UNited NATIONS

World Health Organization
Interim Commission

Organisation Mondiale de la Santé
Commission Intérimaire

WHO.1C/205
WHO.1C/Mal/25
8 June 1948

Expert Committee on Malaria

Report of second session

Pan American Sanitary Bureau Building
Washington, D.C. - May 19-25, 1948

Outline

1. Introduction
2. World Needs
3. WHO Malaria Policy
4. Agriculture and Malaria
5. Use of Insecticides
6. Chemotherapeutics in Malaria Control
7. Research
8. Quarantine
9. Recommended Resolutions
10. Conclusions and Recommendations
SECTION I
INTRODUCTION

The Second Session of the Expert Committee on Malaria of the World Health Organization Interim Commission took place in Washington, D.C. May 19-25, 1948, in the office of the Pan American Sanitary Bureau which very kindly provided full facilities. The following were present:

MEMBERS

Dr. Arnoldo Gabaldón - Venezuela - Chairman
Major General Sir Gordon Covell - U.K.
Dr. Paul F. Russell - U.S.A.
Med. General Marcel Vaucel - France
Dr. D. K. Viswanathan - India

Secretary: Dr. Emilio Pampana - WHO

CO-OPTED MEMBERS

Lt. Col. M. K. Afridi - Pakistan
Dr. J. W. Field - Malaya
Dr. D. Bagster Wilson - Tanganyika

FAO REPRESENTATIVE

Dr. Wallace R. Ayrkroyd

PAN AMERICAN MALARIA COMMISSION OBSERVERS

Dr. Carlos A. Alvarado - Argentina
Dr. Paulo C. A. Antunes - Brazil
Dr. Luis Vargas - Mexico

CONSULTANTS*

Dr. G. Robert Coatney - U.S.A.
Dr. Clay G. Huff - U.S.A.
Dr. Fred L. Soper - U.S.A.
Mr. H. H. Stage - U.S.A.

*co-opted by the Committee for advice in respect of particular sections of the report.
Since the first session of this committee, Dr. N. Hamilton Fairley, U.K., has resigned and the following members have been appointed: Major General Sir Gordon Covell, U.K., Médecin General Marcel Vaucel, France, and Dr. D. K. Viswanathan, India. Dr. Mihai Ciucu, Roumania, a member of the committee, was unable to attend the second session. The seat reserved for a member from U.S.S.R. remained vacant.

In accordance with the terms of reference (WHO.IC/183/Rev.1, February 10, 1948) an informal meeting of malariologists attending the Fourth International Congress on Malaria was convened in Washington by the Expert Committee on Malaria on May 13, 1948. Facilities were provided by the Division of International Conferences of the U.S. State Department. Dr. Arnaldo Gabaldón was in the chair and all members of the Expert Committee, excepting Dr. Ciucu; were present. The agenda (WHO.IC/Mal/13, Geneva, 1 April 1948) had been widely circulated prior to the meeting. A list of those attending is given in Appendix I.

The Chairman invited those present to express their opinions as regards the points raised in the above mentioned agenda and many responded to his invitation. Others later submitted written statements. The Committee in preparing this report has given full consideration to the views put forward.

The Committee took note of the resolutions concerning malaria adopted by the Interim Commission at its Fifth Session (WHO.IC/183, Rev.1, 10 February 1948) and included the items of resolution I in its agenda. The Committee expressed satisfaction at the emphasis placed by the Interim Commission on the importance of malaria as a world health problem.

The Committee further agreed with the opinion of the Interim Commission that a mass attack on malaria in selected areas of food producing countries should be carried out as soon as possible with technical and material assistance and through the WHO regional organizations when these
The Committee also took note of the report of the Fourth Session of the Interim Commission (WHO.IC/124/Rev.1, 19 September 1947) and particularly of resolution 16 in part D of Section III. The last part of the resolution refers to the Darling Prize and the Committee wishes to call attention to the fact that this does not follow a resolution recommended at the First Session of the Committee in Geneva, (WHO.IC/79 - WHO.IC/Mal/4. 30 June 1947, Section X, Part II, Para. 2, page 18). The Committee agrees that, as it previously suggested, the World Health Assembly should award the Darling Prize, but it desires to reiterate its opinion that the selection of the candidate should be entrusted to the Expert Committee on Malaria. This procedure would be in accord with the generally accepted principle that recipients of such prizes should be nominated by experts in the field to which the prize relates.

A drafting sub-committee was appointed (Sir Gordon Covell, Dr. Paul F. Russell).

SECTION II

WORLD NEEDS

An international programme for malaria control on a world wide basis is urgently required in view of the high incidence of the disease throughout a large portion of the globe, resulting in hundreds of millions of cases each year with millions of deaths; the widespread condition of mental apathy and general physical deterioration caused by malaria among the populations of many countries; the serious loss on working efficiency among malaria ridden populations which contributes directly to the critical world shortage of food and causes grave interference with industrial and agricultural activities and development; the availability of new and effective techniques and agents for control of malaria which are not as yet widely exploited; the record of effective international action by the
the League of Nations Health Organization and other agencies; and
the interest expressed by governments in receiving technical assist-
tance in this field.

The Committee wishes to emphasize the points presented in
Section II of the first report (WHO.IC/79 - WHO.IC/Mal./4, 30 June
1947). In particular it desires to note that it is now possible
to attain a degree of practical malaria control, and even of malaria
eradication, utterly impossible 15 years ago. To the realization
of these possibilities there are however grave obstacles, namely,
a widespread dearth of information about the new techniques, a
serious lack of suitable governmental organizations to carry on the
work, and a critical shortage of trained personnel. It is particu-
larly in regard to the removal of these three obstacles that the
Committee believes that WHO can assist a world-wide drive against
malaria.

SECTION III
WHO MALARIA POLICY

A. OBJECTIVES

The Committee finds itself in agreement with the malaria con-
trol objectives expressed by the Interim Commission (WHO.IC/181/
Add.1, of 2 February 1948, Off.Rec.WHO No. 10, 12.1.3.2, 5).
Briefly stated it appears to the Committee that the fundamental
purpose of the WHO malaria policy should be to assist governments
to accomplish effective malaria control along modern scientific
lines. The Committee believes that this should be done through
WHO regional organizations and that it involves practical assistance
in formulating programmes and in setting up adequate governmental
machinery for malaria control, in training skilled personnel, in
disseminating relevant information, in developing uniform inter-
national procedure and nomenclature, and in promoting measures to
protect countries against the introduction of anophelines from the
outside.

B. METHODS

1. Organization

The first essential for effective control of malaria in any
country is the establishment on a permanent basis of a malaria con-
trol organization of adequate size, staffed by adequately paid and adequately trained personnel. The remarkable diminution of malaria in the U.S.A. during the last 30 years has been due in a large measure to the existence of organizations of this character. The type of malaria control organization will vary according to the area, population and economic resources of the country and the nature of the local malaria problems, the primary object being effective control of malaria at the lowest feasible cost.

For example, in India, as an integral part of the Central and Provincial Health Services, an organization constituted on the following lines has given excellent results:

(a) A central institute under a director, with two Deputy Directors, six Assistant Directors, one Entomologist, one Assistant Entomologist and appropriate subordinate staff. Its principal functions are:

(i) to advise the Central Government on all aspects of the malarial problem and of the control of malaria and to advise Provincial Governments as and when required;

(ii) to conduct regular annual courses in malariology for malaria officers, malaria inspectors and engineers of all branches;

(iii) to carry out field and laboratory researches on parasitology, mosquito bionomics, laboratory techniques, and methods of malaria control, including the testing of insecticides and antimalarial drugs;

(iv) to provide instructional manuals on malaria surveys, entomology, antimosquito measures and other aspects of malaria investigation and control, and to produce a Journal of Malariology edited by the Director;

(v) to promote liaison between the central and provincial malaria organizations and with malariologists working in other countries.

The control of malaria in Delhi urban area and the organization of antimalarial measures for all coal fields throughout India is included among the functions of the central institute.

(b) A provincial malaria organization for each province, consisting of:
(i) a headquarters unit with a Director having the status of an Assistant Director of Public Health, an Entomologist, and appropriate subordinate staff. Its functions in regard to advisory and training activities are similar to those of the Central Institute. In addition it provides material for propaganda and issues popular pamphlets in the local vernacular.

(ii) a small number of investigatory and a larger number of control units, each under a malaria officer with appropriate subordinate staff, for the purpose of carrying out demonstration control projects in selected areas based on the headquarters unit. The number of control units varies according to the size of the province and the magnitude of its malaria problem, from two or three in Delhi Province, Coorg and Ajmer-Merwara, to 50 or more in the larger provinces such as Bengal.

An essential feature of the organization is its elasticity, so that further units can be added from time to time as required. The malaria organization of Bombay Province, constituted on a permanent basis on these lines five years ago, is carrying out a control programme over an area of 6000 square miles with a population of one million. This has proved so effective that the government has now sanctioned an expansion of the programme to include another large district, with a view to extending its operations eventually so as to cover all malarious areas throughout the province. Two investigatory and 13 control units so far have been employed in Bombay Province.

In South and Central America antimalaria organizations, within the national and State Health Departments, have been established on the following lines. In small countries such as El Salvador, Panama, and Trinidad (B.W.I.) where malaria is an important problem, the national or island public health departments have established a malaria service as one of their primary divisions. Each service has a central staff adequate to carry out the study of local problems and actually to execute control programmes. The staff includes at least one malariologist and one entomologist competent to identify the local anophelines and antimalaria engineers are employed when drainage projects are under consideration. Engineers are also sometimes in charge of insecticide programmes.

In larger countries where intensive nation-wide malaria control programmes are carried out (Argentina, Venezuela), the central headquarters of the service is devoted to the promotion of uniform standards, general direction, and to supervision. It is divided into different sections, each one headed by a specialized officer, and assigned to one or another
of the following activities: protozoology, and entomology, epidemiology, mosquito control, anti-malaria engineering, research and administration. In one of them (Venezuela) there has been established an international school of malariology, where a course of four and a half months duration is held each year. The Venezuelan Government has given one fellowship to each of the American countries for this course. Another feature of these organizations is the nation-wide distribution of drugs free of charge, which is carried out through medical posts, schools and post and telegraph offices. For local work the countries are divided into zonal organizations with appropriate staff (malarialogist, entomologist, engineer) in charge of executive activities. The number and area of these zonal units depend on the population present and on the budget to be devoted to the work.

In still larger countries such as Brazil, the organization of the central headquarters of the malaria service is essentially similar to that described above, but its direct supervisory activities are limited by distance. Therefore, between the central headquarters and the state organizations, regional headquarters have been established, similar in structure to the central ones and especially designed to implement the general policy. The number of these regional organizations depends on the area of the region and on the scope of the anti-malaria activities carried out in it.

The Committee emphatically endorses the principle that a central organization, in addition to its other functions, should at all times be in close touch with field control activities. In this respect, the assumption of responsibility for the control of malaria in Delhi and in the coal fields throughout India by the Malaria Institute of India has proved of extreme value. The same principle is followed by the Central and South American organizations named above.

The above are examples of differing types of governmental control programmes now in operation. They illustrate the essential similarity of the organizations required to combat malaria in different parts of the world, but they also make it clear that these must be subjected to considerable modification in order to meet the needs of widely differing local conditions.

The Committee recommends that WHO be prepared to assist governments on request, through regional organizations when these
are established, in setting up malaria control projects suited to local needs. The Committee points out that this will often require surveys and recommendations by expert malarialogists provided by WHO and followed by training schemes implemented by WHO.

2. Training

Antimalaria personnel requiring training may be classified as follows:

(a) Directive professional staff
(b) Assistant professional staff
(c) Subordinate personnel

The training of directive professional staff should be carried out in special schools of malarialogy, where the basic principles of protozoology, entomology, epidemiology, therapy, mosquito control, and organization are taught in detail. There are certain schools already in existence which fulfill these requirements, for example, the Malaria Institute of India in Delhi, the School of the Division of Malarialogy in Maracay, Venezuela, the Institute of Malarialogy and the Institute of Public Health in Rome.

Such courses should be supplemented by study in the zoogeographical area where the student is going to work or in other areas where antimalaria programmes similar to those required by the problems which the student is likely to encounter in his own country, are in operation. Specialists in other fields of medicine are not produced in a short time, and the same is true of malarialogists. The period of training, including study tours, should not be of less than six months duration.

The training of assistant professional personnel should be implemented by means of practical work and provision of adequate library facilities. It is advisable, in countries where control programmes are already in operation, that students should receive training in the field methods actually in use before attending the special schools or courses in malarialogy.

The provision of well indoctrinated and disciplined subordinate personnel is one of the most essential requirements for successful malaria control. These objectives may be greatly aided by the provision of manuals describing every technique and step to be followed. The WHO may assist by promoting the
exchange of such manuals and other technical aids as may be available. It is important, however, that such manuals be adapted to local conditions and kept up to date by the issue of new editions at frequent intervals. The Committee wishes to draw attention to the admirable system in force in Venezuela, where mimeographed manuals are issued in loose leaf form so that a new edition of any section can be inserted as required.

With the purpose of facilitating this training programme by every possible means, the Committee recommends that WHO consider the feasibility of:

(i) Assisting on request schools of malariology now in operation by providing expert lecturers who would participate in the teaching programme, or by other help as indicated.

(ii) Assisting in setting up courses in malariology in regions not now provided with such facilities, i.e. in Central Africa and in Southeast Asia. For example, a revival of the International Malaria Courses formerly held in Singapore under the auspices of the Health Organization of the League of Nations might be considered as meeting certain immediate needs in Southeast Asia. Similar courses might be instituted in Central Africa.

(iii) Providing fellowships and travel grants for training in malariology.

(iv) Providing malaria control teams or individuals as required to demonstrate how to set up and to carry on malaria control work in practice.

(v) Disseminating reports and manuals dealing with malaria control measures.

3. Individual experts and operational demonstration teams

The Committee considers that in order to foster the development of national and local malaria control programmes, the services of individual experts and operational demonstration teams should be made available to give adequate advice and practical assistance to governments. It notes with satisfaction that the Interim Commission at its Fifth Session resolved to insert in the 1948 and 1949 budgets appropriations for these purposes.
The Committee recommends that this service should be constituted on a temporary basis and that its function should be to carry out malaria-economic surveys of the area concerned, to put in practice a control programme based on these surveys and to assess results and costs in terms of malaria, general health, and economics. Such control demonstrations should be planned on a scale which could be adopted and expanded by the respective governments within the limits of their budgetary capacity. The size and composition of the teams would depend on the character of the local malaria problem, the extent of the area to be protected, the adequacy of data already available and the needs of the local organization.

If malaria control in the area is non-existent or inadequate, plans should be made for the team to remain in the area for at least two years, to enable them to appraise the value of their recommendations and to advise as to any modifications in the control programme which may be found necessary. As a general rule, the team should not be withdrawn until the control programme is established and the preliminary results assessed.

The Committee does not believe it possible to lay down the composition of the team in detail, beyond stating that a malariologist, an entomologist, and possibly, in areas where increased food production might follow malaria control, an agronomist should be included. A malaria or a sanitary engineer to direct spraying operations may also be found essential. The Committee wishes to stress the importance of elasticity in this respect, in order to meet varying local conditions. The Committee believes that these teams should primarily demonstrate the use of residual insecticide spraying as a method of malaria control.

The Committee recommends that governments be required to appoint local officers to understudy each member of the team provided from outside sources. This should be made a condition of WHO cooperation. In any case, assistant and subordinate staff should be recruited locally and paid by the government concerned.
The Committee recommends that whilst it may be necessary for the WHO Secretariat to assist in procuring the services of individual experts, the constitution of the terms and the arrangements for their despatch to the area to be protected should be the responsibility of the regional organization. Indeed, in certain regions malaria might well be the initial activity of the regional organization. These organizations will be best informed regarding the needs of the different countries which make up their regions.

The Committee wishes to emphasize the vital necessity for all necessary equipment, material and adequate motor transportation for the operational demonstration teams to be included in the initial budgets for such teams. Experience has proved on many occasions that in the absence of adequate transport an operational demonstration control programme cannot possibly be carried out.

The Committee recommends that three operational demonstration teams be formed as early as possible and that they should be allocated, on request by governments, to selected areas in (i) Central Africa, (ii) South East Asia, and (iii) the Tropical Americas.

4. Education of the public

An expression of opinion was requested from the Malaria Committee as to how WHO might aid malaria control through the education of the public. The Committee realizes that Public Health
propaganda is an art simple in theory but complex and subtle in practice and that therefore it is not possible in this report to do more than make certain broad suggestions.

The Committee agrees that every effort should be made by a governmental malaria control organization to obtain full co-operation from the public and that such help depends in some measure upon appropriate propaganda. It is **recommended** therefore that in any malaria courses or malaria control demonstrations aided by WHO, due attention be given to the education of the public in this subject. It must be emphasized, however, that by far the most effective propaganda is a successful demonstration of practical malaria control. Moreover, experience has shown in many countries that people who have once been freed from household insect pests through the use of residual DDT and spraying not only demand continued periodic service but also act as important propaganda agents for surrounding areas.

**The Committee recommends** that WHO, through its Secretariat, should attempt to collect and to distribute to official public health organizations such material on malaria propaganda as is available from all over the world.

**The Committee recommends** that attention be given to the feasibility of building up in each regional organization of WHO a lending library of cinema films, film strips, lantern slides, and other educational material on the subject of malaria and its control. It calls attention to the excellent facilities of this sort offered by the Communicable Disease Center of the U.S. Public Health Service to health agencies in the United States.

Finally, the Committee would emphasize that even more important than educating the general public is the vital need to acquaint administrative officers and engineers of all branches with the basic principles of malariology.
C. CORRESPONDING MEMBERS AND REGIONAL ORGANIZATIONS

The Expert Committee on Malaria believes that the appointment of specialists from various countries as "corresponding members" as called for article 14 of the "Draft Regulations Applicable to Expert Committees and their Sub-Committees" (WHO.IC/140,Rev.1, 7 February 1948) is of great importance on account of the many different regional problems presented by malaria throughout the world.

The Committee considers that the primary function of these specialists should be to communicate to the Secretariat information on scientific malaria research and its practical application within their own special fields or areas. In addition, they would constitute a panel from which members of regional malaria commissions under the regional organizations of WHO could be selected. It is believed that there are a number of malaria problems which may better be solved on a regional basis than at the central.

The Committee would like to assist the Director General in selecting such corresponding members, and would undertake to prepare a list of malarialogists from which nominations of corresponding members might be made. The Committee suggests that when the corresponding members to be chosen do not represent special fields of malarialogy, but are needed to represent geographical areas, their selection should be made through the regional organizations when constituted. For this objective an appropriate modification of article 14 of the Draft Regulations named above is required.

D. BUDGETS

The Committee considers that the distribution of the WHO budget devoted to antimalaria activities on a world-wide basis should be made proportionate to the importance of regional problems. The Nearctic Region and the European, Siberian and Manchurian provinces of the Palearctic Region may be considered
for practical purposes malaria-free. The needs of the Mediterranean, Ethiopian, Indian, Indo-Malayan, Australian, and Neotropical zones should be taken into careful consideration on the basis of population and degree of malarial incidence.

At this early stage, it is possible that requests for aid from WHO may be received from some quarters and not from others and there is danger that undue attention may be focussed on certain regions, to the exclusion of others who are equally in need of assistance. The Committee wishes to emphasize the importance of assuring the distribution of the funds available in a manner proportionate to the needs of regions where malaria constitutes a serious health problem. This consideration demands careful study, otherwise the malaria policy of WHO may incur adverse criticism. A similar policy should be adopted in regard to the distribution of fellowships.

To obtain a general idea of where WHO's help is most needed the Committee recommends that the Secretariat, through the regional organizations, should carry out relevant studies of national, and in larger countries, of state or provincial budgets, paying due regard to the proportion of each budget spent on health activities in general and on malaria control in particular. It is believed that in many countries there is not actually a lack of funds, but rather, that there exists an improper allocation of them due to an inadequate evaluation of the malaria problem.

SECTION IV
AGRICULTURE AND MALARIA

As noted in the introduction, the Expert Committee on malaria invited the FAO to send representatives* to the second meeting of:

*Dr. W.R. Ayrkoyd - Director, Nutrition Service
Mr. F.L. McDougall - Counsellor
Sir Bernard Binns - Agriculture Division
Dr. C. Logothetis - Agriculture Division
Mr. W.H. Pauley - Economics and Statistics Division
its second session for joint discussion of the relation between agriculture and malaria. After these discussions, the following memorandum was presented to the Committee by representatives of FAO:

"PROVISIONAL MEMORANDUM PREPARED BY FAO AT THE REQUEST OF THE EXPERT COMMITTEE ON MALARIA.

"The principal objectives of FAO are the raising of levels of nutrition and standards of living, improving the efficiency of the production and distribution of agricultural products and the bettering of the conditions of rural populations. The elimination or reduction of malaria in areas of the world devoted to food production would undoubtedly assist greatly in the fulfilment of these objectives because good health among the rural population is both an important factor in efficient production and also a potent contribution to rural welfare. FAO will, therefore, warmly welcome the opportunity to co-operate with WHO in the selection of suitable areas for the demonstration of the effect of malaria control on food production.

"It must not, however, be overlooked that the elimination of malaria is not the only factor—though a most important one—in the improvement of the health of a rural population, and that such improvement is only one factor—though again important—in increasing agricultural production and furthering rural welfare. There are also many other hindrances to efficient production, e.g., adverse climatic conditions, poor soils, lack of water, inefficient agricultural methods, attacks on crops and livestock by diseases and pests, economic handicaps, such as lack of capital or credit and unsatisfactory marketing arrangements, lack of incentive to effort due to such causes as the farmer being unable to obtain the consumer goods he needs, difficulties arising from systems of land tenure and taxation, etc. Equally there are positive means of increasing production other than improvement of health, e.g., improvement of plants and animals by selective breeding, better feeding of animals, improvement
of soils by the use of fertilizers, improvement of water conditions by irrigation, drainage and flood control, etc.

"The maximum improvement in agricultural production will be achieved not by isolated effort in a single direction but by the co-ordination of effort along many lines simultaneously. In planning any particular measure to increase agricultural production it is therefore necessary to consider the prospects of simultaneous and co-ordinated action in other directions. This point is made not to deprecate in any way the great importance of the control of malaria to agricultural progress, but to draw attention to the complications involved in selecting areas suitable for the purpose under consideration.

"From the point of view of agriculture, malaria creates two separate types of problems. The first is the case where malaria is endemic in a thickly populated area already under agricultural occupation, where the effect of the malaria is to sap the energy of the working population, and to increase, often at critical periods, the number of working days on which the worker is incapacitated by ill-health. The second is where malaria is preventing the development of an area otherwise suitable for agricultural development. Both these cases may again be divided on the one hand into the situation in which other factors are already favourable to the development of agriculture, on the other into one in which they are at present unfavourable. Thus in a naturally rich agricultural area which already supports a farming population as efficient as health conditions permit, or in a potentially rich undeveloped area readily accessible to a congested agricultural area, it may be that the removal of the handicap of malaria will produce quick and spectacular development. In other areas there may be adverse natural or economic conditions which will check progress even if the malaria is eliminated; examples of this are poor soils, adverse climatic or water conditions, unsuitable tenure systems, lack of agricultural knowledge, lack of credit, etc., and especially, in undeveloped areas, inaccessibility, lack of supplies or amenities, insecurity of person or property and the like. In such areas, from the standpoint of food production, it may scarcely be worth while
to eliminate malaria unless other large-scale improvement plans are in prospect such as an important irrigation or drainage project or a comprehensive plan for organized settlement or colonization.

"It should also not be forgotten that there are areas in which malaria is not at present a serious problem, but which may become infested areas as the result of change due to human or natural agencies. It is for example a well-known fact that the irrigation of new areas is often followed by the spread of malaria into those areas.

"Again, there are a number of questions related to world economy and the distribution of agricultural production which are relevant to the present study. Instances of this are the difficulties in distribution due to the present conditions of international exchange and the risks involved in the too great concentration of agricultural production in a few countries which may render the world food supply dependent to a dangerous degree on the vagaries of the climate or economy of these countries.

"It would be possible to continue this list of important considerations further, but enough has been said to indicate the intricacy of the problems involved and to underline the need for their close and detailed examination. FAO is not at present familiar with conditions in all parts of the world and may have to collect additional facts before it can advise effectively. Moreover, since the help that international organizations can give to a country depends directly on the willingness to co-operate and the capacity of the government of the country concerned to carry out action programmes, it may well happen that the selection of areas may depend to some extent on considerations of a non-technical nature.

"Roughly speaking, we think that it may be said that malaria impairs human efficiency to varying extents in practically all the tropical and sub-tropical countries of the world and also in some temperate countries such as those of the Mediterranean region. In most countries in these regions there is need for improvement in agriculture and rural welfare
and greatly expanded agricultural production is feasible. Thus, it would be possible to point to almost any country in the region and to say 'Here there is malaria' and also 'Here there are possibilities of improving agricultural production'. The choice of demonstration areas must therefore depend on other factors than those two basic ones.

"To assess the effect of malaria control, economic surveys should be made in rural areas selected for demonstration malaria control projects. Such surveys should be made before the initiation of control measures and again at a later date when they have taken effect. FAO will be glad to give advice or assistance within the limits of its resources, regarding the organization and execution of these surveys.

"It is suggested that when the time comes for selecting demonstration areas the simplest procedure may be for WHO to select a number of areas and for FAO to advise on the prospects of increased production in the areas named. A final choice could then be made after appropriate consultation."

The Committee has taken careful note of the above memorandum and welcomes the prospect of collaboration between WHO and FAO in malaria control in selected areas. It heartily endorses the view that malaria control in certain regions would result in increased food production and in betterment of conditions of rural life. In the words of the U.S.A. Secretary of State, George Marshall, at the opening session of the Fourth International Congress on Tropical Medicine and Malaria, "the conquest of disease which hold millions weak and inefficient, and the maximum production of foodstuffs in lands now yielding little, are tremendously important requirements of the world situation."

The Committee agrees that the choice of suitable demonstration areas involves consideration of many and diverse factors and recommends
that the two secretariats (WHO and FAO) should collaborate in examining the problem of selecting areas on the bases of (1) feasibility of effective malaria control and (2) potentiality as regards increased food production. The Committee also recommends that these secretariats should prepare a joint report for its further consideration.

SECTION V
USE OF INSECTICIDES

A. INTRODUCTION

The steady development of malaria control by anti-mosquito methods has progressed along certain well-defined lines. Initially, the measures employed were mainly those directed against the aquatic stages of mosquitoes, namely the application of larvicides such as oil, paris green and copper cyanide, the manipulation of water and the utilization of naturalistic methods. While this line of attack is still of the utmost importance in concentrated urban centres and in anopheline eradication and other special schemes, its chief drawback has been that it is not a practical proposition in scattered rural populations.

The next phase was the development of spray-killing of adult mosquitoes with pyrethrum insecticide for malaria control in rural areas. The value of this method has been demonstrated by the results achieved in South Africa, India, the Netherlands and Brazil. Pyrethrum has however definite insecticidal limitations in that while it has a potent immediate knockdown effect, it possesses practically no residual action. For effective results this insecticide has, therefore, to be applied systematically and repeatedly, the intervals varying from once a day to once a week depending on the peculiarities of behaviour of
the vector species of anophelines concerned. None the less, the use of this insecticide marked an important step in malaria control methods and is still of considerable value in situations were rapid disinsectization is desired such as in treating aircraft and possibly in controlling a short and sharp malaria epidemic.

With the recent discovery of the residual action of the newer insecticides, the outlook has once again undergone a complete change inasmuch as spraying operations need only be carried out at extended intervals. A proper exploitation of this feature of the new insecticides has greatly simplified procedure to the extent that the control of malaria in vast rural areas has now become economically and technically feasible.

Of the numerous chemicals in this group of residual insecticides tested, DDT has so far given the most outstanding performance. Another residual insecticide to which reference may be made is benzene hexachloride (gamma isomer) on which an extensive field test is reported to be in progress. In the formulations now available, however, this insecticide has the serious drawbacks of a relatively shorter period of residual action and a disagreeable odour.

Of the remaining insecticides in this group, DDD or TDE (Tetrachloro-diphenylethane) can be recommended as a larvicide especially in situations where the safety of fish or other aquatic life needs consideration. Chlordane (a chlorinated hydrocarbon) and chlorinated camphene do not possess as long an effective residual action as DDT. Combinations of pyrethrums with piperine compound (piperonyl cyclonene or cyclohexenone and piperonyl butoxide) increase the effectiveness of pyrethrum both in its knock-down effect and residual action, but further work is essential before their general adoption can be considered. Parathion is too toxic for warm-blooded animals for practical use at present.

In the existing circumstances DDT thus appears to possess many of the essentials of an ideal insecticide for the control of malaria, in that, in the dosage required, it is cheap, has a prolonged residual action, is non-toxic to man and domestic animals and confers collateral public health benefits through the simultaneous destruction of other disease-carrying insects.
Mention should, however, be made of the reported prevalence, in Sweden and Italy, of *Musca domestica* resistant to DDT and the development of resistant strains of this species after spaced exposure to DDT in the laboratory. There is therefore need for close observations on its effects on mosquitoes, although, so far, no resistant anophelines have been reported.

B. FEASIBILITY OF EFFECTIVE MALARIA CONTROL ON A WIDESPREAD BASIS

There is definite and overwhelming evidence that the recently introduced insecticides can be relied on as a basis for a widespread attack on malaria with the expectation of a significant reduction of morbidity in areas where they are properly applied. This opinion is based on the results available from many countries where DDT has been used as an indoor residual spray and where its effectiveness has been demonstrated against different vector species of anophelines with wide variations in resting and feeding behaviour. Doubt has, however, been raised as to the efficacy of this insecticide against *A. gambiae* in Africa, but a final opinion on this point must await the results of further trials now in progress.

C. PRODUCTION AND DISTRIBUTION OF INSECTICIDES

DDT is at present manufactured mainly in U.S.A., U.K. and Switzerland. The production capacity in U.S.A. (100 million pounds) has sufficient surplus over local needs to have influenced the price of DDT which has recently touched the low figure of 26 cents per pound. This figure, however, gives a fair margin of profit only in large plants working continuously at full capacity production. As regards the two remaining countries, exact production figures are not available, but it is known that they export considerable quantities of DDT.

The Committee is not aware of actual shortage through low production, or of the available supplies being insufficient to
meet the current demands of the countries where malaria
control projects are in progress or are under consideration.
Nevertheless the Committee is unable to view the position
with equanimity since the manufacture of DDT is at present
concentrated in non-malarious parts of the world, whereas in
the malarious countries where this chemical is most needed there
is hardly any local production. In these circumstances, any
interference with the free flow of trade through any cause will
have disastrous consequences, as severe and epidemic forms of
malaria will appear in areas dependent upon control with DDT.
There is therefore an emphatic need for planning and stimulating
the production of DDT on a regional basis particularly in the
malarious parts of the world. For this purpose, the Committee
recommends that this question be referred for an early and
detailed study to the appropriate bodies of the Economic and
Social Council of the United Nations. The Committee recommends
also that definite standards and specifications be laid down for
DDT technical powder and its formulations used in malaria control.
For this objective and for all questions relating to the proper
use of insecticides, the Committee recommends that an expert
Sub-Committee on Insecticides be set up as early as possible.

As regards the distribution of DDT, apart from the
handicaps on world trade imposed by existing conditions, the
imposition of local customs duty which, in some countries,
ranges around 36%, places serious limitations on the use of
DDT. The waiving of such duty would, therefore, be an
important step towards stimulating the extension of malaria
control with DDT and as such also deserves the immediate attention
of the appropriate Bodies of the Economic and Social Council.

The above remarks concerning the regional production
and distribution of DDT apply equally to solvents and
emulsifying and wetting agents used in the preparation of
spraying formulations.
D. RELATIVE VALUE OF INSECTICIDES AND CONTROL ORGANIZATION

In evaluating insecticides in relation to malaria control, it is necessary to consider them separately as adulticides and as larvicides.

Adulticides: The application of DDT as an adulticide is the most effective method of a mass attack on malaria in rural areas, so far evolved. The widely experienced success of this method in many parts of the world has advanced it well beyond the experimental stage and it should now form a sure basis to undertake extensive control programmes in all malarious countries.

In formulating such programmes, however, it is essential that spraying operations be organized on proper lines keeping in view the various factors such as the natural history of the local vector species, the nature of sprayed surfaces, the formulation and dosage of DDT, the frequency of spraying and the selection of suitable equipment. In countries where the above factors have already received a detailed study, extension of control to new areas should be encouraged immediately. In others, where sufficient data are still lacking, it would be desirable to institute pilot control schemes in large and compact areas so as to evolve the most economic method of applying DDT under the local conditions prevailing.

The importance of such a study cannot be over-emphasized particularly as factors influencing the efficient application of DDT are diverse, complex and intimately related to each set of local conditions. Thus, the effective dosage of DDT employed in different countries has ranged from 60 mg. per square foot to 200 mg. and the frequency of spraying from once in six weeks to once in twelve months. Similarly the nature of treated surfaces influences not only the dosage and frequency of spraying
but also the selection of DDT formulation. Rough surfaces such as mud and adobe walls require relatively larger doses to compensate for irregularities of surfaces and for the loss of DDT due to absorption and have more prolonged lethal action against insects when treated with emulsions or suspensions than with solutions. In using suspensions special care is necessary to ensure that the wettable powder contains particles of the requisite size and that the DDT is uniformly dispersed both in the powder and in the fluid at the time of spraying.

As regards equipment, the Committee is of opinion that an efficient type of spraying apparatus which would suit local conditions in all countries is yet to be evolved. Indeed, it is doubtful if a sprayer standardized on a world-wide basis can be produced considering that the development of such equipment must have reference to ready handling by local labour and the facilities for repair which vary from region to region. The Committee therefore recommends that the Sub-Committee on Insecticides referred to on page 23 should assist in standardizing suitable patterns for each region and in stimulating their local manufacture. In this regard, the most urgent need of the greater part of the Eastern tropics is to design a simple and improved hand sprayer with fan-shaped spray nozzle, whereas in mechanically advanced countries progress should be along the existing lines of developing standardized power-operated machines capable of mass delivery of DDT.

Outdoor sprayings from the air by means of aircraft including helicopters, or on the ground by aerosols and fog spraying machines have considerable value in certain countries but are unlikely to have much practical application in most eastern countries. Even in those countries where these methods are in use, care has to be taken to avoid the destruction of the beneficial insects and to eliminate the danger to wild life through overdosage.

Finally, the Committee wishes to draw particular attention to the paramount need for proper organization and planning of a DDT spraying campaign and the adequate training of the personnel. While the actual composition of a spraying unit must conform to
the resources and means of communication in each country, the provision of adequate transport is essential to its successful working as, otherwise, it will be impossible to evolve an economic organization capable of treating a wide circle of villages in rapid succession. How far DDT spraying can be left to the individual householder will depend upon the status of the local inhabitants, but in most malarious countries it has been found essential to engage permanently employed spraying gangs. In planning a spraying programme, advantage must therefore be taken of variations in transmission season, if any, so as to keep these gangs fully occupied. In connection with the training of personnel, special emphasis must be laid on evolving a simple technique for ensuring the application of the requisite dosage of DDT.

Larvicides: While the older larvicides, such as oil, paris green and copper cyanide still play an important role, DDT and benzene hexachloride (gamma isomer) have such pronounced lethal action on both the culicine and anopheline larvae that they can effectively replace them. The main advantageous feature of the latter insecticides is the relatively small dose necessary for the destruction of all larvae in the breeding places, a feature which greatly simplifies the important problem of transportation and supplies.

In the case of DDT, the effective dosage is 5 quarts of a one per cent solution in kerosene or fuel oil per acre in stagnant water and one part of DDT per million parts of water in running streams. Alternately, an emulsion concentrate prepared by dissolving DDT in xylene or medium kerosene extract and adding a suitable emulsifier diluted with water to a final concentration of 5% DDT has proved effective as a larvicide in comparable doses. The use of such an emulsion has the advantage of simplifying the transport problem still further.

Applied as dust, both DDT and benzene hexachloride (gamma isomer) are lethal to larvae. In the case of DDT, however, a serious drawback in using it in this form on a large scale is the difficulty of grinding the technical powder to the requisite degree of fineness without special diluent and apparatus.
For treating extensive breeding areas of stagnant water, mechanical sprayers have been employed but these have to be fitted with special nozzles which deliver a fine spray at a slow rate. This was found essential as the prevailing tendency is towards overdosage which apart from wastage involves a real danger to fish and other wild life. For the majority of breeding areas, however, hand atomizers of the flitgun type have proved satisfactory whereas for small scattered rain water pools simple devices such as squirt cans and shake drop bottles have been used with success.

For residual larvidical action, the dosage employed in stagnant water is one pound of DDT dissolved in \(2\frac{1}{2}\) gallons of oil per acre of breeding surface. Such heavy dosage can however be used only in situations where danger to fish and other wild life does not enter into consideration.

The choice between the larvicidal and adulticidal control methods would be determined mainly by relative costs. Generally speaking, in scattered rural populations, residual spray killing of adult mosquitoes is the more economical method, but in large urban areas antilarval measures may prove cheaper, unless residual spraying restricted to the periphery or to particular sections of the area might alone suffice for malaria control. Residual spraying may also be preferred if its collateral benefits are desired.

In campaigns aiming at the eradication of vector species adequate indoor residual spray may, by itself, prove sufficient in the case of highly anthropophilic and indoor-resting species, but with respect to others it is frequently necessary to supplement such spraying with antilarval measures.

E. PRICE OF INSECTICIDES

The cost of insecticidal materials varies widely in different countries, from 39 to 91% of total expenditure. Factors which affect this proportionate cost are the price of DDT, solvents and of wetting and emulsifying agents, set against labour and supervisory costs, transport and type of spraying equipment. The cost of DDT varies from $0.26 to $1.44 per pound, at present, in
various countries. There is therefore a considerable need for concerted action to effect a reduction in the high prices, not only of the technical powder, but also of the solvents and other ingredients required for various formulations. In selecting a suitable formulation its local cost must be given due consideration. The high cost of DDT has in some countries been offset by the relatively lower labour costs but, with the increasing demand for high labour wages, there is still further need for reducing the price of DDT and its formulation to the lowest possible level. Regional standardization of spraying equipment is also another step that may affect economies in controlling malaria.

SECTION VI
CHEMOTHERAPEUTICS IN MALARIA CONTROL

A. PART THAT MODERN CHEMOTHERAPEUTICS CAN PLAY IN MALARIA CONTROL.

The Committee, considering the part that modern chemotherapeutics can play in malaria control, agrees with the following propositions:

1. Measures directed against the mosquito transmission of malaria are, in the existing state of knowledge, the only methods which give permanent control. They should take priority wherever possible.

2. Chemotherapy and chemoprophylaxis have an important part in the clinical control of epidemic malaria.

3. Chemoprophylaxis, however efficient, can be considered in general only as palliative.
4. Preventive drugs have, and will retain, an important part in personal prophylaxis.

5. Therapy plays a secondary role in the prevention of malaria.

The Committee, considering that there would be general agreement that the primary consideration in the communal control of malaria is the interruption of transmission at the mosquito level, recommends that measures so directed should be given priority by health authorities wherever possible. The epidemic situation, which can arise only when the above measures are not used or adequately applied, is an exception, for here immediate clinical control has an urgency which can be met most quickly by the use of drugs under appropriate supervision. But here also simultaneous efforts should be made to organize the destruction of adult anophelines.

The Committee, while recognizing the high efficiency of modern synthetic drugs both for suppression and, as regards falciparum malaria, for radical prevention, is agreed that apart from the epidemic situation, the useful application of mass chemoprophylaxis is restricted to special circumstances, where supervision is good and adequate mosquito control is not feasible. The following are examples:

(a) Aggregations of labour living under conditions in which an effective attack on transmission is not feasible or has not yet been undertaken;
(b) Mobile groups operating in malarious territories;
(c) Certain easily supervised social groups, such as school children living in endemic areas where control measures are not yet operative;
(d) Armies in the field.

The Committee, however, wishes to emphasize the impermanence of such measures. Moreover, the safety of synthetic drugs when taken for many years, and the possible repercussion of a loss of immunity under conditions highly endemic still remain to be assessed. Further information on these points is required.

Personal prophylaxis remains, in the view of the Committee, an important field for the application of drugs. The precision of action and the power of certain new synthetic compounds, and their relative safety when used for limited periods, is now generally accepted. For suppression of all forms of malaria and for radical prevention in falciparum infection they remain an important measure of personal defence.
The Committee has raised the question of the cost of antimalarial drugs. It notes that the price of the synthetic compounds has been greatly reduced within the last few years, but that such cost might still be a heavy burden for impoverished countries. The Committee has not at its disposal sufficient data for a profitable discussion of this point and suggests that it be considered at a later session.

B. PRESENT-DAY KNOWLEDGE OF THE USE AND DOSAGE OF MODERN CHEMOTHERAPEUTICS

Many drugs produced over the past few years have shown promise from screening tests in avian and simian malaria, but relatively few are well enough known to justify other than experimental use in human malaria. The Committee, therefore, restricts consideration to the following drugs:

1. SCHIZONTICIDES: Quinine
   Atebrin (a)
   Chloroquine (b)
   Paludrine (c)

2. GAMETOCIDES: Plasmoquine (d)
   Pentaquine (e)
   Iso-pentaquine (f)

Synonyms:
(a) mepracrine (U.K.), quinacrine (France, U.K., U.S.A.) Atabrine (U.S.A.), Italchina (Italy), Metoquina (Latin America), acriquine (U.S.S.R.).
(b) SN 7618 (U.S.A.) Resochin (Germany), Aralen (U.S.A.) Mivaquine-B (France).
(c) Chlorguanide (U.S.A.), Palusil (Italy), 3359 RP (France), M-4888 (U.K.), Guanatol Drinupal (Western Hemisphere)
(d) Pamaquin (U.K.), Praequine (France), Gamefar (Italy)
(e) SN 13276 (U.S.A)
(f) SN 13274 (U.S.A)

1. Schizonticides

QUININE: The merits and limitations of quinine are so well known that repetition here would be superfluous. Quinine has been displaced for certain purposes by the newer more potent synthetic
compounds, yet, in the view of the Committee, it still remains a valuable drug in all forms of malaria and, particularly, for the immediate treatment of serious falciparum infection. The Committee recognizes that certain new compounds offer better prospect of permanent cure and are to be preferred in many situations. It is realized, however, that in impoverished malarious countries, raising their own Cinchona, quinine or alkaloid mixtures may remain the sheet-anchor of treatment for many years to come.

The value of quinine as a suppressive is less certain. The newer drugs are so much more active that few health authorities would be prepared to consider the use of quinine for this purpose. The Committee discourages the use of suppressive quinine by non-immunes exposed to infection, but is prepared to admit that partially immune residents of endemic areas may derive great benefit from this drug, which can be given safely even for many years.

**Atebrin:** The therapeutic action of atebrin in all forms of human malaria is so well known that it is scarcely necessary to consider it here. In general terms it's speed of action is about the same as that of quinine, particularly now that a loading dose \(^1\) on the first day of treatment is standard practice.

\(^1\) There is variation in the amount of the loading dose commonly employed from a minimum of 0.6 g. to a maximum of 1.0 g. on the first day. Four schemes widely applied are summarized below:

<table>
<thead>
<tr>
<th></th>
<th>1st day</th>
<th>2nd day</th>
<th>Succeeding days</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-immunes</td>
<td>(1.0)</td>
<td>0.3</td>
<td>0.3 x 5 days</td>
<td>2.8 g.</td>
</tr>
<tr>
<td></td>
<td>(0.9)</td>
<td>0.6</td>
<td>0.3 x 5 days</td>
<td>3.0 g.</td>
</tr>
<tr>
<td>Immunes</td>
<td>(0.6)</td>
<td>0.6</td>
<td>0.3 x 5 days</td>
<td>2.7 g.</td>
</tr>
<tr>
<td>Partial</td>
<td>0.6</td>
<td>0.3</td>
<td>0.3 x 3 days</td>
<td>1.8 g.</td>
</tr>
</tbody>
</table>

These amounts are for adults and are administered in three or more daily doses.
It is for suppression that atebri in has made its most distinct contribution. Non-immunes may be fully protected even under conditions of intense transmission, at low cost and with no more than slight risk or inconvenience (staining of skin and eyes, gastrointestinal disturbance and, rarely, lichenoid skin eruptions and transient psychoses). The Committee emphasizes the importance of the observations that suppressive doses of atebri eradicate falciparum malaria, but information is still needed on the long term effects after many years of administration.

CHLOROQUINE: This drug is a 4-amino-quinoline developed in Germany before World War II under the name of Resochin. Like quinine and atebri it is an active schizonticide against all forms of human malaria. In general terms, the clinical activity of chloroquine resembles that of atebri, but the toxicity is lower. Its advantages are: that it does not stain the skin and eyes; that it does not produce gastrointestinal disturbance; and that, in very short courses of treatment, 2 to 4 days, it may produce radical cure of falciparum infection. The two-day treatment has special value for self medication because a dose usually adequate for radical cure of falciparum infection is

---

1 There is general agreement that the optimal suppressive dosage for non-immune adults is 0.1 g. daily; a preliminary build-up of 0.3 g. daily for 5 days has been recommended. For suppressive cure of falciparum infection, the daily dose of 0.1 g. should be continued for at least three weeks after the last exposure. With partially immune populations, particularly in areas of low endemicity, suppressive doses of 0.3 g. given once weekly, or 0.2 g. twice weekly, have given a high degree of suppression. With this dosage, however, the possibilities of suppressive cure of falciparum infection are unknown.

2 American experience indicates that the optimal adult dosage, expressed as base, is as follows:

<table>
<thead>
<tr>
<th>Location</th>
<th>Dose Details</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S.A</td>
<td>0.6 g. (divided in two doses)</td>
<td>1.5 g.</td>
</tr>
<tr>
<td></td>
<td>0.3 g. daily for three days</td>
<td></td>
</tr>
<tr>
<td>Venezuela</td>
<td>0.9 g. (divided in three doses)</td>
<td>1.8 g.</td>
</tr>
<tr>
<td></td>
<td>0.9 g. on second day only in three doses</td>
<td></td>
</tr>
</tbody>
</table>

(The tablets of 0.25 g. of chloroquine diphosphate contain 0.155 g. of base).
consumed while the patient still feels ill. Like other schizonticides it does not prevent relapses in vivax malaria, but its slow elimination prolongs the period between relapses. The use of a loading dose is recommended.

Chloroquine is an extremely effective suppressive drug. A single dose given once weekly affords a high degree of protection in vivax malaria and suppressive cure in falciparum malaria. In this respect, it is superior to atébrin which has to be given daily to non-immunes to produce comparable effects.

PALUDRINE: Paludrine is a biguanide compound with a molecular pattern which differs radically from the quinoline or acridine systems upon which are based quinine and atébrin. The drug was introduced towards the end of World War II and was quickly shown to be an active schizonticide in human malaria giving a high cure rate in falciparum infection. The toxicity for man is low and the dosage which produces clinical cure is but a small fraction of the maximum tolerated dose. There is no general agreement yet as to the speed of action which appears, as a rule, to be slower than that of quinine, atébrin or chloroquine. There is furthermore difference of opinion as to the optimal dosage and the duration of treatment.

Available evidence on paludrine treatment in falciparum infection, and particularly in severe falciparum infection, is still inadequate. Further information is needed.

Clinical cure has been reported in falciparum and vivax malaria with single doses ranging from 5 to 1000 mgs. These

---

1. For suppression 0.3 g. of base (i.e., 0.5 g. of chloroquine diphosphate) are the dosages advised; they are given once weekly on the same day of the week.

2. There is such wide difference in the effective range of dosage that the indications which follow must be regarded as provisional:
   (a) For standard therapy, in adults: paludrine monohydrochloride, 0.3 g. daily for five to ten days (the monohydrochloride contains 86.5% of paludrine base).
   (b) For single dose therapy, in adults: 0.3 g. of monohydrochloride in one dose, followed by a weekly suppressive dose of 0.1 g. to 0.3 g. on the same day of the week.
reports show that many attacks are clinically cured by a single dose of 100 mgs. or more, but that the clinical response is slow. Clinical relief, obtained by a means so simple, so safe and at so small cost may well prove to be of great benefit to rural populations, not disposed to take, or unable to afford or obtain regular or systematic treatment. The single dose method cannot be recommended with confidence for the routine hospital treatment of *falciparum* malaria. The Committee notes, however, that good results are recorded from a single dose of 300 mgs. of paludrine given as the routine immediate treatment for overt attacks of *vivax* malaria, and followed at weekly intervals by the same dose, or even lower doses, for the suppression of relapses.

The most striking and distinctive action of paludrine is that which suggests destruction of the pre-erythrocytic forms of *P. falciparum*. A single dose of 50 mgs. or less, given between the third and six day after the bites of infective mosquitoes, has been shown to sterilize a high proportion of infections of *P. falciparum*. This observation was made on S.W. Pacific strains; recent work suggests that the Roumanian strains do not exhibit such high sensitivity.

Field experiments designed to test the preventive value of paludrine are not numerous but indicate that a single dose of 300 mgs. given weekly on the same day of the week affords complete protection.\(^1\)

The Committee, impressed by the fact that the best results appear to have been obtained in the Far East, draws attention to the possibility of differences in strain response to paludrine. This difference is particularly striking in the precisely controlled experiments carried out with the Roumanian and South West Pacific strains of *P. falciparum*.

---

1. Doses of the order of 0.1 g. given once weekly have been shown to be insufficient in some parts of the world; in Indochina, doses of 0.1 g. given twice weekly are apparently highly efficient; likewise, in Malaya, doses of 0.2 g. once weekly have given no more than an occasional break-through; in Malaya, and in hyperendemic areas in India, 0.3 g. once a week has given full protection.
Hopes have been raised by the observation that the sporogonic cycle, in mosquitoes fed on gametocyte carriers receiving paludrine daily, does not proceed to the production of sporozoites. No evidence is yet available of the effect of paludrine on sporogony when given in suppressive weekly or biweekly doses. Further knowledge is needed to assess this effect and its possible significance not only with paludrine but also with other new drugs.

2. Gametocides

The Committee considers under this heading only the following 8-amino-quinolines: plasmoquine, pentaquine and isopentaquine.

These drugs have a similar molecular pattern; all are active gametocides against \textit{P. falciparum}; all produce high cure rates in \textit{vivax} malaria when given with active schizocytocides; all are toxic; none has any place in the prevention of malaria in the field.

**Plasmoquine:** The Committee is agreed on the following point:

(a) Plasmoquine, in association with an active schizontocide, still offers one of the best hopes of radical cure in \textit{vivax} malaria;

(b) Plasmoquine renders the case of \textit{falciparum} malaria non-infective to mosquitoes and still has some place in routine treatment for cases in, or returning to, areas where transmission is possible.

**Pentaquine:** Pentaquine is an American drug introduced in 1946 and still restricted to experimental use. It resembles plasmoquine and has the same general field of utility. Toxicity is somewhat lower than that of plasmoquine but the toxic effects are similar. Haemolytic anaemia has been described in a small proportion of cases.
Combined quinine and pentaquine treatment is reported to have produced cure rates in *vivax* malaria (S.W. Pacific strains) of the order of 80-90%.

**ISO-PENTAQUINE**: Iso-pentaquine is another 8-amine-quinoline developed in the United States in 1947. It has the same field of activity as pentaquine but is slightly less toxic.

Administered with quinine, the drug has given cure rates in *vivax* malaria (S.W. Pacific strains) as high as, or higher than, that of pentaquine.

Iso-pentaquine is at present reserved for experimental investigations.

---

**SECTION VII**

**RESEARCH**

---

**A. INTRODUCTION**

The Committee considers that for the present at least the aspects of malaria research to which WHO should give support are those that contribute most directly to the elimination of the disease.

The extent to which WHO can contribute to this objective requires careful consideration. While there are undoubtedly many ways in which international cooperation, and even direction, may accelerate the clarification of particular problems, there is at the same time a certain danger to be apprehended from the mere canalisation of thought and outlook to which emphasis, on particular lines of investigation by this Committee, may lead. On the other hand, isolated workers, or groups of workers, may well be glad of advice on the direction that their studies may most profitably take. Also there are many lines, more particularly in the field of applied investigation, where parallel studies may lead to results that could not otherwise be achieved. Some notable results were achieved by such studies under the auspices of the Malaria Commission of the League of Nations.

---

1. American experience suggests, for adults, a fourteen day course of 0.06 g. of pentaquine base daily given concurrently with 2.0 g. quinine sulphate. Higher dosages have been employed - up to 0.12 g. base with the same amount of quinine - in order to raise further the cure rate, but at this dosage there is a danger of abdominal pain and moderate haemoglobinuria. Hospital observation is necessary whenever the daily dose of base exceeds 0.03 g. (The monophosphate of pentaquine contains 75% of base).
Perhaps the circulation of well considered questionnaires would, in this field, lead to a crystallisation of knowledge, a revelation of the gaps in knowledge, that could not otherwise be attained.

While some basic problems are to be approached only on a world wide basis, there are many other more immediate problems, particularly those concerning the vectors of malaria and their control, which should at any rate in the earlier stages be dealt with on a regional basis.

B. BASIC RESEARCH

The Committee wishes to emphasize that most of the questions arising under this head cannot be greatly advanced by any direct contribution of WHO. Progress in their solution is most likely to be made by the individual worker of the right calibre and training. Basic studies of the whole range of animal parasites protozoa may yield further results of importance equal to the outstanding leads already given to the elucidation of human malaria, by the study of simian and avian malarias.

The WHO could greatly foster such research by emphasizing the needs to the various research granting
agencies, such as the Rockefeller Foundation, Indian Research Fund Association, and British Colonial Research Committee.

Examples of studies requiring such emphasis are outlined below:

1. Parasite-animal relationships
   a. Behaviour of different strains of human parasite in different races.
   b. International identification and designation of parasite strains.

2. Vectors and insecticides
   a. Study of varying behaviour of the same vectors in different parts of the same region;
   b. Exact method of determining the age of adult mosquitoes;
   c. Coordination of bionomics and taxonomic studies;
   d. Development of new insecticides;
   e. Study of insect physiology in relation to insecticidal action.

3. Epidemiology
   a. Relationship between infective vector density and human malaria morbidity.

4. Chemotherapy and Chemoprophylaxis
   a. Development of causal prophylactics against P. vivax.
   b. Development of drugs for radical cure of vivax malaria.
   c. Effect of antimalarials on tissue forms and sporogony.

C. APPLIED RESEARCH

The subjects considered under this head offer a special opportunity for cooperative research investigated by WHO. It is considered that such combined results may in some cases be achieved by the collation of replies received in response to a questionnaire on the subject selected. In other cases, an outline of an investigation of regional significance might be circulated to suitable institutions or individuals in specified areas, with a view to elucidating problems of general importance to the regions concerned. These problems are as follows:

1. Choice of control method:

   Study of factors influencing the choice between antilarval and antialdult measures of control in different regions.
2. Insecticides:
   a. Study of factors influencing the dosage and frequency of application of DDT under varying local conditions;
   b. Comparison of costs of control in different sizes and types of community;
   c. Appraisal of collateral benefits derived from residual spraying for malaria control.

3. Organization and equipment:
   a. Comparative study of antimalaria organizations in different parts of the world;
   b. Development of ideal spraying equipment on regional basis.

4. Chemotherapy and Chemoprophylaxis
   Comparison of action of chloroquine and paludrine against varying strains of malaria parasites (a) therapeutically and (b) prophylactically.

D. PROPOSED EXPERIMENTS

The Committee considers that the under-mentioned research programmes are of major importance and recommends that they be initiated as early as possible under the auspices of WHO.

1. Coordinated field and hospital trials in malaria chemotherapy and chemoprophylaxis.

The Committee draws attention to the very valuable results achieved by the series of coordinated field trials of various antimalarial drugs under the auspices of the Health Organization of the League of Nations prior to World War II, and recommends the institution of investigations similarly coordinated as follows:

   a. Comparative prophylactic trials under field conditions of chloroquine and paludrine, extending over a period of one year if possible, or failing this, over as long a period as local circumstances permit.

   b. Comparative therapeutic trials of paludrine and chloroquine in all forms of malaria to assess relative activity and to determine differences in strain response.

The Committee suggests that such trials might be carried out in South and Central America, India, Pakistan, Malaya, Indochina, Southern Europe, North Africa, and possibly Central Africa.
2. Species eradication in the absence of natural barriers

There are two main concepts in modern malaria control programmes, namely species eradication and the prevention of malaria transmission by the use of insecticides without attempting actual eradication of the vector species. Except in instances where countries have been invaded by exogenous anophelines, species eradication has so far been attempted only in areas where natural barriers make re-invasion improbable, e.g. the islands of Sardinia and Cyprus. The Committee considers that these methods should be combined in a selected area where natural barriers are non-existent, the objectives being the eradication of the vector species in the centre and the creation of an artificial barrier at the periphery by the application of residual insecticides. The Committee suggests that Central Africa would be a suitable region for the conduct of such an experiment.

SECTION VIII
QUARANTINE

In response to a request to WHO.IC from the Expert Committee on International Epidemic Control, the Expert Committee on Malaria discussed in detail Item 6 of the agenda (WHO.IC/Mal/18, Rev.1, 26 April 1948) which related to a draft international agreement aiming at preventing importation of anophelines into an island (Sardinia) where a campaign for the eradication of anophelines is in progress (Documents WHO.IC/Epid./3; WHO.IC/Mal./21 and WHO.IC/Mal./22).

The Epidemic Control Committee referred the matter to the Malaria Committee with a request that the latter should communicate its views and recommendations directly to the First World Health Assembly.

1. The Expert Committee on Malaria emphasizes the necessity of preventing the introduction of anophelines, by sea or by air, into areas where a campaign of species eradication has been completed, or is in progress, as in Sardinia.

2. Experience has shown that inspection of a ship for the presence of mosquitoes is unreliable in that even after lengthy search it is impossible to be sure that none is present. The Committee recommends, therefore, that the local authority be empowered to carry out immediate
disinsectization of any ship which does not possess a valid disinsectization certificate.

3. The Committee, however, is of opinion that the production of a valid disinsectization certificate should not preclude subsequent inspection of the ship by the local authority while the vessel is in port.

4. The Committee considers that ships which in the opinion of the local authorities require disinsectization on arrival in Sardinian ports should be treated by the most rapid methods available, such as aerosols, but suggests that the technical questions relating to the best methods of disinsectization of sea or aircraft be referred to the Sub-Committee on Insecticides proposed in section V of this report.

5. The Committee recommends that whenever regulations be enforced regarding the disinsectization of seacraft or aircraft, rigid anti-mosquito sanitation should, as far as practicable, be maintained within the mosquito flight range of ports and airports of the country to be protected, so that no imported mosquitoes will be able to survive.

6. With the above reservations, and the deletions or modifications given in the footnote¹, the Committee approves in general the provisions of the Draft International Sanitary Agreement (WHO/IC/Mal./22) and recommends to the World Health Assembly that steps be taken to put into effect immediately the measures envisaged in the draft.

7. The Committee, moreover, recommends also that, apart from the specific case of Sardinia, a draft International Sanitary Regulation to prevent importation of anophelines and applicable to all areas requiring such protection, be studied by the Expert Committee on International Control, jointly with the Expert Committee on Malaria.

¹ The Committee recommends the deletion of:

"as well as the absence or presence on board of insect vectors of human malaria" (Art. 3, par. 2)

"or if the inspection shows that the ship is absolutely clear of insect vectors of human malaria" (Art. 6, par. 1)

"and if, in any case, it is free of anophelines" (Art. 8, par. 2)
SECTION IX
RECOMMENDED RESOLUTIONS

The Expert Committee on Malaria submits the following
Recommended Draft Resolutions for the consideration of the First
World Health Assembly:

I

Whereas the World Health Organization, in order to perform
its statutory functions in relation to malaria control throughout the world, would benefit by the advice of a group of competent malarialogists experienced in the several branches of malarialogy and in various parts of the world,

The First World Health Assembly resolves

1. That the Executive Board be instructed to establish during its first session a Committee to be called: "The Malaria Committee of the World Health Organization", with the following terms of reference:

   (a) to act as an expert advisory body to the World Health Organization.

2. That the World Health Organization set up within its Secretariat a Malaria Section adequately staffed, with a view:

   (a) to assist in implementing the malaria policy of the World Health Organization, and particularly such recommendations of the Malaria Committee as are approved by the World Health Organization; and

   (b) to make it possible for the World Health Organization to function as an international coordinating and intelligence centre in the field of malaria.

II

Whereas the Darling Foundation was created by private Funds with a view to honouring the memory of Dr. S.T. Darling, killed

* See page 4.
by accident during a study mission of the Malaria Commission of
the League of Nations;

Whereas the Darling Foundation had the purpose of granting
periodically a medal and a prize to a malarialogist who particu-
larly distinguished himself with his work;

Whereas, with the liquidation of the League of Nations, the
Statutes of the Darling Foundation are no longer applicable;

The First World Health Assembly resolves:

1. That the Malaria Committee of the World Health Organization,
in consultation with the Director-General, draft the new
statutes of the Foundation and submit these for approval to
the Executive Board;

2. That such statutes should delegate to the Malaria Committee
the responsibility for recommending to the World Health
Organization the name of the candidate to whom the medal
and the prize should be attributed;

3. That the medal should be solemnly awarded by the World
Health Organization;

4. That the Director-General should be the administrator of
the Fund of the Darling Foundation.

SECTION X

CONCLUSIONS AND RECOMMENDATIONS

The following are the conclusions and recommendations
approved by the Committee during its second session:

1. WHO Malaria Policy. With reference to the inter-
national programme for malaria control on a world wide basis,
the Committee deems it advisable to recommend:

(a) that WHO be prepared to assist governments on request,
through regional organizations, when established, in
setting up on a permanent basis malaria control services
suited to local needs, and that these services should be of adequate size, staffed by adequately paid and adequately trained personnel;

(b) that the main objective of the services mentioned above should be effective control of malaria at the lowest feasible cost and adapted to the limitations of the budgetary capacity of each government;

(c) that the services of individual experts and operational demonstration teams be made available to give adequate advice and practical assistance to governments in order to foster the development of local and national malaria control programmes;

(d) that the services mentioned in the preceding paragraph be constituted on a temporary basis; and that in reference to teams, their function should be to carry out malaria economic surveys of the area concerned, to put in practice a control programme based on these surveys and to assess results and costs in terms of malaria, general health and economics; that such control demonstrations should be planned on a scale which could be expanded by the respective governments within the limits of their budgetary capacity. Plans should be made for each team to remain in the area until the control programme, which will be primarily carried out by residual insecticide methods, is established and the preliminary results assessed. This service should not be of less than two years' duration.

(e) that when operational-demonstration teams be sent to a country, a condition to obtain WHO cooperation should be, that the governments be required to appoint local officers to understudy each member of the team from outside sources;

(f) that whilst it may be necessary for the Secretariat to assist in procuring the services of individual experts, the constitution of the teams and their arrangement for their dispatch to the area to be protected should be the responsibility of the regional organizations as soon as they are established;

(g) that all necessary equipment and adequate motor transportation for the operational demonstration teams be included in the initial budgets for such teams;
(h) that three of these teams be formed as early as possible and that they should be allocated on request by governments to selected areas in (i) Central Africa, (ii) Southeast Asia, and (iii) the Tropical Americas;

(i) the assistance on request to schools of malariology now in operation by providing expert lecturers who would participate in the teaching programme, or by other help as indicated;

(j) the assistance in setting up courses in malariology in regions not now provided with such facilities, i.e. in Central Africa and in Southeast Asia. For example, a revival of the International Malaria Courses formerly held in Singapore under the auspices of the Health Organization of the League of Nations might be considered as meeting certain immediate needs in Southeast Asia. Similar courses might be instituted in Central Africa;

(k) the provision of fellowships and travel grants for training in malariology;

(l) the provision of teams or individuals as required for training purposes in the application of particular techniques of malaria control;

(m) the dissemination of reports and manuals dealing with malaria control measures;

(n) that in malaria courses or malaria control demonstrations aided by WHO, due attention be given to education of the public on this subject, and that even more important is the vital need to acquaint administration officers and engineers of all branches with the basic principles of malariology;

(o) that WHO, through its Secretariat, attempt to collect and to distribute to official public health organizations such material on malaria propaganda as is available from all over the world;

(p) that attention be given to the feasibility of building up in each regional organization of WHO a lending service of cinema films, film-strips, lantern slides, and other educational material on the subject of malaria and its control;
Corresponding Members

(q) an appropriate modification of article 14 of the "Draft Regulations Applicable to Expert Committees and their Sub-Committees" (WHO.IC/140, Rev.1, 7 February 1948) to provide for the "corresponding members" to work on a regional basis within the regional organizations, when they will be established;

Budgetary studies

(r) that the Secretariat, through the regional organizations, should carry out relevant studies of national, and in larger countries, of state or provincial budgets, paying due regard to the proportion of each budget spent on health activities in general and on malaria control in particular.

2. Agriculture and malaria. With reference to this problem, the Committee recommends:

(a) that when the time comes for selecting demonstration areas the simplest procedure may be for WHO to select a number of areas and for FAO to advise on the prospects of increased production in the areas named, the final choice made by appropriate consultations;

(b) that the two Secretariats (WHO and FAO) should collaborate in examining the problem of selecting areas on the bases of (1) feasibility of effective malaria control, and (2) potentiality as regards increased food production, and prepare a joint report for further consideration.

3. Insecticides. The Committee considers that the application of DDT as an adulticide is the method of choice in a widespread attack on rural malaria, and that by its use a significant reduction of morbidity may be effected in the majority, if not in all malarious countries. Further investigation is required to assess the efficacy of this insecticide against A. gambiæ in Africa.

In order to stimulate the use and production of DDT and to render it available to all malarious countries, the Committee recommends:

(a) that the question of regional production of DDT, solvents and wetting and emulsifying agents and the waiving of customs duty on these insecticides in non-manufacturing countries be
referred to the appropriate Bodies of the Economic and Social
Council of the United Nations;

(b) that an Expert Sub-Committee on Insecticides be set up to specify
international standards for insecticides and their formulation, to
stimulate the development of standard spraying equipment on a
regional basis, and to deal with all other questions relating to
the proper use of insecticides;

(c) that research on insecticides be encouraged with special emphasis
on determining their stability, effective particle size, duration of
residual action in different surfaces, optimum formulations,
toxicity to beneficial insects and wildlife, and the possibility of
development of resistant strains of mosquitoes;

(d) that literature be interchanged on spraying techniques, formulations
equipment, organizational details, costs and results of spraying
operations.

4. Chemotherapeutics in malaria control.

(a) The Committee agrees that the primary consideration in the
communal control of malaria is interruption of transmission at
the mosquito level, and recommends that measures so adopted
should be given priority by health authorities wherever possible;
agrees on the value of drug administration (apart from clinical
indications) under special circumstances which are briefly:
(i) the immediate clinical control of epidemic malaria;
(ii) the clinical control, under restricted conditions, of
endemic malaria;
(iii) the suppression and suppressive cure of existing human
infection.

(b) The Committee is not prepared at the present time to give firm
recommendations for the use and dosage of the new compounds but
has summarized information in Section VI which may serve as a
provisional guide.

5. Research

The Committee recommends:

(a) that coordinated hospital and field trials on malaria chemotherapy
and chemoprophylaxis be carried out under the auspices of WHO in
different countries;
(b) that an experimental project of species eradication in the absence of natural barriers be carried out in Central Africa under the auspices of WHO.

6. Quarantine against reimportation of anophelines.

The Committee recommends:

(a) that the World Health Assembly take steps to put into effect immediately, with the reservations expressed in Section VIII of the present report, the measures envisaged in the Draft International Agreement concerning steps for the prevention of importation of malaria vectors into regions cleared of anophelines (Sardinia). (Doc. WHO.IC/Mal/22);

(b) that the local authority be empowered to carry out immediate disinsectization of any ship which does not possess a valid disinsectization certificate;

(c) that whatever regulations be enforced regarding disinsectization of seacraft or aircraft, rigid anti-mosquito sanitation should, as far as practicable, be maintained within mosquito flight range of ports and airports of the country to be protected, so that no imported mosquitoes will be able to survive;

(d) that apart from the specific case of Sardinia, a draft International Sanitary Regulation to prevent importation of anophelines, and applicable to all areas requiring such protection, be studied by the Expert Committee on International Epidemic Control jointly with the Expert Committee on Malaria.

7. Vote of thanks.

The Committee recommends to the Executive Secretary to convey officially to the Director of the Pan American Sanitary Bureau its appreciation for the hospitality and the active cooperation that the Bureau has offered to the Committee during its present session.
APPENDIX 1

LIST OF MEMBERS WHO ATTENDED THE MEETING ON MALARIA


<table>
<thead>
<tr>
<th>NAMES</th>
<th>COUNTRIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFRIDI, M.K.</td>
<td>Pakistan</td>
</tr>
<tr>
<td>ALVARADO, Carlos A.</td>
<td>Argentina</td>
</tr>
<tr>
<td>ALWING, A.S.</td>
<td>Illinois, U.S.A.</td>
</tr>
<tr>
<td>ANNECKE, David</td>
<td>Union of South Africa</td>
</tr>
<tr>
<td>AZIZ, M.</td>
<td>Cyprus</td>
</tr>
<tr>
<td>BARNES, Milford</td>
<td>Iowa, U.S.A</td>
</tr>
<tr>
<td>BISHOPP, F.C.</td>
<td>Washington D.C., U.S.A</td>
</tr>
<tr>
<td>BOYD, Mark L.</td>
<td>Florida, U.S.A</td>
</tr>
<tr>
<td>BUSTOS, Castellanos, Jose</td>
<td>Mexico</td>
</tr>
<tr>
<td>CAMBOURNAC, P.J.C.</td>
<td>Portugal</td>
</tr>
<tr>
<td>CANAPERIA, Giovanni A.</td>
<td>Italy</td>
</tr>
<tr>
<td>CHWATT, L.J.</td>
<td>Nigeria</td>
</tr>
<tr>
<td>CLAVERO, DEL CAMPO, Gerardo</td>
<td>Spain</td>
</tr>
<tr>
<td>COATNEY, G. Robert</td>
<td>Maryland, U.S.A</td>
</tr>
<tr>
<td>COLL, Hector</td>
<td>Argentina</td>
</tr>
<tr>
<td>COOPER, W. Clark</td>
<td>Maryland, U.S.A</td>
</tr>
<tr>
<td>COVELL, Gordon</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>DAGGY, Richard</td>
<td>Saudi Arabia</td>
</tr>
<tr>
<td>DE CAIRES, P.F.</td>
<td>British Guiana</td>
</tr>
<tr>
<td>DECOURT, Ph.</td>
<td>France</td>
</tr>
<tr>
<td>DOWNS, Wilbur G.</td>
<td>Mexico</td>
</tr>
<tr>
<td>DY, Francisco J.</td>
<td>Philippines</td>
</tr>
<tr>
<td>EARLE, C. Walter</td>
<td>Georgia, U.S.A</td>
</tr>
<tr>
<td>EYLES, Don E.</td>
<td>Georgia, U.S.A</td>
</tr>
<tr>
<td>FIELD, J.W.</td>
<td>Malaya</td>
</tr>
<tr>
<td>GABALDON, Arnold</td>
<td>Venezuela</td>
</tr>
<tr>
<td>GALVAO, A.L.</td>
<td>Brazil</td>
</tr>
<tr>
<td>GILLETTE, H.P.S.</td>
<td>Trinidad</td>
</tr>
<tr>
<td>HACKETT, L.W.</td>
<td>Argentina</td>
</tr>
<tr>
<td>HERMS, William B.</td>
<td>Californis, U.S.A</td>
</tr>
<tr>
<td>HILL, Rolla B.</td>
<td>Florida, U.S.A</td>
</tr>
<tr>
<td>HINMAN, Harold</td>
<td>South Carolina, U.S.A</td>
</tr>
<tr>
<td>JETTMAR, H.M.</td>
<td>Austria</td>
</tr>
<tr>
<td>JOHNSON, Penny A.</td>
<td>Tennessee, U.S.A</td>
</tr>
<tr>
<td>KNOPPERS, A.T.</td>
<td>Netherlands</td>
</tr>
<tr>
<td>KUMM, Henry W.</td>
<td>Brazil</td>
</tr>
</tbody>
</table>
LANDERRO, Fausto Lunes
LEACH, Charles N.
LEPRINCE, J.A.

MacDONALD, G.
MacKIE, J.B.
MATHESON, Robert
MISSIROLLI, A.
MORIN, Henri G.S.

MIETO, Gasparino M.

OTTO, Gilbert F.
PAMPAENA, E.J.
PINOTTI, Mario
PUTNAM, Persis

QUINCY, Griffith E.
RAFFAELE, C.
ROSEBOOM, Llyod
RUSSELL, Paul F.

SANHERALLI, E.J.
SCHAEFF, J.W.
SCHMEHEL, Frances L.
SCHWETZ, J.
SHANNON, James A.
SINGH, Jaswant
SINTON, J.A.
STOKER, W.J.
SUTTER, Victor A.
SWELLENGREBEL, N.H.

VAUCÉL, Marcel
VISWANATHAN, D.K.

WALKER, Arthur J.
WILCOX, Timée
WILSON, D. Bagster

YOUNG, Martin D.

Portugal
New York, U.S.A
Tennessee, U.S.A

United Kingdom
Hongkong
New York, U.S.A
Italy
France

Venezuela
Maryland, U.S.A

WHO
Brazil
New York, U.S.A
Georgia, U.S.A

Italy
Maryland, U.S.A
New York, U.S.A

Trinidad
United Kingdom
D.C., U.S.A
Belgium
New Jersey, U.S.A
India
United Kingdom
Indonesia
Brazil
Netherlands

France

India

Louisiana, U.S.A
Tennessee, U.S.A
Tanganyika

South Carolina, U.S.A