LEAGUE OF NATIONS.

C.H./Malaria/Fourteenth Session/P.V.4.

HEALTH ORGANISATION.

MALARIA COMMISSION.

FOURTEENTH SESSION.

Provisional Minutes of the Fourth Plenary Meeting held Friday, June 29th, 1928, at 10 a.m.

Dr. LUTRARIO in the Chair.

Present: All members who had attended the preceding meeting.

Report of the Second Sub-Committee

(Document C.H./Malaria/12/Extract 2.)

The Report of the Second Sub-Committee was read.

The MEDICAL DIRECTOR said that, by an error, the proposal of Professor Swellengrebel concerning anophelism without malaria had not been inserted in the Report. He read this proposal, which would be added to the list of questions in the Report to be made the object of an international investigation, as was proposed by Professor Pittaluga.

Definition.

Anophelism without malaria exists in regions where both anopheles and men exist, but where the insects for some unknown reason do not transmit malaria. The factors which prevent this transmission are the causes of anophelism without malaria.

Limitation of the scope of observation.

In large areas from which malaria has disappeared for many years and to which there is not a great influx of carriers of gametes, it is clear that these conditions alone are sufficient to produce the phenomenon. It is, therefore, suggested that the observations be limited to districts where the phenomenon exists, but which are situated in the neighbourhood of malarious areas.

Enumeration of possible causes.

Without wishing in any way to limit the scope of the inquiry, it is important to begin by asking what are the factors which might cause the phenomenon and which are active in the district under consideration. Amongst these factors the following may be mentioned:

(a) Differences in the anopheline density of the malarious and non-malarious regions.
(b) Morphological and biological differences of the anopheline population of these regions; especially with regard to selection of food (animal or human blood), shelter (animal or human habitations), and breeding places (hydro-tellwise conditions).
(c) Differences in relation to receptivity, of both anopheline faunas, with regard to malarial infection.
(d) Differences in relation to the human host and its surrounding, e.g.
    (i) Numerical relationship between man and domestic animals, in stables, especially an animal instict, by means of the precipitin test or otherwise, should prove most attractive to anopheles.
    (ii) Conditions of housing, especially with regard to the shelter offered to anopheles.

The MEDICAL DIRECTOR, as the result of the discussion at the preceding meeting, had drafted a note concerning the subject which he thought might be made the object of an international investigation. He would read it after the Commission had discussed the Report of the Third Sub-Commission.

Professor BRUMPT, recalling the proposal of Professor Marchoux, and the observations made by Professor Ottolenghi on the attraction in stables of anopheles by the proper use of colour, drew attention to the part played by spiders' webs in the capture of mosquitoes. Spiders' webs were generally of a neutral tint, and thousands of anopheles were found in them. During a tour which he had made in the Camargue, in Corsica and in Brittany, Professor Brumpt had been asked by peasants whether they ought to sweep the cobwebs from their stables. They had said that veterinary officers had urged them to do so. This was a question which would have to be settled. It was quite true that not all spiders lived upon anopheles, but it was equally true that a large number did so, as was proved by the number of carcases of anopheles found in the webs. It could therefore be considered that the part played by the spider in the campaign against the anophelis was important, and should be studied on an international basis. If they were not destroyed by the spider, the anopheles caught in a web might be destroyed by means of fly-tox, or other similar liquids. Professor Brumpt suggested, therefore, that a proposal should be added on this point to the list already given.

Professor OTTOLENGHI pointed out that although it might be true that spiders' webs played an important part in the destruction of anopheles it should also be realised that if the spiders webs were removed they reappeared some days afterwards in fine weather. It was easy therefore to consult the requirements of veterinary officers and malariologists.

Professor NOCHT thought that attention should also be drawn to the importance of humidity in the measures taken to combat the anophelis. Various investigations had shown that the anophelis lived by preference upon the borders of the dampest part of the district.

The Report of the Second Sub-Committee was adopted, the Commission postponing the discussion on the subjects to be chosen as capable of being made the object of an international investigation.

Report of the Third Sub-Committee.
(Document C.H./Malaria/12/Extract 3).

The CHAIRMAN read the Report, Item 4, which was connected with the controversial question raised in the Report of the Second Sub-Committee in regard to which the Bureau of the Commission intended to make a proposal. He proposed that the discussion of this paragraph should be reserved.

Professor MARCHOUX thought that since quiniostovarsol was not so dangerous as plasmochin there was no need to reserve the administration of this drug solely for the doctor, as was recommended in paragraph 3.

Professor ASCOLI, Chairman of the Third Sub-Committee, recalled that it had considered that experiments in treatment by quiniostovarsol had not yet been conducted on a sufficiently wide scale to make it possible to recommend the distribution of this remedy to the general public.

Professor MARCHOUX recalled that it was at the request of Professor Nocht that the Sub-Committee had demanded that the use of plasmochin should be submitted to the direct control of doctors, though the use of this drug occasionally caused accidents, and steps should be taken to prevent the general public from acquiring the distrust of a drug which might be of excellent value. Quiniostovarsol, on the other hand, was inoffensive. There could be no objection, therefore, to distributing it, to a certain extent, among the population. Even if it were improperly used, it did not create the same danger as plasmochin. It was undeniable that in all cases the supervision and observation of the doctor were useful, but they were not indispensable in the case of quiniostovarsol.

Professor ASCOLI said that the reason why the Sub-Committee had decided to include quiniostovarsol among the remedies recommended as capable of giving good results in malarial cases was because it was intended to pay a tribute to the experience of Professor Marchoux. Quiniostovarsol had not yet been experimented with on a large scale. It was known that it had given excellent results in cases of benignant tertian fever, but it was also known that its use in the case of malignant tertian fever sometimes caused accidents. He thought, therefore, that the use of these drugs ought still to be submitted to the supervision of doctors, for to do so would in no way affect the opinion which the general public might have of the remedy. It was indisputably true that the experience so far gained made it impossible to recommend its distribution to the general public.

Professor MARCHOUX did not think that paragraph 3, as drafted, contained a recommendation favouring the use of any particular drug. Personally, the only interest he had in the use of quinhostovarsol was a purely scientific interest due to personal research and experience. He was aware that the remedy had been used in Madagascar with no ill result, and that at the moment it was distributed to the population of that island.

Dr. KLIGLER considered that since the two remedies quiniostovarsol and plasmochin were still in the experimental stage, their use could scarcely be recommended before definite information had been obtained on the results they gave. He proposed that all references to either drug should be entirely deleted. The Commission could, however, ask that more detailed experiments should be carried out in connection with these drugs, but it should not assume the responsibility in any way of recommending their use.

Professor MISSIROLI said that the silence of the Report in regard to the two remedies in question might be interpreted as a criticism.

Professor ASCOLI said that the Sub-Committee had regarded it to be its duty to deal with plasmochin in view of the fact that this drug had been placed upon the Agenda. The Sub-Committee had taken the responsibility of mentioning the drug in question, for experience had shown that it was effective, and it would be unjust to make no mention of it. The same was true in the case of quiniostovarsol, which provided a certain basis of treatment in benignant cases. The Sub-Committee thought it could therefore mention the two remedies, which were not

specialities but scientific preparations of which it had been possible to control the good results.

The MEDICAL DIRECTOR desired to interrupt the discussion in order to remind the Commission of the practice followed by the Health Committee when a discussion of this kind took place. Paragraph 3 of the Report of the Third Sub-Committee was clearly distinguishable from the three other paragraphs in which the Sub-Committee gave its views on certain methods of treatment and on certain methods of study. Doubts might arise in regard to the third paragraph, and a doctor reading it might wonder whether the Commission intended to recommend doctors to study the use of the two remedies mentioned, or whether it intended to undertake the study of these two remedies on its own account. Up to the moment, the Health Committee had always avoided making recommendations of a general kind influencing in any way the treatment of a disease. All doctors treating malaria were aware of the two remedies in question, and had had to read the literature on their subject. The Committee should avoid, therefore, making any mention of them in the Report if it did not intend to make a special investigation of them - a perfectly legitimate suggestion in view of the importance of the two drugs. If the Commission decided in favour of this investigation, a Report would then be asked for from the competent organisation for submission at the next Session.

Professor NOCHT pointed out that experience gained in treatment of plasmochin and quiniostovarsol was, at the

moment, on so wide a basis that public opinion would be astonished if the Committee refrained from making any mention of these drugs. It was impossible to compare these two remedies to any fanciful preparation in use, for they had already proved their worth. Some means must therefore be found of mentioning them in the Report, without, however, causing the Commission to make recommendations in regard to them.

The MEDICAL DIRECTOR asked whether the Malaria Commission thought that the Health Committee should undertake a study of these two remedies, in view of the fact that several members thought that they should still only be used with prudence.

Professor ASCOLI, Chairman of the Third Sub-Committee, replied that the Third Sub-Committee agreed to consider paragraph 3 to be a request to undertake a study of the two drugs in question, such a study to be carried out under the auspices of the Health Committee.

The Report of the Third Sub-Committee was adopted with certain drafting amendments.

The Second Sub-Committee Programme of International Studies.

The MEDICAL DIRECTOR recalled that on a proposal of the Third Sub-Committee and of Colonel James, Dr. Lutrario had been asked to choose two or three subjects capable of being made the object of an international study, which would be absorbed by the Health Committee with all the means at its disposal

An unofficial meeting which had discussed the anti-malaria campaign in the United States suggested the following subjects:-

1. Dwelling places and malaria.
2. Study of the anophelis maculi pennis and quadri maculatus.

1. Dwelling places and malaria.

Information would be collected by the Secretariat which would take into special account conditions in tropical, sub-tropical and southern countries. On the basis of this information, a plan of study could be drafted by Dr. Evans and M. Bonamico. On the other hand Mr. Hackett made a proposal which would be classed as a chapter in the study of the above subject, namely, the investigation of the degree of contact between anopheles and man in areas of different malarious intensity; the relative proportion of anopheles in stables and bedrooms, and the proportion of anopheles attacking man as discovered by the precipitation test.

This experimental and epidemiological study might be entrusted to three groups each having two members of the Commission:

Professor Brumpt and Professor Carlos Chagas
Stazione Sperimentale in Rome and Dr. de Buen
Colonel Christophers and Dr. Kligler
Dr. Maxcy and Dr. Sfarcic.

2. Study of anophelis maculi pennis and quadri maculatus.

A systematic biological study carried out in Europe and in the United States of anophelis maculi pennis and quadri

maculatus from the point of view of the transmission and prevention of malaria could be entrusted, in the first place, to the laboratories and research works in America, chosen by the Federal Health Service of the United States and by the International Health Division of the Rockefeller Foundation, on the one hand, and the Amsterdam Institute and Colonel James' laboratory on the other.

When the investigations had been sufficiently advanced a wider co-operation would be required on the basis of a provisional report. Any other member of the Commission who desired to undertake similar work would be asked to forward his observations to the Secretariat to be communicated to the above-mentioned group of research workers.

The Third Sub-Committee proposed a plan of studies regarding the practical importance of intensive treatment of malarial patients by quinine in the prophylaxis of malaria. This plan provided for:

a) A critical study of the data available up to the present;

b) Epidemiological and statistical study of the frequency of pre-epidemic relapses in individuals who had undergone an intensive quinine treatment.

These two studies might be undertaken by the Secretariat, who would obtain such advice and invite such expert collaboration as was found necessary for the preparation of this report.

c) Experimental study of the effects of this treatment on:

   a) the time of appearance, the persistence, the rhythm of reappearance and the number of gametocytes;
   b) the possible loss of evolutionary capacity of the gametes found in treated persons.

It was obvious that this experimental investigation could only be carried out in laboratories in close and daily contact with hospitals possessing sufficient material.

This investigation could be entrusted to three groups formed by a representative of the two institutions:-

1. Professor Nocht - for the Institute of Tropical Hygiene in Hamburg,
   Professor Ascoli - for the clinics, and
   Professor Ottolenghi - for the Institutions of Italy.

2. Colonel Christophers - for the Institutions of British India, and
   Dr. An Kingbay - for the Institutions of the Federated Malay States.

3. Professor Pittaluga - for the Hospitals and Institutions of Spain, and
   Dr. Sergent for the Institution of Algeria.

The other subjects of study proposed during the course of the Session might be classified, and the attention of members of the Commission and other malariologists might be drawn to the usefulness of such a study. In that case, the Commission would be anxious to be kept informed, from time to time, of the progress of these studies. If the proposals just made were accepted, the Chairman of the Commission and the Medical Director would undertake to explain them to the health organisation. Since the programme of investigations proposed was very wide, the Medical Director suggested further that the other questions should be classified in order to place them in a special note annexed to the report.

They would thus be brought to the attention of malariologists, who would be asked to keep the Committees carrying out the investigations informed of their researches and discoveries.

The CHAIRMAN referred to the very special importance of the subjects chosen, which though not numerous, were of vast scope. For financial reasons, the Commission had had to renounce enlarging the programme still further. He would be delighted to support the plan of study when the Health Committee met if the Malaria Commission agreed to it.

Dr. HACKETT recognised the excellence of the choice made in the questions to be studied.

Professor Swellengrebel, having studied at great length the question of the contact of the anophelis and man in direct connection with the Institute at Rome, Dr. Hackett said he would be happy to see him associated in the investigations into this question to be carried out by the Sub-Committee just appointed.

The MEDICAL DIRECTOR took note of the suggestion of Dr. Hackett and proposed that, in order to include the United States of America and Yugoslavia, Dr. Maxcy and Dr. Sfarcic should constitute a new study group.

Dr. MAXCY replied that he would be happy to undertake, on his own responsibility, the study which the Commission desired him to make. He was not certain to be able to supervise it directly himself, but he would be careful to see that it was carried out in the best possible conditions.

Dr. SFARCIC also accepted the appointment which had been offered to him.

Professor BRUMPT drew attention to the present wording of the question concerning the study of anopheles. It appeared that the study of the anophelis maculi pennis should be limited to Europe. The true maculi pennis, however, was to be found in Canada, and in the United States, where it had not been sufficiently studied from the pathological and biological points of view. It would be useful to establish a parallel between the studies carried out into the maculi pennis in those regions and the studies in Europe.

Dr. BOYD said that a collection of American maculi pennis had been sent to the British Museum where the insect had been identified and declared to be the same as the European maculi pennis. The area of the dispersion of this mosquito extended over Canada, the North of the United States, as far as New York, and the Pacific Coast as far as California.

Colonel JAMES thought the matter to be merely a question of drafting. In the intention of the Sub-Committee the study of the maculi pennis should be carried out wherever that insect was to be found.

Professor SWELLENGREBEL asked, though he would not press the point, whether the Indo-Dutch Hospital, comprising twelve hundred beds, should not be included in the institutions called upon to make the suggested researches. Dr. Walsch, its Director, would certainly collaborate with pleasure.

The MEDICAL DIRECTOR replied that he would have been happy to include it in the list of laboratories and

hospitals capable of furthering the study of these questions. He had been limited in his choice not by financial considerations but by the desire to obtain speedy results. It was for this reason that he had proposed a system by which investigations would be entrusted to certain laboratories grouped by pairs. He had no objection to the proposal that the Dutch-Indies should associate itself with the investigations, and he would remind the Commission that the question had been raised during the discussion with Colonel James, The experience gained from the study undertaken into the subject of secondary alkaloids, which had been undertaken several years previously, had shown that such a study, if carried out at too many points simultaneously, only achieved results after a long period of time had elapsed.
The Commission was therefore obliged to limit the field itself if it wished to obtain practical results.
He was sure that all institutions capable of influencing the progress of the investigation undertaken by means of their research work would be asked to communicate to the organisations specially instructed to carry out the investigation in question the results obtained by them.

The programme of work proposed by the Medical Director was adopted.

The MEDICAL DIRECTOR proposed to entrust the study of plasmochin and quiniostovarsol to a number of clinics and Institutes of Colonial Medicine. He asked Professor Nocht and Professor Maxcy to make proposals in regard to this matter for submission at the next meeting.

Report of the First Sub-Committee. (Continuation of the discussion).

The CHAIRMAN recalled that the Commission had not yet reached agreement on the text of the ninth resolution contained in the report of the first Sub-Committee. He proposed a formula adopted by the Bureau which took account of the various opinions expressed.

Dr. KLIGLER pointed out that there was a certain degree of difference between the text proposed and the fundamental principle adopted by the Commission, of only recommending one or two treatments of the disease at a time. He thought that the present proposal recommended the simultaneous use of all measures in the campaign against malaria.

The MEDICAL DIRECTOR replied that the formula proposed could be very widely interpreted. The simultaneous use of all measures was not recommended, but on the contrary, the use of measures suitable to conditions in the various districts, with the exception of measures of mechanical protection which were recommended in the case of all countries.

The CHAIRMAN added that in the minds of the persons who had drafted the resolution the first paragraph referred to an unchanging factor, that was to say, the treatment of the diseased persons, and the second paragraph to a reduction of the chances of infection by the treatment of sick persons, and by the adoption of the measures suitable to the local conditions of each district.

Professor MISSIROLI accepted the proposed draft.

Dr. KLIGLER would have preferred the last paragraph to suggest the adoption of the system of explicit and direct recommendations made to the population.

Dr. BONAMICO pointed out that recommendations to the population were hardly ever effective.

Dr. HACKETT agreed with Dr. Kligler, and said there was a difference between a campaign of organised destruction carried out at great cost, and destruction carried out by the population itself in its dwelling places.

Professor SWELLENGREBEL referred to the danger which might be created by the use of the term "temporary measures". It might be considered that the only durable measures were those requiring continuous supervision.

Professor PITTALUGA, while recognising that some of the observations made should not be forgotten, and improved the draft proposal, thought that since the Commission had asked certain members representing various points of view to draw up a text capable of being applied to the various countries and summarising the general opinions expressed, it would be good not to re-draft this text in detail, but to respect the effort made by the drafting committee to take account of the opinions expressed.

Colonel JAMES urged that in the text of the resolution it should be clearly stated that the object of the investigation was to choose the most effective methods and those which were least costly and best adapted for the local solution of the problem of the campaign against malaria.

M. MISCIROLI accepted this suggestion.

The following wording was adopted unanimously for paragraph 2 of Resolution 9 of the Report of the First Sub-Committee:

a. The Commission considers that the first duty of administrations which have to organise anti-malarial measures is to provide for the treatment of the malarious sick with the additional object of reducing sources of infection.

Simultaneously, or subsequently, according to the circumstances and conditions of the various regions, a study of the causes of endemicity should be undertaken with the object of choosing and carrying out the most efficacious, the cheapest and best adopted method or methods in its solution. Provision should also be made either for radical measures (large bonification, drainage) or for other measures (anti-larval measures).

The Commission is of the opinion that in all cases the use of mechanical protection and measures against the adult insects are desirable.

Point 8 of the Report of the First Sub-Committee.

The CHAIRMAN read the following text, which was adopted without observations:

8. The improvement of the conditions of the inhabitants which result from the development of widespread "bonification" is one of the determining factors in the regression of malaria. The work done is only efficacious in so far as it leads to intensive cultivation of the ground.

It is certain, however, that the use of antilarval measures whilst more extensive works are being carried out is of great value inasmuch as it reduces the anopheline density and serves to bridge the dangerous period which accompanies and follows such undertakings.

The discussion on anti-malarial hygiene was of a special nature. This was not the case to the same degree in regard to the other departments of hygiene, and this had been obvious in the work of the Commission. There was no subject which led to more divergence of view; there was no subject which inspired a stronger final agreement. The divergences of view were apparent as long as special cases were discussed. Agreement was necessarily reached when an endeavour was made to lay down general principles. The methods recommended consisted in the connection to be established according to actual conditions between the general principles and the special cases. The Commission could not achieve a formula in which an endeavour would be made to discover ready-made solutions mechanically, but should adopt dynamic principles which would have a continuous appeal on the initiative and discernment of the health specialist. The conclusions laid down by the Commission were all the more valuable in practice in view of the fact that they were based on the widest, most different, and most personal experiments. Each member had contributed his effective and definite share to the final result.

Report of the Third Sub-Committee.

The Commission adopted the following text for paragraph 3 of the Report; "Use of drugs other than quinine, with special reference to Plasmochin".

The Third Sub-Commission has taken note of the results of work done in connection with the parasiticudal action of other substances, notably plasmochin and quiniostovarsol.

It recommends that the Malaria Commission should include in its programme a study of the value of plasmochin and quiniostovarsol in the treatment of malaria - the enquiry being carried out in hospitals or in circumstances permitting of direct daily medical supervision. This experimental study would be under the control of:

Professor Ascoli	-	Rhone
" Nocht	-	Hamburg
Colonel Christophers	-	India
Professor De Langen	-	Weltevreden
The Anti-Malarial Service of Madagascar		
Dr. Barber	-	United States of America
Professor Pittaluga	-	Madrid
United Fruit Companies of Central America.		

Professor NOCHT understood that Mr. Barber was to go to Central America to carry out clinical investigations. It would therefore be useful to add the name of Mr. Barber to the list of persons entrusted with the study in question, for the experiments in Central America were of special use. He also proposed that Professor Pittaluga should be added to the list on account of the great amount of work he had done on this question.

This proposal was adopted.

The Commission rose at 1 p.m.