncer this scheme. Further, 39, 36, 12 and 10 towns were added during 1977-78, 1978-79, 1979-80 and 1980-81 respectively and a total of 43 million people spread over 125 towns are now under this scheme which is spread over 16 States and two Union Territories.

Operational Aspects of the Scheme

Organisational set up — The Directorate of NMEP at Delhi is the headquarters of the UMS which provides administrative and technical guidance, field research, training and evalution of the scheme. The scheme is operated through State/Union Territory Governments. Health Directorate of the State/Union Territory executes the programme either through the municipalities or directly through its own organisation.

Financial arrangements — UMS to start with was a centrally sponsored scheme. The financial arrangements of central assistance under this scheme was an operational cost and cost of material and equipments.

Operational cost of the scheme is the expenditure on staff. The cost is an additional subsidy to the committed level of expenditure incurred by the local bodies/states. Under the pattern of assistance, material and equipments were procured centrally and supplied directly to towns with intimation to States and Union Territories. No cash subsidy for such expenditure was envisaged till 1978.

From 1979 onwards, this scheme has become a centrally assisted programme on 50 : 50 sharing basis with the states. Under the new pattern of assistance, states have to procure larvicides like Mosquito Larvicidal Oil (MLO), superior kerosene oil, transports and sprayers in addition to operational cost, while Centre is providing larvicides other than the two indicated above.

Operational Methods

Broadly speaking, the scheme is the supplementary to mosquito control operation particularly at the aquatic stages of mosquitoes, with special emphasis on malaria control. Various methods are being used in the larval control operation.

Engineering methods — Drainage (subsoil, surface) and other sanitary engineering work come under the major category and no budget has been provided under the scheme to undertake these measures. Temporary measures such as cleaning and deweeding, channelling, filling and drying water collections as well as management of waste water fall under the minor category of engineering measures.

Larviciding—Due to extensive urbanisation, practically all the cities and towns are growing with increasing boundary with shanty township conditions in the periphery. This facilitates extensive breeding of mosquitoes and the problem is becoming more acute day by day. As a result, town planning work is not keeping pace with the need. The chemical larviciding is the only answer to such situation. Mineral oil, now Mosquito Larvicidal Oil (MLO) and paris green (copper acetate arsenite) are the oldest larvicides. To these larvicides new additions like temephos, fenthion and pyrethrum based emulsifiable oil have been made in the programme. The larviciding operations are carried out at weekly intervals throughout the year.

Biological control—The biological method of control is supplementary to the chemical larvicidal measures. A large number of pathogens, parasites and predators of mosquito as well as larvae have been recorded but except the larvivorous fishes other organisms have not been seriously tried in the field. One of the limitations of the biological control agents including the larvivorous fishes is the need to rear them in large number. The larvivorous fish once adjusted to an environment may produce dramatic results. Sitaraman *et al.* (1975) have used *Gambusia affinis* in Hyderabad city (AP) at the rate of five per square metre and reported remarkable control over malaria transmission. Similarly Sitaraman *et al.* (1976) have pointed out that the use of *Poecilia reticulatus* at the rate of 50-100 fish per well has reduced *A. stephensi* breeding and kept at a low level up to 48th day. Joshi *et al.* (1976) as well as Sasa *et al.* (1965) have used *Poecilia reticulatus* in the control of *C. quinquefasciatus* breeding near Delhi and in Bangkok respectively and were able to bring down the larval density to a very low level. Programme officers of all the states having urban malaria problem have been requested to introduce both *Gambusia affinis* and *Poecilia reticulatus*. But due to environmental and organisational difficulties, the application is not yet uniform.

Adulticide operation—Though indoor residual spray with insecticides like DDT, BHC or malathion is not taken up in the urban areas, the peripheral areas of a town or city are covered with adulticide on getting the report of the malaria case. UMS provides for the focal adulticide spray of two per cent pyrethrum extract in 50 houses around the malaria case.

Application of insecticides by Ultra Low Volume (ULV) and Thermal Fogging techniques have been recently taken up in some towns. The vector species and almost all other mosquitoes, whether resting indoor or outdoor are exposed to the action of ULV and fogging.

Surveillance—As per Chadha Committee recommendations the active case detection in urban areas, particularly in towns with more than 40 000 population, was withdrawn

and there was substantial black out of malaria information except in case of passive case detection. Now under the modified plan of operation, Govt. of India has agreed to provide one surveillance worker per 20 000 population in each urban areas and also to intensify the PCD activities.

The scheme is proposed to be integrated with that of National Filaria Control Programme, wherever these two diseases co-exist, as larviciding is common to both the diseases in urban areas.

Discussion

Farid (1976) pointed out that for the control of urban malaria, permanent engineering works like drainage filling and water management would prove more useful and UMS does not provide funds for this aspect due to the enormous cost involved.

For successful implementation of the scheme, two pronged attack is necessary, i.e., health education as well as strict enforcement of bye-laws for reducing the mosquitogenic conditions. The success of the scheme in Bombay was largely due to the second approach. Health education is also very essential as even domestic water containers have been found to provide a profuse source of breeding of *A. stephensi*. In rich houses in cities, water coolers, etc. also create a problem and the awareness of the malaria problem and means to prevent stagnation of water can go a long way in reducing the menace. Multiplicity of administrative units within a given Municipality or a Corporation also causes the problem of effective coordination. Efficient functioning of the coordinating bodies under the direct and constant watch of the top administrative functionary is a must and has given dividents. The suggestions given by Covell (1928, 1930) holds good even today after five decades.

With increased urbanisation, it appears that the problem will be a matter of still greater concern in days to come if not properly tackled. It is a big public health challenge and creation of the UMS component filled a much needed gap. In spite of various constraints, good work is being done by the workers for keeping the disease under control. As the operations are similar in many respects, there is a proposal to integrate the National Filaria Control Programme and the UMS, especially the mosquito control component.

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Investigation on Simian Malaria in India, and its Potential as a Source of Zoonosis*

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An enzootic of simian malaria in which 51 per cent of the monkeys were found infected was detected in Nilgiri district of Tamil Nadu, India. The vector responsible was *A. elegans* which belongs to the *A. leucosphyrus* group. The investigation on the bionomics of this species revealed extreme preference of these mosquitoes to simian blood. They were never captured indoor or collected from monkey baited net traps kept at ground level or on platforms kept at some height. They readily fed on wild monkeys roosting on top of arecanut trees at night. In the laboratory, these mosquitoes were found to be extremely reluctant to feed on human volunteers even when kept hungry. From these, it appears that this focus of simian malaria is not likely to act as a zoonotic reservoir for human infection.

Introduction

Eyles *et al.* (1960) reported accidental infection of *P. cynomolgi bastianelli* in laboratory workers. Since then, successful inoculations of *P. cynomolgi bastianelli, P. cynomolgi* (M. strain) and *P. brasilianum* into human volunteers have been reported in USA (Beye *et al.*, 1961; Coatney *et al.*, 1961; Schmidt *et al.*, 1961; Contacos *et a.l*, 1962 and 1963).

The finding of natural infection of *P. knowlesi* in an American white man working in the jungles of Malaya has conclusively proved that simian malaria could be a zoonotic disease under certain environmental conditions (Chin *et al.*, 1965). Deane *et al.* (1967) and Fong *et al.* (1971) have further confirmed the above findings. Natural infection of *P. simium* and *P. knowlesi* in man has been reported in Brazil and Malaysia respectively by them.

Ramakrishnan and Mohan (1962) reported an enzootic of simian malaria in *Macaca radiata radiata* monkeys in Nilgiri district of Tamil Nadu, India. Pattanayak (1963) also found a reservoir of simian malaria in Kozhikode district of Kerala state adjoining the Nilgiris. Choudhury *et al.* (1963a) incriminated *A. elegans* as the vector of simian malaria in the Nilgiris and considered this species to be responsible for the enzootic focus in the local monkeys.

In order to determine whether this reservoir could act as a source of zoonosis, an investigation was carried out in a small hamlet covered with dense tropical forest in the foot hills of the eastern side of the Nilgiris. The fruit gardens consisting of mango and jackfruit trees and the arecanut plantations contained in the hamlet were frequently being visited by the monkeys. The results of the

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investigation have been presented in this paper.

Material and Methods

All the links in the chain of transmission of simian malaria, *viz.* the infected monkeys, the species of simian malaria parasites and *A. elegans* mosquitoes were indigenous to the Nilgiris.

The monkeys were *Macaca radiata radiata* Geoffroy which is synonym of *Silenus sinicus*. *P. cynomolgi* and *P. inui* found in the local monkeys were utilised for the investigation. Wild caught *A. elegans* mosquitoes and some laboratory reared mosquitoes obtained from the eggs of this species were used. Frequent attempts to colonise this species failed.

Marking of the mosquitoes for the release experiments was carried with printer's gold and silver dust in the way mentioned by Majid (1937) and Russell *et al.* (1944). The marking was also done by a new method. The dorsum of the thorax of three days old *A. elegans* mosquitoes was painted with a dilute solution of aluminium paint in ether after lightly anaesthetising the mosquitoes. The paint left a bright silvery spot on the thorax.

Results

Infection in the monkeys — One hundred and seventy *Macaca radiata radiata* monkeys were trapped in the Nilgiris during the investigation. Table 1 shows the malarial infection in them. It can be seen that 51% of these monkeys were showing infection on capture, the predominant species being *P. inui* (52.8%). Among the remaining infections, 36.7% were a mixture of *P. cynomolgi* and *P. inui*. Except Knowles (1919) who found simian malaria parasites in Assam, all other workers detected simian malaria parasites in *Silenus sinicus* monkeys in South India.

Natural infection in the mosquitoes — A total of 3 476 anopheline mosquitoes consisting of 14 different species was collected and dissected for the presence of sporozoites in them. Out of these, 55.8% were *A. tessellatus* and 10.3% were *A. elegans*. Natural infections of simian malaria parasites were only found in *A. elegans* (Choudhury *et al*, 1963a). Though *A. tessellatus* was not incriminated, this species was found to be good experimental vector of simian malaria (Choudhury *et al*., 1963b). Hence attention was attracted to this species because of their abundance in the investigation area.

Table 1 — The Species of Parasites in *Macaca radiata radiata* Monkeys Captured from Different Places of Nilgiris

No. of monkeys captured	No. found infected	Per cent infected	Prevalence of species of parasites (%)		
			P. inui	*P. cynomolgi*	*P. cynomolgi* and *P. inui* (mixed)
170	87	51.2	52.8	10.3	36.7

Table 2 — Results of Precipitin Tests of Blood Meals of *A. elegans* and *A. tessellatus* Collected from the Investigation Area

Species of mosquitoes	No. of blood meal tested	Per cent positive			Remarks
		Monkey	Bovine	Human	
A. elegans	125	100.0	0.0	0.0	Simiophilic index 100.0
A. tessellatus	639	0.0	83.2	0.3	

Table 3 -- The Results of the Release Experiment Carried out with *A. elegans* Mosquitoes

Sl. No.	Date & time of release	No. of mosquitoes released	No. recaptured on subsequent day	No. found fed	Distance between point of release and capture (metres)		No. of wild unmarked *A. elegans* captured		
					Minimum	Maximum	Freshly fed	Unfed	Total
1	15.5.64 (7.30 a.m.)	51 Lab. reared with gold dust	11 (21.5)	2 (18.1)	15	400	Nil	Nil	Nil
2	29.7.64 (7.00 p.m)	63 Wild with gold dust	9 (14.2)	9 (100)	150	300	37	Nil	37
		32 Lab. reared with silver dust	24 (65.6)	24 (100)	150	300	—	—	—
3	3.8.64 (6.45 p.m.)	60 Lab. reared with aluminium paint	7* (11.6)	6† (85.7)	10	25	28	6‡	34§

* Search was made only for two hours in the morning.
† One unfed mosquito was found injured and was not in a fit condition to fly.
‡ Containing partially digested blood.
§ 33 Out of 34 showed sporozoites.

Note: Figures in parentheses are in percentages.
All fed mosquitoes showed monkey blood by precipitin test.

Feeding preference of A. elegans and A. tessellatus — The results of the precipitin tests carried out with the blood meals of these two species of mosquitoes are given in Table 2.

It can be seen that 88.2% of *A. tessellatus* showed preference for bovine blood. Not a single blood meal of this species showed monkey blood. Whereas all the 124 blood meals of *A. elegans* mosquitoes showed monkey blood only. This extraordinarily high figure recorded here showed a very selective affinity of this species for monkey blood. Surprisingly not a single *A. elegans* mosquito could be collected during this investigation from monkey baited net traps kept at ground level or on a platform kept at a height of 5 metres.

Bionomics of A. elegans — In the investigation area, breeding of *A. elegans* was detected in the arecanut garden during the months of June to september, 1963 and 1964 in association with *A. tessellatus*, *A. maculatus*, *A. hyrcanus* and *A. barbirostris*. They were found in temporary water collections at the base of the arecanut trees, formed as a result of intermittent irrigation practised in these gardens. The adults were found resting on the exposed roots of the arecanut trees in the caved-in-channels connecting one arecanut plot with another lying on a lower level.

They were never collected indoor from human dwellings, cattle sheds, or outdoor from monkey baited net traps. But freshly engorged *A. elegans* were collected from the day time resting places in the morning in the arecanut gardens. The blood meals of these mosquitoes showed monkey blood. To solve this, release experiments with marked females were undertaken. The data of the release experiments are shown in Table 3.

It can be seen from the Table that in the first series, out of 51 laboratory reared and gold dusted *A. elegans* mosquitoes released in the morning in one of the arecanut gardens, eleven were recaptured on the subsequent day. Two of these mosquitoes were freshly fed

and showed the presence of monkey blood. The results were inconclusive except the finding that some of the released mosquitoes had fed on the monkeys.

The second release experiment was carried out at dusk and planned in such a way that the released mosquitoes could imbibe a blood meal from a caged monkey kept on a platform about 6 metres above the ground level or from wild monkeys found roosting on nearby arecanut trees. The released mosquitoes included 32 laboratory reared, dusted with silver; and 63 wild caught, dusted with gold. The point of release was 25 metres from the caged monkey and about 150 metres from the wild.

All the released mosquitoes were found to fly upwards on release. One gold dusted mosquito came and settled on the outside of the monkey baited net trap but left without making an attempt to feed on the monkey.

Searches were made during the night from the monkey bait but no *A. elegans* mosquito was collected. Thirtythree marked mosquitoes fully fed, were collected next morning from the bottom of the arecanut trees on which the monkeys were resting during the night. Two mosquitoes were actually seen in the process of coming down fully engorged. Thirtyseven unmarked *A. elegans* fully fed were also collected during this period from the same spot. The blood meals of all the fed mosquitoes showed the presence of monkey blood.

The above observation showed that this species has a strong preference for monkey blood. They are most probably attracted by smell of the monkeys and fly upward to about 15 to 20 metres in search of the host. They feed at that altitude and rest on the arecanut leaves during the night. Being disturbed by the monkeys in the morning, they come down almost vertically as too much engorgement does not allow them any liberty to fly in any other direction.

Out of a total of 95 mosquitoes released, 33 were captured back giving a capture rate of 34.7%. In case of laboratory reared silver dusted mosquitoes, the capture rate was even higher, the figure being 75%. Since these mosquitoes were reared from eggs, they were earnestly looking for their first blood meals. It appears fantastic to capture them in such large number taking into consideration the place of capture which was full of weeds and other vegetations. The possibility of the sucking tubes being contaminated with the printer's dusts was considered.

Hence in the third release experiment, 60 three-days old painted mosquitoes were released at dusk just below the arecanut trees where monkeys were found resting for the night. Next morning between 5 to 7 a.m., seven painted mosquitoes, six fully fed and one unfed were captured. The unfed mosquito was found to be injured and was unable to fly properly. Thirtyfour unmarked *A. elegans* mosquitoes, of which 28 were fully fed were also captured during this period. No attempt was made to collect any more mosquitoes after the initial collection. The percentage of capture of the released mosquitoes was 11.6% in this series. It could have possibly been higher if the searches were continued for a longer period All the blood meals showed the presence of monkey blood.

The above experiments conclusively showed that these mosquitoes were attracted to the monkeys roosting on tall arecanut trees and remained with the host of predilection during the night and fed on it during this period. Out of 34 unmarked *A. elegans* mosquitoes collected during the last experiment, 33 showed sporozoites. This shows the magnitude and efficiency of this species as a vector of simian malaria.

Table 4 — Details of the Volunteers, the Dose of Inoculation and the Species of Parasites Employed*

No. of human volunteers (male)	Age (years)	Date of infective bite	Dose of inoculation†	Period of observation (in months)	Untoward symptoms
1	28	27.08.1963	3	6	Nil
2	20	09.09.1964	3	7	Nil
3	21	09.09.1964	2	6	Nil

* Mixed infection of *P. cynomolgi* and *P. inui*.

† Presence of sporozoites was detected by post-prandial dissection.

These mosquitoes somehow feel shy to enter a trap containing a monkey both on the ground as well as on platform kept on some height. This is contrary to the finding of Wharton *et al.* (1962) of *A. leucosphyrus* and *A. pujutensis*, other natural vector of simian malaria being collected from monkey baited net traps in Malaya. *A. hackeri*, another natural vector of simian malaria in Malaya, was caught in monkey baited net traps one hour after sunset. Macdonald and Traub (1960) reported that both *A. leucosphyrus* and *A. balabacensis introlatus* would attack man and were actually collected from human baited traps at ground level and in forest canopy in the hill forest of Malaya. *A. elegans* appears to be definitely different in this respect. Not a single specimen of this species could be collected from human baits or dwellings. Even in the laboratory, it was very difficult to coax them to feed on human volunteers. Many times, it was seen that they died without taking a blood meal when attempts were made to feed them only on human volunteers.

Experimental transmissibility of simian malaria to human volunteers — Human volunteers were bitten by infected *A. elegans* mosquitoes having sporozoites in their salivary glands. The details of the transmission studies are given in Table 4. None of the volunteers showed any demonstrable parasites by microscopical examination. The reluctance of the infected mosquitoes to feed on human volunteers did not allow a heavy dose of infection to be given to the volunteers. No further intensive effort was made as this species did not absolutely show any evidence of contact with man during this investigation.

Discussion and Conclusion

The aim of this study was to explore the possibility of simian malaria acting as a zoonotic disease under Indian conditions. There was certain amount of urgency in this respect and apprehension also. In recent years, it has definitely been established that simian malaria parasites could be transmitted to human volunteers. The chain of events started with the accidental infection in 1961 of few workers engaged in research on simian malaria in USA with *P. cynomolgi bastianelli*. This parasite has got fairly good resemblance to *P. vivax*. Since then, *P. cynomolgi* (M.strain) and *P. brasilianum*, a quartan parasite of the monkeys of the New World were successfully transmitted to human volunteers. Matters reached the peak, when Chin *et al.* (1965) described the natural infection of a white man in Malaya with *P. knowlesi*.

In India, the finding of natural infection in the monkeys was mostly restricted to the

southern part. In the north, thousands of *S. rhesus* monkeys examined for experimental work, did not reveal any natural infection in them. Donovan (1920) reported one infection of *P. cynomolgi* out of 89 monkeys examined in the Nilgiris. Mulligan and Swaminath (1940) reported the finding of one *S. sinicus* monkey infected with *P. inui* in the foot hills of the Nilgiris. During the course of another two decades, the small focus has expanded into an enzootic proportion among the monkeys. Attention was naturally attracted to this enzootic simian malaria and investigations were planned to find out whether there was any possibility of this reservoir of simian malaria parasites acting as an extra human source of infection to man.

Close association between man and monkey was mostly found to exist in different plantations of the Nilgiris. In the foot hills in Kallar, there is a good acreage of arecanut plantation where many people are employed. They come from distant villages in the plains and work in the garden during the day. The coffee plantations located between 2 000 to about 4 000 feet employ comparatively less labour as the work is mostly seasonal.

Careful examination of the captured monkeys revealed that 51% out of a total of 170 examined, were infected in nature. Not a single monkey was trapped which was showing an acute infection. This is most probably due to the fact that during the acute illness they must be very quiet and would avoid getting into a trap. When kept in captivity some of them had bouts of parasitaemia during which mosquitoes could be infected by feeding on them. Thus, it appears that a ready source of infection is available to the vector mosquito in nature.

The vector responsible for this enzootic simian malaria has been found to be *A. elegans* which belongs to the *A. leucosphyrus* group. The study of the bionomics of *A. elegans* has revealed that this species is comparatively shy and less aggressive in nature in contrast with four other members of the *A. leucosphyrus* group which have been incriminated as vectors of simian malaria. Some of them were found to attack man and others were readily collected from human baits. In contrast, not a single *A. elegans* mosquito was found on human bait during this study. The precipitin tests carried out with blood meals of these mosquitoes revealed the presence of only monkey blood in them. Under laboratory conditions, it was observed that most of the laboratory reared *A. elegans* mosquitoes would prefer to die without a blood meal than to feed on human volunteers. The complete dependence of these mosquitoes on monkey was farther corroborated by the following findings.

Laboratory reared marked *A. elegans* mosquitoes released on the ground level went upto an altitude of 10 to 15 metres for the monkeys which were resting on the top of arecanut trees situated about 100 yards from the point of release.

From above, it can be concluded that transmission of simian malaria to man in the Nilgiris is probably not possible due to the presence of a vector which is shy, reluctant to feed on man and completely dependent on monkeys for their blood meal.

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A Focus of Chloroquine Resistance in *Plasmodium falciparum* in Shaktinagar Area of Mirzapur District, Uttar Pradesh

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In Shaktinagar, a focus of chloroquine resistance in *P. falciparum* was detected in 1980. In one ***in vivo*** test carried out with 600 mg and two with 1500 mg base (adult dose); 8 out of 9, 4 out of 7, and 2 out of 11 cases respectively were showing persistent asexual parasitaemia on Day 7. The results were confirmed with ***in vitro*** macro tests in Shaktinagar as well as in a neighbouring village of Waidhan PHC of Sidhi district of Madhya Pradesh. Steps taken to control the spread of disease were partially successful.

Introduction

Shaktinagar area of Mirzapur district, Uttar Pradesh, was hyperendemic for malaria, and despite NMEP's activities since 1958, the area persistently remained in attack phase. With the progress of construction activities in the area by the National Thermal Power Corporation (NTPC), there was a steady rise in malaria cases with two suspected deaths due to cerebral malaria in 1979. Enquiries made with local medical officers revealed a lack of proper response to chloroquine from the middle of 1979, and many clinicians were using sulfalene + pyrimethamine combination to cure the disease.

In view of the recent reports of chloroquine resistance in *P. falciparum* in north eastern parts of India (Sehgal *et al.*, 1973 and Chakraborty *et al.*,1 979), and as part of NMEP's countrywide programme for monitoring the chloroquine resistance in this plasmodial species, investigations were undertaken in the Shaktinagar area to ascertain (i) the sensitivity of *P. falciparum* to chloroquine, (ii) the impact of remedial measures to control the disease, and (iii) the status of insecticide resistance of the probable vectors.

Material and Methods

Description of study area — Shaktinagar is located at the tri-junction of Uttar Pradesh, Madhya Pradesh and Bihar, and is separated from MP by a small stream (Ballia Nala). It is a hilly terrain of about 10 km^2 area, with a population of about 38 000 inhabitants, of which three-fourth consists of labour force drawn from Uttar Pradesh, Madhya Pradesh, Bihar and Orissa. Shaktinagar is now a growing industrial complex. The project was started in 1978 and is likely to be completed by 1985. There are 2 super thermal power stations, along with KJB railway construction project and Bina Coal Mines. The area is under Mirzapur Primary Health Centre (PHC) and 3 more medical institutions look after the medical needs of the workers.

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Monitoring technique — P. falciparum cases were selected by biased mass blood surveys between February to June 1980. Individuals who had shown the presence of chloroquine in urine (Lelijveld and Kortmann, 1970) before the administration of drug, or gave history of taking other antimalarials, were not included in this study.

This *in vivo* and macro *in vitro* tests for drug resistance were carried out as per standard technique (WHO, 1973). The adults (15 years and above) received full dose, depending upon the test (600 mg or 1500 mg chloroquine base), and the children in the age groups 1, 1-4, 5-8 and 9-14 years were given 1/8, 1/4, 1/2, and 3/4th of the adult dose respectively for the *in vivo* test. The potency of the chloroquine tablets was tested at the Central Drug Research Institute, Lucknow.

As a rule, one-hundred thick blood smear field were examined for the detection of the asexual parasites, and their density per microlitre (μl) was estimated on the basis of count against 300 leucocytes (i.e., count $\times$ 25).

Remedial measures—Attempts were also made to control malaria and prevent the spread of chloroquine resistance by: (i) intensification of active and passive case detection of the malaria cases with presumptive chloroquine treatment; (ii) four rounds of mass blood surveys in six months to detect missed cases; (iii) two rounds of mass drug administration (MDA) with chloroquine, and one round with sulfalene + pyrimethamine providing 90 to 95% coverage in each round. For MDA, 600 mg base of chloroquine was given to adults; other received as per the agewise proportion. Two tablets of sulfalene + pyrimethamine (each having 500 mg base of sulfalene and 25 mg base of pyrimethamine) were given to adults, and younger age groups were given proportionately low dosages. This drug combination probably used for the first time in India; (iv) prompt radical treatment of all malaria cases, adults with *P. falciparum*, 600 mg chloroquine base and 45 mg primaquine base were given simultaneously on the same day and *P. vivax* with a total of 600 mg chloroquine base + 75 mg primaquine; (v) screening of all new labourers for *P. falciparum* and treating with sulfalene + pyrimethamine; and (vi) mosquito control by: (a) spraying malathion at the rate of 2 g/m^2 in January, February, and three rounds of DDT at the rate of 1g/m^2 in March, May and August 1980, (b) pyrethrum fogging once a week in the entire project area from March, 1980, and (c) weekly application of larvicidal oil at all suitable places from March, 1980. The oil was applied at the rate of 170 to 225 litre per hectare or one litre per 50 linear metre for channels or 20 ml/m^2 on other water collections not used for drinking purposes.

Results and Discussion

Chloroquine resistance — Results of *in vivo* tests are given in Table 1, and *in vitro* macro tests in Table 2 and 3. In February 1980 the "alternative test" with 600 mg base (adult dose) showed persistence of asexual parasites in eight out of nine cases (88.8%) on Day 7, whereas with 1500 mg base (adult dose) asexual parasites persisted in four out of seven cases (57.1%) on Day 7 i.e., RII response in Day 7 test. In March-April 1980, another *in vivo* study with 1500 mg base (adult dose) at the same place revealed persistence of asexual parasites in two out of eleven cases (18.2%). On Day 14, two more cases showed reappearance of asexual parasites. Thus four out of eleven cases (36.3%) showed either lack of parasite clearance or reappearance of the same within 28 days of the observation period.

Table 1—Results of *in vivo* Tests Carried out in Shaktinagar Super Thermal Power Construction Project (NTPC) for Determining Chloroquine Sensitivity during February-April, 1980

Period of test		Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 10	Day 14	Day 21	Day 24	Day 28
(A) Alternative test (adult dose 600 mg base)														
Feb. 1980	(a)	9/9	9/9	9/9	8/9	8/9	8/9	8/9	8/9					
	(b)	100.0	100.0	100.0	88.8	88.8	88.8	88.8	88.8	.....Study closed				
	(c)	5 489	4 603	3 272	2 836	2 436	2 089	1 856	1 850					
(B) 28-Days extended field test (adult dose 1500 mg base)														
Feb. 1980	(a)	7/7	7/7	7/7	6/7	6/7	4/7	4/7	4/7					
	(b)	100.0	100.0	100.0	85.7	57.1	57.1	57.1	57.1	.....do.....				
	(c)	3254	2521	1829	1393	886	596	525	532					
March-April, 1980	(a)	11/11	11/11	11/11	11/11	9/11	5/11	2/11	2/11	1/11	4/11	4/11	3/9	3/9
	(b)	100.0	100.0	100.0	100.0	81.8	45.4	18.2	18.2	11.1	36.4	36.4	33.3	33.3
	(c)	3 729	1 777	818	577	179	104	100	145	370	463	547	100	230

Note : (a) No. positive for asexual stage/No. examined.

(b) Per cent positive.

(c) Mean arithmetic asexual parasite density of the whole group per microlitre.

N. B. : *in vivo* Test using 1500 mg chloroquine schedule in May 1981 revealed that out of the 19 cases examined, 17 were positive for asexual parasite on Day 7, i.e. RII level of resistance.

Table 3 — Results of *in vitro* Test Carried out in Shaktinagar in September, 1980

Case No.	Pre-culture count Parasite/ mm³ blood	Large %	Small %	Control K_1	Control K_2	Mean	Schizont count per 300 WBC and % control on exposure to various chloroquine concentration (nmol) 0.25	0.50	0.75	1.0	1.25*	1.50	2.0	3.0
1	7 245	33	67	77	83	80	33 (41.3)	14 (17.5)	9 (11.3)	3 (3.8)	2 (2.5)	0	0	0
2	75 225	47	53	143	135	139	96 (69.0)	63 (45.3)	49 (35.2)	17 (12.2)	9 (6.5)	3 (2.2)	0	0
3	19 125	35	65	33	39	36	—	7 (19.4)	—	2 (5.5)	—	0	0	—
4	14 400	31	69	36	30	33	11 (33.3)	7 (21.2)	5 (15.1)	3 (9.1)	1 (3.0)	0	0	0
5	11 400	34	66	47	49	48	9 (18.7)	5 (10.4)	2 (4.2)	0	0	0	0	0
9	14 275	36	64	127	115	121	89 (73.5)	57 (47.1)	41 (39.9)	11 (9.1)	—	2 (1.6)	—	—
Mean	23 617	64	36	77	75	68	(47.6)	(25.5)	(21.2	(6)	(3)	(0.8	0	0

* Discriminatory concentration of chloroquine.

Note : Figures in parentheses are % control.
K_1 & K_2 = Control No. 1 & 2.

Table 3—Results of *in vitro* Macro Test in Village Sakhanwa (Waidhan PHC), Sidhi District, Madhya Pradesh (near Shaktinagar NTPC) during June, 1980

Case No.	Pre-culture count			Control			Schizont count per 300 WBC and % control on exposure to various chloroquine concentration (nmol)					
	Parasite/ mm³ blood	Large %	Small %	K_1	K_2	Mean	0.25	0.50	0.75	2.0	1.25*	1.5
1	2 100	28	72	119	91	105	62 (59.4)	39 (37.1)	23 (21.9)	12 (11.4)	3 (2.8)	2 (1.9)
2	6 350	29	71	67	73	70	11 (15.7)	8 (11.4)	4 (5.7)	3 (4.3)	2 (2.8)	1 (1.4)
3	3 150	20	80	36	44	40	9 (22.5)	7 (17.5)	5 (12.5)	3 (7.5)	2 (5.0)	1 (2.5)
Mean	3 867	26	74	74	67	72	(41.6)	(27.4)	(16.2)	(9.1)	(3.6)	(2.1)

* Discriminatory concentration of chloroquine.

Note : Figures in parentheses indicate % control.
K_1 & K_2 = Control No. 1 & 2.

In September 1980, the *in vitro* macro test at Shaktinagar showed schizont maturation in three out of six cases examined (Table 2). In the adjoining Shakhanwa village of Waidhan PHC of Sidhi district (Madhya Pradesh), schizont maturation was noted in all the three cases at 1.50 n mol (Table 3). Current studies have clearly shown positive evidence of chloroquine resistance in Shaktinagar area which was not noticed in 1979 (Dwivedi *et al.*, 1979). In the absence of any other known focus in the vicinity, it is rather difficult to explain whether chloroquine resistance was introduced recently or was missed in earlier studies. The circumstantial evidence indicates that the resistant strain of *P. falciparum* came to Shaktinagar through the labour force from Orissa where chloroquine resistance in *P. falciparum* has already been reported (Guha *et al.*, 1979).

Remedial measures— The mass drug administration with sulfalene + pyrimethamine showed some side effects, since 10% of the patients complained of "giddiness and hot sensation". One group of 840 persons was negative for malaria parasite before MDA, but 9.6% of them showed *P. vivax* between 9 to 14th day after the MDA, though none showed *P. falciparum* infection during this period. The efficacy of this drug combination, as a suppresant against *P. vivax* after single dose administration of two tablets (adults) needs further study. Bruce-Chwatt (1968 and 1980) had cautioned against MDA of such combination but advocated its use in project areas where resistance of *P. falciparum* had existed to 4-aminoquinolines.

The slide positivity rate (SPR) was 20.6% in January 1980 and *P. falciparum* constituted 90.4% of the cases. In spite of the remedial measures the SPR remained quite high (30.51%) in August 1980 but the proportion of *P. falciparum* cases declined and fluctuated between 8.95 and 16.45% during June to

August 1980. The administration of the drug combination appears to have affected *P. falciparum* since despite high SPR, the falciparum cases had considerably declined after MDA.

Entomological studies — Mosquitoes collected from the area showed a high density of *A. culicifacies* though some specimens of *A. fluviatilis* were also found. One hour exposure of *A. culicifacies* to 4% DDT and 0.4% dieldrin killed 47.5 and 72.5% mosquitoes respectively, indicating intermediate resistance on 4% DDT and 0.4% dieldrin.

In the project areas the control of malaria which is not easy under the best circumstances, has been further complicated at Shaktinagar by chloroquine resistance in malaria parasite and resistance in vector species to DDT and dieldrin.

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Immunological Studies in Benign Tertian (*P. vivax*) Malaria

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In the present work humoral and cell-mediated immune responses were studied in patients with confirmed benign tertian malaria and compared to controls. Parameters studied for humoral immune response included serum immunoglobulins, C3, rheumatoid factor, autoantibodies to various tissues and red blood cells, antibody responses to typhoid vaccine and screening for circulating immune complexes. The status of cell-mediated immune response was tested by 1-chloro-2,4-dinitro-benzene (DNCB) skin sensitisation.

The results indicated significant increase of serum IgG and IgA, depressed antibody response to 'O' antigens of *Salmonella typhi* but normal response to 'H' antigens, higher frequency of rheumatoid factor and depressed response to DNCB skin sensitisation in benign tertian malaria patients. Serum complement, circulating immune complexes and autoantibodies were comparable to controls. It was concluded that in benign tertian malaria only minor perturbations in the immunological status occur.

Introduction

Gross perturbations in the immunological parameters have been reported in chronic malaria (Verrier-Jones and Talwar, 1974). However, critical review of the literature shows that the parameters have been studied mostly in chronic falciparum malaria patients (Greenwood and Brueton, 1974; Strichaikul *et al.*, 1975; Houba *et al.*, 1976). On the other hand, little attention has been paid to the immunological status in *Plasmodium vivax* infection.

In India *P. vivax* infection is most prevalent and accounts for up to 90% of cases in many areas (WHO, 1969). Therefore, the present study was aimed at screening the immunological perturbations in this disease.

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Material and Methods

Blood smear positive patients suffering from *P. vivax* infection were taken in the study. Controls were drawn from the staff members of the institution. Past infections were recorded by way of history of fever and positive blood smear examination. As the area under study is completely covered by AIIMS Rural Health Scheme, it has been reasonable to rely on such data.

Serum immunoglobulins and C3 levels were estimated by standard single radial immunodiffusion test (Fahey and McKelvey, 1965) using monospecific antisera obtained commercially (Chemapol, Czechoslovakia). Statistical analysis was carried out as per recommendations of Malaviya (1972).

Rheumatoid factor (RF) was screened in the serum by standard latex agglutination test using commercially available kits ('Rheuma-Wellcotest', Wellcome Research Laboratories, UK).

Among autoantibodies antinuclear antibody (ANAB), thyroid microsomal antibody (TMA), smooth muscle antibody (SMA), parietal cell antibody (PCA), and mitochondrial antibody (MA) were screened by standard indirect immunofluorescence test (IFT) of Holborow (1967). The antigen substrate used included rat kidney, rat stomach and human thyrotoxic thyroid in a composite block. Commercially available fluorescein conjugated anti-human IgG+IgA+IgM (Chemapol, Czechoslovakia) was used and stained cryostat sections were read in 'Reichert' Immunopan fluorescent microscope with 100 Watt 6 Volt halogen lamp, FITC-exciter filter and GG-9 barrier filter. The details of technique have been described in earlier papers from this laboratory (Narayanan *et al.*, 1976; Bala *et al.*, 1977).

Thyroglobulin antibody (TGA) was screened using the passive hemagglutinin technique with the commercially available 'kit' (Fujizoki Pharmaceutical Co., Tokyo, Japan). The instruction of the suppliers were followed in detail and microtitre system (Cook Engineering, USA) was used for the test.

Autoantibodies to red blood cells were screened using the standard antiglobulin (Coomb's) test. The commercially available 'Selectogen cells' (Ortho Diagnostics Inc., USA) were used as antigen substrate. The test instructions provided by the manufacturer were followed rigorously.

Antibody response to *S. typhi* antigen was tested by giving 0.1ml of commercially available typhoid vaccine (Central Research Institute, Kasauli) intradermally. The serum was tested for "O" and "H" antibodies before, and 2 weeks after the vaccine. Standard 'Widal' flocculation test was carried out for the antibody determination using commercially available antigens (Central Research Institute, Kasauli). The values were compared using Students 't' test.

The screening for serum immune complexes was carried out using the IgG-coated latex agglutination inhibition technique (Lurhuma *et al.*, 1976). Human sera containing rheumatoid factor (RF) in the titre of 1:320 was used. IgG coated latex particles were obtained from M/s Burroughs Wellcome UK. Limiting dilution of the rheumatoid factor was used in the technique and patient's sera showing clear inhibition of latex agglutination at the highest dilution of rheumatoid factor (taking into account the dilution factors) were considered positive for immune complexes. Sera showing positive tests for RF were not used because RF interferes with the reaction. The DNCB skin sensitisation was carried out as per technique of Catalona *et al.* (1972).

Results

A total of 74 patients were studied along with 44 controls. Among patients there were 35 females in the age range of 14 to 45 years (median 28 years) and 39 males in the age range of 14 to 60 years (median 30 years). Among controls there were 24 females with an age range of 12 to 55 years (median 31 years) and 20 males with an age range of 16 to 55 years (median 30 years).

The patients were clinically heterogeneous with approximately one-third studied only after one apparent attack of benign tertian malaria, another one-third had at least two apparent attacks before the study, and another one-third had more than three apparent attacks. All the parametres could not be studied in all the patients.

Table I shows the results of serum immunoglobulins and C3. The levels of IgG and IgA were found to be significantly elevated in

Table 1- Serum immunoglobulins and C3 Levels in *P. vivax* Infection (Mean ± S.D.)

	IgG	IgA	IgM	C3
Patients				
n	43	41	38	42
	2.29 ± 0.15	2.05 ± 0.18	2.31 ± 0.12	1.97 ± 0.17
Controls				
n	25	25	25	25
	2.23 ± 0.08	2.03 ± 0.17	2.24 ± 0.07	2.00 ± 0.10
	t = 2.18	t = 3.80	t = 0.47	t = 0.90
	p < 0.05	p < 0.001	p > 0.05	p > 0.05

N. B. : Values of IgG, IgA and IgM have been expressed in WHO activity units and converted into logarithm. C3 Values have been expressed as per cent of normal pool and converted into logarithmic values.

the patients than in controls ($p < 0.05$ and < 0.001 respectively). No significant difference was found in the IgM and C3 levels between patients and controls ($p > 0.05$).

Rheumatoid factor was positive in a titre of 1:20 or more in 4 out of 31 patients whose it was tested (approx. 13%). None of the 44 controls showed a positive RF test. The difference was statistically not significant ($p > 0.05$).

Seventyfour patients and 44 controls were screened for antinuclear antibody (ANAB), parietal cell antibody (PCA), smooth muscle antibody (SMA), mitochondrial antibody (MA), thyroid microsomal antibody (TMA), thyroglobulin antibody (TGA) and antired blood cells antibody (ARBCA). The results are given in Table 2. No significant difference was noted in the frequency of these autoantibodies between patients and controls ($p > 0.05$ in all comparisons).

Immune response to typhoid vaccine could be tested in 12 patients and an equal number of controls. The mean increase of 'O' antibody titre in patients after vaccination

Table 2- Autoantibodies in *P. vivax* Malaria

Autoantibodies	Patients (74)	Controls (44)
Antinuclear	0	0
Parietal cell	3	4
Thyroid Microsomal	1	1
Tavroglobulin	0	1
Mitochondrial	0	0
Smooth Muscle	0	0

$p > 0.05$ in every comparison.

was 1.8484 while in controls it was 2.5415 (titres expressed in natural logarithm). The difference was statistically significant ($p < 0.05$). The mean rise of 'H' antibody titre after vaccination was 2.8303 in comparison to 2.7148 in controls. The difference was statistically not significant ($p > 0.05$).

Circulating immune complexes could be detected in 4 out of 31 patients (13%) and in 5 out of 25 controls (20%). The difference was statistically not significant ($p > 0.05$).

Table 3—DNCB Skin Sensitisation in *P. vivax* Malaria

Subjects	DNCB Response				
	4+	3+	2+	1+	Negative
Patients (19)	4	6	5	3	1
Control (55)	34	9	10	2	0

Chi Square = 11.93; $p < 0.01$.

Skin sensitisation to DNCB was carried out in only 19 patients and a large number (55) of controls. The results are given in Table 3. The patients showed a significant degree of inability to respond to DNCB sensitisation ($p<0.01$).

Discussion

The present study was aimed at the assessment of immune status in patients with benign tertian (*P. vivax*) malaria. Both the humoral and cell-mediated immune responses were studied. Some degree of perturbation was seen in both of these. Thus some abnormalities were seen in the levels of serum immunoglobulins, IgG and IgA were high whereas IgM was comparable to normals. McGregor *et al.* (1970) reported selective rise of IgG in falciparum malaria in adults and showed that IgM increase is seen only in malaria occurring during the first two years of life.

C3 levels as well as circulating immune complexes were within normal limits in patients with vivax malaria. It would thus appear that in contrast to *P. falciparum* and *P. malariae* infection where low C3 and immune complex disease including nephropathy has been reported (Greenwood and Brueton, 1974; Strichaikul *et al.*, 1975), no immune complex mediated tissue injury seems to be occurring in *P. vivax* infection.

Similarly, the prevalence of autoantibodies in *P. vivax* malaria was also found to be comparable to that of controls. This finding is in contrast to a high prevalence of autoantibodies reported in falciparum infection (Greenwood *et al.*, 1970; Wells, 1970). The absence of autoantibodies and immune complex mediated tissue injury may be indicative of a less severe degree of immunoinflammation seen in *P. vivax* infection.

Rheumatoid factor is known to occur in several non-rheumatoid conditions usually associated with chronic infective conditions (Glynn, 1975). A variable frequency of rheumatoid factor in malaria from 8% to 21% has been reported by other workers (Sharper *et al.*, 1968). In the present study, only 4 out of 31 patients showed the presence of RF and this difference was statistically not significant.

Haemolytic anaemia is not generally a feature of *P. vivax* infection. Therefore, the absence of anti-red cell antibody in these patients may be expected. However, if the antibodies are directed to malarial antigens coated or complexed with red blood cells *in vivo* then the test would be falsely negative because the red cells used in the test (Selectogen) do not contain malarial antigen.

Antibody response in *P. vivax* infection seems to be partially affected as shown by poor response to 'O' antigen but normal response to 'H' antigen. Heavy load of malarial antigen leading to antigenic competition would be the most obvious explanation though

other mechanisms may be considered (Tanabe *et al.*, 1977). Greenwood *et al.* (1972) have also reported poor response to immunisation in malaria.

Some degree of suppression of cell-mediated immune response was demonstrated in *P. vivax* infection by way of relatively poor response to DNCB skin sensitisation. It would appear to be a secondary non-specific immuno-suppression as is seen in several chronic diseases like tuberculosis (Malaviya *et al.*, 1975) leprosy and others (Bryceson, 1974). On chemotherapy, when the bacterial load becomes less, the responses start reverting to normal. It would, therefore, be interesting to test DNCB in those patients who have had *P. vivax* infection in the past but got cured and did not get the infection again for a significant period of time.

It would thus appear that some degree of immunological perturbations do occur in *P. vivax* infection. However, the degree and extent of abnormalities are much milder than that reported in falciparum infection by other workers (Greenwood *et al.*, 1972; Williamson and Greenwood, 1978).

The generalisation that in malaria only the humoral immune responses are suppressed and cell mediated immunity is not affected (Verrier-Jones and Talwar, 1974) also does not hold true in benign tertian form of the disease.

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Response of *P. falciparum* to Chloroquine in Andaman-Nicobar Islands, India

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An *in vivo* 28 day extended field test was carried with 1500 mg base of chloroquine in *P. falciparum* cases in Campbell Bay (Great Nicobar), Hut Bay (Little Andaman) and Port Blair (South Andaman) during April-June 1980. On Day 7, 5 out of 49 (10.2 per cent) were found positive for asexual parasites (RII type of resistance) in Hut Bay only. By the end of the observation period of 28 days, 9 out of 19, 10 out of 49 and 1 out of 3 were positive for asexual stage on some day or other in Campbell Bay, Hut Bay and Port Blair respectively. Though clear cut evidence of resistance (RII) was found in Hut Bay only, RI type of resistance is strongly suspected in all the three islands.

Introduction

After the detection of chloroquine resistance in *P. falciparum* in Assam and subsequent spread to some other parts of India, it became necessary to continue the monitoring work in other parts of India which still remained unsurveyed (Sehgal *et al.*, 1973; Das *et al.*, 1979; Chakraborty *et al.*, 1979; Guha *et al.*, 1979; Pattanayak *et al.*, 1979). The present note gives the details of the findings of the studies carried out in three places of Andaman-Nicobar group of islands during April-June 1980.

Material and Methods

Description of study area — Andaman-Nicobar group is a centrally administered territory comprising of over 300 islands and is situated in the Indian Ocean within the latitude of 6° 39' and 13° 34' covering an area of 3 215 square miles. North Andaman, Middle Andaman, South Andaman, and Little Andaman are prominent amongst the Andaman group. Car-Nicobar, Teressa, Little Nicobar, and Great Nicobar are prominent amongst the Nicobar group. The 10° channel separates the Nicobar from the Andaman group. The total population of the entire union territory was 1 15 000 (1971 census).

The indigenous population of aborigines of the Negrito type is small and most inhabitants are former Indian prisoners of the old penal settlements and their descendants. Since 1947, refugees from Bangladesh (former East Bengal/East Pakistan) have been settled in the islands after clearing the jungles. Fresh batches of refugees from Bangladesh have also been settled during 1971-74 particularly in the Little Andaman.

The study was carried out in Campbell Bay (Great Nicobar islands), Hut Bay (Little Andaman island) and Port Blair (South Andaman islands).

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Table 1—Results of *in vivo* Tests (28 Day Extended Field Test) with Chloroquine in Andaman-Nicobar Islands (1980)

Sl. No.	Locality and island	Number of cases		Number examined, number positive for asexual stages and parasite density per microlitre of blood									
				Day 0	Day 2	Day 4	Day 7	Day 10	Day 14	Day 17	Day 21	Day 24	Day 28
1	Campbell Bay (Great Nicobar)	19	(a)	19/19	7/19	1/19	0/19	2/19	3/19	4/19	9/19	ND	6/19
			(b)	6 343	104	50	0	400	208	3 132	1 722	--	15 491
2	Hut Bay (Little Andaman)	49	(a)	49/49	37/49	9/49	5/49	3/49	8/49	7/49	10/49	3/49	3/49
			(b)	1 2341	1 378	153	3 575	2 867	2 800	3 529	6 878	508	2 608
3	Port Blair (South Andaman)	3	(a)	3/3	3/3	0/3	0/3	0/3	1/3	0/3	0/3	0/3	0/3
			(b)	5833	475	0	0	0	3500	0	0	0	0

Note : (a) Numerator indicates the number positive and denominator indicates the number examined.

(b) Mean density of asexual parasite of the whole group including the negatives.

ND = Not done

Survey technique — Initially, a mass blood survey was carried out in all the three places for selecting suitable cases. Persons thus selected and having asexual parasitaemia were taken up for *in vivo* test. Test procedures and interpretation of results were as per the recommendation of WHO. Adults received 1400 mg chloroquine base in divided doses on Day 0, Day 1 and Day 2. Children received the drug in proportional smaller doses. Urine was examined for the presence of chloroquine as per the technique of Dill and Glazko (Lelijveld and Kortmann, 1970). Only those who were negative initially for chloroquine in their urine were selected for the study. In all cases, absorption of drug was confirmed by urine test following drug administration. One hundred thick smears fields were examined for the detection and density of asexual parasites. Three per cent Giemsa was used for staining in phosphate buffer at *p*H 7.2.

Malaria in Andaman-Nicobar is confined to 2-3 km belt of coastal areas, and interior areas are rather free from the disease. *Anopheles sundaicus* is the only vector in the area and the distribution of human cases broadly follows the distribution of this vector species which breeds in brackish water or saline water swamps and creeks in the coastal areas (Covel, 1927; Kalra, 1980).

Results and Discussion

Mass blood surveys carried out showed a slide positivity rates of 11.0, 38.0 and 5.0% out of 1223, 527 and 241 examined respectively in Campbell Bay, Hut Bay and Port Blair. Proportion of *P. falciparum* cases to total cases was 35.2, 81.1 and 23.0% respectively in these three places.

On Day 7, a critical day for classifying the cases as sensitive or resistant, 5 out of 49 (10.2%) were found positive for asexual parasites in Hut Bay (Little Andaman) only. In Campbell Bay (Great Nicobar), it is suspected that RI level of cases do exist, even as early as on Day 10, two cases out of 19 were positive for the ring stage. At Port Blair, out of three cases, only one case showed asexual parasites on Day 14 but cleared up due to treatment taken privately by the patient. At Campbell Bay and Hut Bay between Day 7 and Day 28, 9 out of 19 and 10 out of 49 were positive respectively on some day or other during the follow-up period. All the cases were of indigenous origin and no history of movement was given by any of the patients (Table 1).

How many of them were due to recrudescence and how many due to reinfection remained unknown, as transmission was not interrupted during the study period. Frequent recrudescence after chloroquine therapy was reported by the patients and physicians in all the three islands where the study was carried out. *in vitro* Study can give an answer to this problem.

How this resistant strain got established in Hut Bay of Little Andaman is not precisely known. The present test is the only one done so far in these islands. Bangladeshi refugees were settled there during 1971-74. The resistant strain may have been brought from Bangladesh from where this phenomenon has already been reported (Rosenberg and Maheswary, 1976).

Out of the places from where chloroquine resistant *P. falciparum* has been recorded from India so far, this is the only place where *A. sundaicus* is involved in the transmission of malaria.

In view of the above findings, it is necessary that all the islands are frequently monitored to find out the resistance status to chloroquine,

amodiaquine and other antimalarials like pyrimethamine and sulfa + pyrimethamine combination.

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Short Note

Water Mites (*Arrenurus* sp.) Parasitising Mosquitoes in Uttar Pradesh Terai, District Nainital

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Among the acarine parasites found parasitising mosquitoes, water mites are the most common although a few terrestrial mites have also been reported (Mullen, 1975). In India such records are scanty and require our attention because of their role in parasitising mosquitoes in their natural habitats. The only available reports are from *Culex pipiens* (Fearside, 1900); *Anopheles* sp. (Chatterjee, 1901); and *A. stephensi*, *A. maculatus* and *A. splendidus* (Sinton, 1917). The mites recovered from these mosquitoes were not identified. Recently Rahman *et al.* (1979) observed water mites (*Arrenurus* sp.) parasitising *A. annularis* in Delhi.

In September, 1980 extensive mosquito collections were made from a large number of villages as well as forest areas of UP Terai using the suction tube and pyrethrum space spray. During the identification of these mosquitoes, larvae of water mites were found attached to the body of six species of mosquitoes (Table 1). These mites were identified as *Arrenurus* sp. with the help of Mullen's key (1974), and further identification is awaited. Most of these mites were found attached laterally between the abdominal tergites. A few mites were also found on lateral and posterior aspects of thorax and cervical region of *A. hyrcanus*. In the other five mosquito species mites were found attached on the abdomen. The attachment site of these mites therefore, did not vary with host species.

The mite infestation rate was 3.28 per mosquito, highest being 3.8 in *A. hyrcanus* and their number on each mosquito varied from 1-29. The infestation rate of *Arrenurus* sp. on *A. annularis* was 2.85 per mosquito and the number of mites attached to single host varied from 1-4 (Rahman *et al.*, 1979).

In the present study mites were mainly found attached to the abdomen, whereas Rahman *et al.* recovered them from thoracic region of mosquitoes. Mullen (1976) also reported that the most common attachment site of water mite (*Thyas barligera* and *Thyasides sphagnorum*) was thorax and they were rarely found attached to the abdomen. This variation may be due to the possibility of a different species of *Arrenurus* mites found in UP Terai. Reisen and Mullen (1978) observed that water mites exhibit a wide host range and show preference for attachment sites on their hosts which varied significantly with host taxa and sex.

The role of these mites in the regulation of mosquito population in their natural habitats is not known, which needs to be investigated. From the present studies it can be concluded that these mites show preference for *A. hyrcanus* in this niche.

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Table 1—Mosquitoes Found Parasitised by *Arrenurus* sp. Mites in U P Terai—September, 1980

Host species	Collection site (village)	No. of mosquitoes		No. of mites recovered	
		Examined	Parasitised	Total	Mean (range)
A. hyrcanus	Bhimnagar Rampura	80	29(36.2%)	115	3.8(1-29)
A. subpictus	Bhimnagar Fatehganj	28	3(1.7%)	3	1
A. annularis	Bhimnagar	2	1(50%)	2	2(1-2)
C. quinquefasciatus	Bhimnagar	37	2(5.4%)	2	1
C. vishnui	Bhimnagar	29	2(6.8%)	4	2(1-3)
C. tritaeniorhynchus	Bhimnagar	12	2(1.6%)	2	1

This report of infestation of *A. hyrcanus*, *A. subpictus*, *C. quinquefasciatus*, *C. vishnui*, *C. tritaeniorhynchus* by *Arrenurus* mites is the first record from India.

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OBITUARY

Dr Ramakrishnan Simili Ponnuswamy
(22.10.1913 - 18.5.1981)

Dr S. P. Ramakrishnan, former Editor of Indian Journal of Malariology died in Madras on 18th May 1981 at the age of 67.

Dr Ramakrishnan was born in Madras on 22nd October 1913. He was educated at Madras from where he obtained his M.B.B.S. degree. Subsequently he did DPH from Calcutta and was awarded D. Sc. (PH) from Calcutta University as a result of his pioneering work on malnutrition and Malaria.

After graduation he joined the Indian Medical Service, Ministry of Defence and served in Middle East from 1940-46. He retired as Lieutenant Colonel in 1946 and joined the Malaria Institute of India (now National Institute of Communicable Diseases) as Assistant Director. Later he became the Director, a post which he held till 1965 when he joined the World Health Organisation as Assistant Director, Health Services (Communicable Diseases). He became WHO Project Director in Nigeria in 1970 and retired from WHO in 1973. He was Editor of the Indian Journal of Malariology from 1959 to 1963.

As Director of National Institute of Communicable Diseases, his principal aim was to carry out research on different aspects of malaria which had direct bearing on malaria eradication and to train a cadre of Indian workers in the field of malariology.

He was elected Fellow of the Indian Society for malaria and other communicable diseases in recognition of his outstanding contributions especially in malaria and plague. He was also elected Fellow of the Indian Academy of Medical Sciences and a member of the Indian Public Health Association.

In his death the world has lost an eminent malariologist and a great public health administrator. The members of the board of Indian Journal of Malariology, some of whom had the privilege to work with him, mourn his death and extend the deepest sympathy to the bereaved family.

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Books/Monographs

Rao, T. R. (1981). *Anophelines of India* (W. Q. Judge Press, Bangalore).

Landau, I. and Y. Boulard (1978). In *Rodent Malaria*, edited by R. Killick-Kendrie and W. Peters (Academic Press Inc., London) : 53-84.

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