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GENEVA 1927

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GENEVA, July 1927

LEAGUE OF NATIONS.

Health Organisation

Principles and Methods of Antimalarial Measures in Europe

SECOND GENERAL REPORT OF THE MALARIA COMMISSION

Publications of the League of Nations

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In Memory

OF

Dr. Norman V. Lothian,

Secretary of the Malaria Commission of the League of Nations;

OF

Dr. Samuel T. Darling,

of the International Health Board of the Rockefeller Foundation;

OF

Mlle A. Besson,

of the Health Section of the League of Nations,

who died as the result of an accident while engaged in their scientific and humanitarian task at Beit-Mery, Lebanon, May 21st, 1925.

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LIST OF THE MEMBERS OF THE MALARIA COMMISSION.

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SECTION I.

SUMMARY OF THE COMMISSION'S VIEWS ON MEASURES FOR DEALING WITH MALARIA IN EUROPE.

It is not part of the Commission's mandate to suggest appropriate antimalarial measures for countries or localities in which malaria is to be dealt with at any cost as a matter apart from the other public health needs and expenses of the country concerned. Our task is quite different. It is to ascertain what measures are most appropriate in countries where the cost of public health measures is an important consideration, and where, in consequence, the antimalarial measures that can be taken are limited financially in accordance with the relative importance of the disease as compared with the importance of other diseases and conditions which affect the public health. This adds greatly to the interest of the subject, but also makes the task of giving advice more difficult. When the discovery of the mosquito cycle of the parasite was made, it was almost universally believed that a single simple method had been put within our grasp, capable of application in all malarious districts. Since then nearly three decades have passed, and such a method is still to seek.

For these reasons, the Commission is unanimously of opinion that the scientific study of malaria must be continuously pursued in the laboratory and the field. We desire particularly to bring this view to the notice of European Governments and to suggest that each of those Governments which has not already done so should establish a small central permanent organisation of selected workers who would devote their whole time to malaria research. It does not seem to be generally realised in Europe what an immense amount of patient labour remains to be performed before we shall know definitely the lines on which, in different circumstances, antimalarial measures may proceed with hope of success. The history of special "antimalarial campaigns" is chiefly a record of exaggerated expectations followed sooner or later by disappointment and abandonment of the work. This record of failure and disappointed hopes makes it clear that the only prospect of real progress lies in renewed activity in the continuous study of the disease in all its aspects.

Moreover, during our tour, nothing struck us more forcibly than the observation that, in several of the countries which we visited, costly measures were being undertaken with an antimalarial purpose in circumstances in which such action was of very doubtful utility. A central malaria-research organisation continuously occupied with the subject, and in close touch with similar organisations in other countries, would be in the best position to advise as to the kind of measures upon which funds available for antimalarial work could most profitably be spent.

We do not propose to enumerate a list of subjects on which research is needed. Here we shall refer only to certain routine observations which we consider are most likely to advance the knowledge necessary for practical antimalarial work. We think that in every European country at least one area should be selected in which detailed observations on malaria should be made at regular short intervals (say monthly) for several years. The observations should be upon all the matters with which a complete "malaria survey" is ordinarily concerned, but in particular they should include an endeavour to record accurately the amount and character of the disease month by month and year by year, and the numerical prevalence and infection rate of anopheles in the houses at the same intervals. Observations should be made as to the abundance of anopheles larvæ in breeding-places in the neighbourhood of houses at different seasons of the year. The work should include a systematic house-to-house enquiry for cases, for taking blood-films and for collecting anopheles. It is essential that the laboratory staff should have no difficulty in entering and examining the interior of any house, stable or other building. We are convinced that, of all records relating to malaria, the full and definite story of its course and progress from month to month and year to year in selected localities, accompanied by similar information relating to adult anopheles in the houses and other buildings, is the work that is most urgently needed at present from the point of view of prevention.

We desire to refer also to an entirely new field of enquiry which has lately become available in Europe and which, if scientifically tilled and harvested, promises to yield fruitful results. We refer, of course, to the field of enquiry opened up by the use of malaria as a method of treatment. The Commission is unanimously of opinion that, both in the immediate interest of the patients who undergo that treatment and in the ultimate interest of the millions of malaria sufferers in the world at large, it is essential that, in each country where the method is used, there should be central expert control and an officially organised arrangement by which a pure strain of a relatively innocuous organism cultivated in mosquitoes would be available for use. This means that a laboratory shall be established for the continuous provision of infected mosquitoes and that there shall be an official arrangement by which an expert member of the laboratory staff shall take the infected insects personally to the hospitals in which patients are to be treated, and shall have facilities for studying the course of the malarial attacks in those persons. We suggest that, whenever possible, the work in this laboratory should be carried out in close collaboration with the laboratory situated in the same district as the malarious locality which has been selected for continuous routine observations of the natural course of the disease

among the general population. In this way, the factors concerned in the seasonal onset, course and decline of the natural disease (benign tertian, at least) among the population could be correlated with the more exact records of infection of anopheles month by month in the laboratory and the clinical manifestations of infected patients in the hospital. We can imagine no scheme of enquiry which would be likely to give more profitable results from the practical point of view, and no scheme which, in the present state of knowledge, would better justify the initial and recurring expense involved.

But the Commission, knowing that no master-key has yet been discovered which will unlock all the gates at present barring the road to success in antimalarial work, and realising that for this reason research into all aspects of malaria must continue to be pursued with ever-increasing zeal, is very conscious that an impartial and authoritative pronouncement on preventive measures in the light of existing knowledge and experience is expected of them. The collective study tours undertaken by the Commission have afforded an opportunity of ascertaining and of comparing the present position of antimalarial work in a number of countries where an endeavour has been made for some years to follow what is believed to be the teaching of that knowledge and experience. During these journeys, observations made by individual members of the Commission are examined by other members, and the results are discussed in full session by malariologists belonging to very varied schools of antimalarial practice and opinion. In this way, individual views become modified, and the Commission as a whole endeavours to arrive at an impartial judgment regarding what may be the wisest course to pursue in different circumstances when due consideration is given to administrative and social and economic as well as to technical difficulties. In most instances, of course, the final view of the Commission as a whole represents a compromise between opposing tendencies — a compromise which may be called the "average opinion", which, perhaps, as a rule, most nearly approaches the truth. So far as we are aware, our mutual discussions are the first occasion on which the collective thought of malariologists of different countries and different schools of teaching and practice has been brought to bear on local malaria problems studied on the spot.

In view of these advantages, the Commission is of opinion that it can no longer hesitate to state, more definitely than was done in its former report, certain conclusions, based on the documentary evidence collected and on the personal observations made, which may be of service to the public health administrations of the European countries which are concerned with the problem of malaria control.

1. In the first place, we should like to explain that, in our view, the present mandate of our Commission is not concerned with the problem of converting malarious areas into non-malarious ones. The financial limitations, to which we have already referred, justify us in this view. We regard the mandate as being concerned only with the measures to be adopted in order that malaria may cease to be an important cause of sickness and death. There is, of course, a great difference between the two

aims. In a locality (for example, London or Rome[1]) which has been changed as stated in the first aim, malaria fails to spread when imported cases of the disease are introduced: in such a locality the work done has been all-sufficient; no subsequent preventive measures are required. From such places there has been a *real* disappearance of the disease. On the other hand, in a locality to which the second aim refers (for example, the Panama Canal Zone), the potentially malarious character of the locality has not been changed, but the amount of sickness and mortality caused by the disease is effectively kept in check by various measures or circumstances which are continuously in operation. From such places there has been an *apparent* rather than a real disappearance of the disease. It is evident, of course, that the second aim is less satisfactory than the first. As Professor Gosio has written: "No victory is real that does not overcome the endemicity of the disease and suppress its sources; failing this, we can only claim to have scotched an ever-threatening enemy whose re-awakening is an ever-present possibility". This is true, but in the thousand and one small towns and villages of every affected country the "scotching of the enemy" is all that can be hoped for, and, in the present state of knowledge, it is all that should be aimed at. Those who are dissatisfied with this limited aim may derive comfort from the knowledge that it is all that has been accomplished even in countries like England, the Netherlands and Denmark, which geographically and in every other respect are much more favourably situated for obtaining success in the "eradication" of malaria than is any affected country in Central and Eastern Europe. See, for example, the map of England on page 15 showing the areas in which locally contracted ("indigenous") cases of malaria were brought to notice between 1917 and 1926, and on page 14 a map showing what was believed to be the distribution of indigenous malaria about sixty years ago[2]. It will be seen that the geographical distribution of the areas in England which are still liable to the occurrence of locally contracted cases of malaria is very much the same as it was six decades or more ago. This means that in England, except as regards London and similar large cities, we are not able to cite an indubitable example of *real disappearance* in the sense just defined. The rural towns and villages of England which formerly were malarious are still potentially so, as is proved, for example, by the fact that in Queenborough town in 1917, when a large number of malarial patients and carriers were introduced from abroad, a sharp and widespread epidemic of new cases among the local inhabitants occurred. Therefore, we are obliged to admit that what has happened in those areas is not an eradication of the causes of endemicity and of the sources of malaria but a significant reduction, and in some instances a complete cessation, of observed cases of the disease and in particular a cessation of severe and fatal cases. Thus the disease has come finally to be of little or no importance as a cause of sickness and death. This, in our view, is a sufficient

[1] Many examples could, of course, be cited. Recently the Commission saw a good example at Mondello, in Sicily.

[2] Two maps of the Netherlands, found on page 16, illustrate an exactly similar state of affairs.

aim to strive for, and, indeed, in the present state of knowledge, it is the only aim which is possible of accomplishment, except in a small fractional proportion of the numerous localities where malaria prevails.

Conclusion. — In Europe, having regard to the present state of knowledge, the correct antimalarial practice is an endeavour to reduce the incidence and severity of the disease. Measures designed to accomplish more than that (particularly measures aiming at "eradication") are not a wise proposition and can be justified only in very exceptional circumstances.

2. Secondly, we wish to remark upon the belief (which we found to be common in Eastern Europe) that it is always necessary to deal with malaria by a method arising directly out of the knowledge of the evolutionary cycle of the parasite in mosquitoes. Our opinion is that it is very desirable in certain circumstances to throw off the tyranny which that belief has exercised over men's minds during the last thirty years. It is safe to say that in some countries of Eastern Europe with very limited financial resources hardly anything has retarded the effective control of malaria so much as has the belief that, because mosquitoes carry malaria, their elimination should be the object of chief concern and expenditure. We have seen some extreme instances in which so much of the time of the available medical men was taken up by antilarval measures in the field that little or no treatment of the people who were ill in their homes could be carried out. Since the advent of the new knowledge of the transmission of malaria by mosquitoes, there has been a tendency to forget that there are many methods of dealing with the disease, and that some of them are effective even without any attempt being made to reduce mosquitoes. Indeed, it is wise not to forget that some of them were effective long before the malaria parasite and its vital association with a mosquito of any sort had been discovered. In this connection, we may repeat that England, the Netherlands and Denmark are examples of countries in which malaria was robbed of its importance as a cause of sickness and death, without any knowledge of the epidemiology of the disease and without any reduction of anopheles having occurred. In various other parts of Europe this is happening to-day. Quite recently, during our tour in Sicily, we were shown a locality (Rotondella) in which a quite similar change had been effected under the same conditions of absence of measures based on epidemiological knowledge and absence of anopheles reduction.

Conclusion. — It is not always necessary to deal with malaria by a method arising directly out of the knowledge that the disease is transmitted by mosquitoes.

3. A result of our enquiries which is closely related to the conclusion just stated is the recognition that there is not yet a method of malaria control which can be described as being superior to all others and, therefore, to be adopted in every country. There are (as we have already said) a number of methods of control, and some of them are constantly being improved. Each or any of them may, either wholly or in part, render valuable service in a country if it is a method well suited to the local conditions.

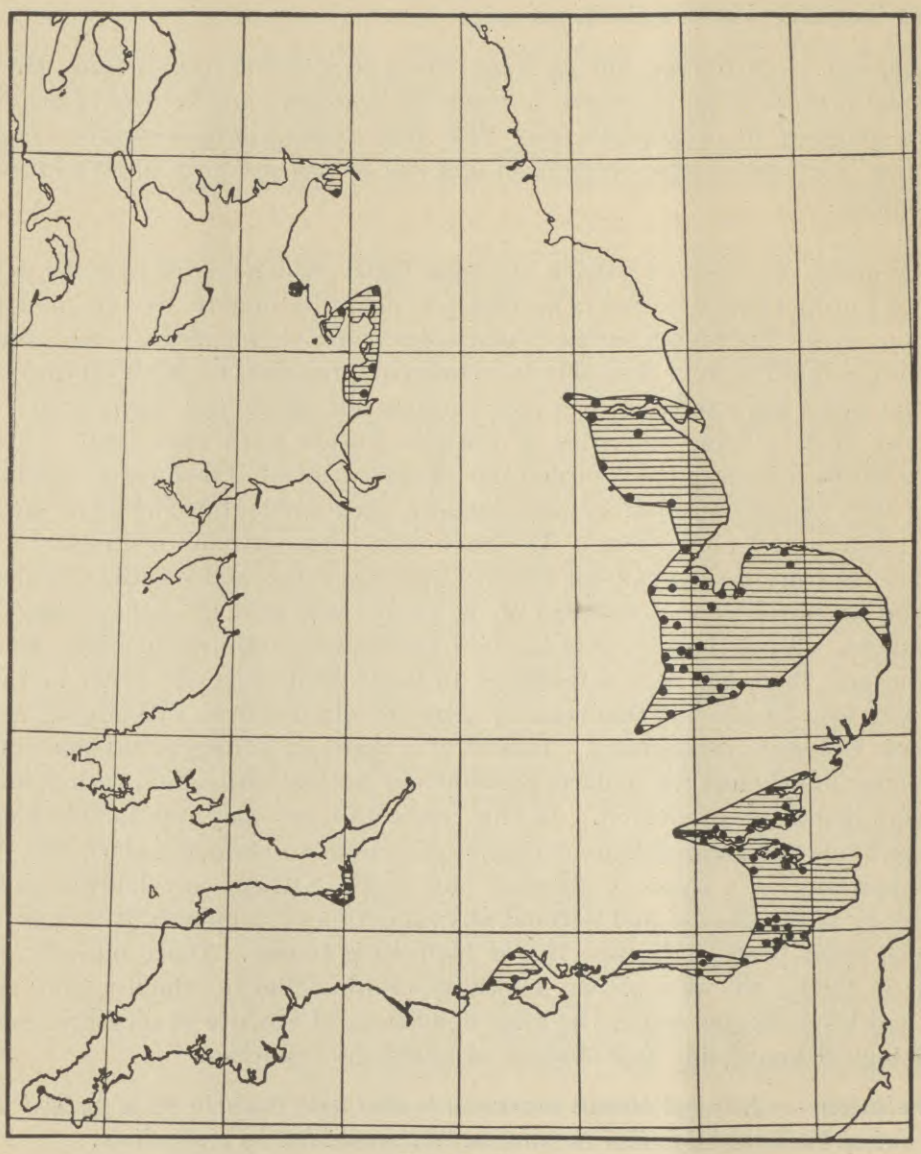


Figure 1.

ENGLAND AND WALES. — GEOGRAPHICAL DISTRIBUTION OF INDIGENOUS MALARIA ABOUT 1860.

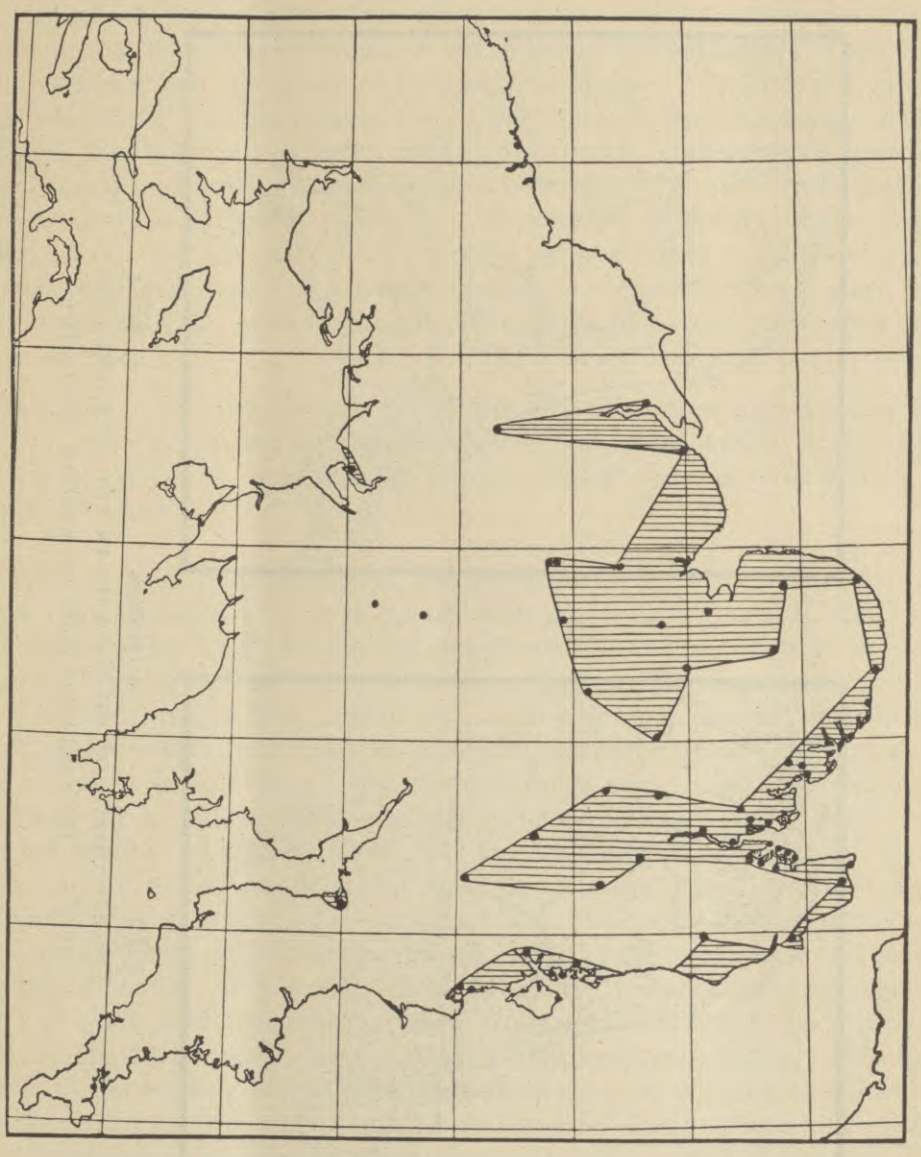
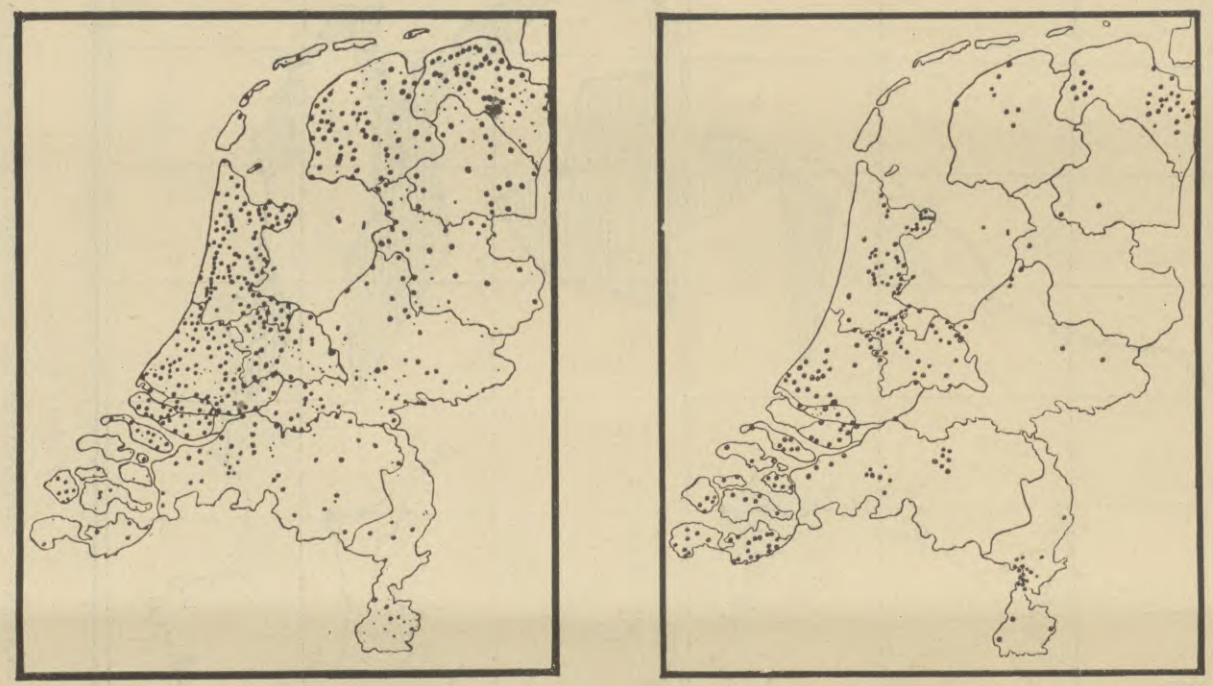


Figure 2.

ENGLAND AND WALES. — GEOGRAPHICAL DISTRIBUTION OF INDIGENOUS MALARIA BETWEEN 1917 AND 1926.



1919 *Figure 3.* 1875

THE DISTRIBUTION OF MALARIA IN THE NETHERLANDS.

1919. — The small dots represent localities malaria-free.

This suitability or adaptability to local conditions is one of the most important matters to be considered in a choice of methods and it is essential to the success of the method chosen. Local conditions differ from place to place, and the differences constitute secondary or auxiliary factors which, as we noted in the beginning of this Section, play an important part in the epidemiology of the disease. They may be concerned with the inhabitants (*e.g.*, race, social status, habits and customs, housing, work, etc.) or with the anopheles (*e.g.*, species, habits, abundance, etc.) or with the soil and environment (*e.g.*, reclamation and clearing of land, character and extent of breeding-places, primitive or intensive agriculture, farming or industries, state of general sanitation, etc.). The necessity of employing a method which takes these secondary factors and their differences in different places into account makes malaria control a *local problem* to a much greater degree than is the case with the control of other infectious diseases.

Conclusion. — In every country and very largely in every area, there must be preliminary examination to ascertain what method is best suited to the local conditions. At present, it cannot be said that for malaria control there is a method of choice superior to all others.

4. This study of local conditions and peculiarities is indispensable, but we do not mean that measures of control cannot be begun until a complete study is concluded. Usually that study is long and complicated and is best done in conjunction with certain "primary measures" which, as we shall see later, are to a considerable degree applicable everywhere. Moreover, a considerable part of the study is of an expert nature which, from lack of a sufficient number of trained workers, can only be done in certain sample areas. For this part of the enquiry we must depend upon the results of the routine examinations made over a prolonged period at the selected observation station or stations which we have already recommended should be established by every European country under the charge of a central expert organisation, as has been done in Spain, for example. With the complete information relating to those sample areas to guide him, the officer in charge of the measures in any particular locality should be able very quickly to ascertain whether they are applicable to his locality and what particular information to supplement them may be required. In any case, he should, of course, arrange at once to ascertain the amount and character of malaria in the locality and to take what steps may be possible to ensure that a continuous record on this subject will be obtained by examinations and re-examinations at frequent intervals or by some other plan best adapted to the local circumstances.

Conclusion. — When the method which has been decided upon has been begun, study of the local conditions and circumstances must be continued uninterruptedly, but its amount and character are unavoidably limited to what the available staff has been trained to do. In any case, it is essential to arrange for a system of ascertaining at frequent intervals the amount and character of malaria.

5. Next we may consider the problem of the actual methods of controlling malaria which, in the existing state of knowledge, it is desirable to recommend. Before doing so, we must say a few words on the vexed question whether it is better to utilise several of the known methods at the same time or to concentrate all available effort on one carefully selected method. This is a question which has been put to the Commission more than once. The public health authorities of several countries which we visited are anxious for a definite indication to be given as to how far it is necessary for them to go in the "antimalarial campaign" to ensure that the disease will be brought under control. In this connection, the observations which the Commission made during its tours proved clearly the danger of putting in action at the same time, and with the limited staff available, too many measures of control. The result of this practice was invariably that not one of the measures was brought to the degree of perfection at which it could possibly begin to have any effect on the incidence of malaria. Action of that kind is doubtless prompted by the laudable desire for quick results, but it is apt to bring discredit on the methods used and even to lead to scepticism of the practical value of modern knowledge. Logically, it seems reasonable to suppose that even a little antimosquito work, or a little screening, or a little distributing of quinine, must inevitably do *some* good, but the results of practical work do not support this conclusion. They show that, as regards any and every measure, there is a "minimal effective degree of perfection". Unless the means and materials available are adequate to bring the work beyond that minimal standard, no result whatever ensues and all that has been done is wasted. Nevertheless, it is true (as we said at the beginning of this Section) that up to the present we know no single method of control which alone suffices to deliver the world from malaria. In this respect, the problem of malaria control is much more like that of plague than that of smallpox — but even the plague problem is probably easier to solve than the malaria problem. Fortunately, our Commission's decision that in Europe, having regard to existing knowledge and to financial limitations, it is not a wise or practical proposition to aim at the "eradication" of malaria makes it easier to answer the question whether it is better to utilise one or several measures. If the aim were the "eradication" of malaria from a locality, we should be obliged to say that it would be necessary to employ at the same time all known methods which, with the means available, could be brought to the standard called "minimal effective degree of perfection". But with the lesser aim — the reduction of the incidence and severity of the disease — the utilisation of all available methods is not necessary, and it is better, in our opinion, to limit the action taken to one or two selected methods, which can then be brought to a high degree of perfection. If, after a fair trial, these one or two measures are found to be insufficient to rob the disease of its practical importance from the public health point of view, further methods can be systematically added to them until the desired end is attained.

Conclusion. — For the reasons stated, the Commission is not in favour of utilising all available methods of control in the same locality at the same time. They consider

it preferable to employ only one or two methods which, with the means available, can be brought above the standard called "minimal effective degree of perfection".

6. We consider that, subject to the above limitations, there should be considerable freedom of choice as regards the particular methods of malaria control to be adopted in any country or area. Each country and, to a more limited extent, each locality must "work out its own salvation" in this matter, and we suggest that they should do so in greater degree than has hitherto been the case. It is chiefly with this end in view that we have laid stress on the necessity of establishing in each country a *permanent* central malaria-research organisation, composed of workers who are intimately acquainted with the local conditions and peculiarities and, at the same time, are in close touch with similar organisations in other countries and, above all, with public health workers in their own countries who have to deal with malaria. The problem is essentially one for experimental treatment separately in each of the countries concerned, and at present we do not see how it can be solved in any other way. There must be continuous investigation, continuous criticism and continuous use of the imagination. It we permit ourselves in this report to criticise in a general way the antimalarial work of the countries which we visited, we may say that, on matters of principle, there is evidence of an endeavour to follow too slavishly the antimalarial policy adopted in some other countries, without ascertaining in the first place whether it is suited to the local circumstances and conditions, and in some instances without interpreting correctly the real purpose which those other countries have in view in carrying out the particular methods adopted. As regards the first point, we think, for example, that the discovery that direct antilarval measures are practicable and produce very good results in one country or locality should not be regarded as a sufficient reason for adopting that measure in another country or locality until it has been ascertained that the conditions are quite similar. As regards the second point, we realise that it is sometimes very difficult to interpret correctly the purpose which a country has in view in carrying out certain measures, and that terms such as *assainissement*, "bonification", *bonifica*, *saneamiento*, *polder*, etc., are almost universally misunderstood and misinterpreted except in the particular country where they originated. It was evident during our tours that in several countries the Italian term *bonifica* was interpreted as meaning a direct antilarval measure, consisting chiefly of large and small drainage works. Nothing could be further from the truth. In the world generally there is a widespread misapprehension of Italian antimalarial methods. This misunderstanding is evidenced by the fact that large bonification works had been carried out with success long before the discovery of the transmission of malaria by mosquitoes. Therefore it may be useful to state categorically here that Italy does not carry out large and small drainage works with the object of getting rid of anopheles mosquitoes, nor does she place antilarval measures in the forefront of her antimalarial programme. Indeed, she places very little reliance on antilarval measures except in certain well-defined conditions where hydraulic work of such a kind can be done as to prevent

all larval growth. We make this definite statement in the hope that it will prevent to some extent the waste of money, energy and time which in some countries is being misapplied in the false belief that the Italian example is being followed.

Conclusion. — Subject to certain defined limitations, there should be considerable freedom of choice as regards the particular methods of malaria control to be adopted. The Commission deprecates the adoption of measures in one country on the ground that they have been successful in another, where, perhaps, circumstances and conditions are quite different.

7. It is usual to classify measures into:

(1) *Direct;*
(2) *Indirect.*

We adopt that classification, but we give to the terms a more precise definition than is usual. For instance, we do not regard antilarval measures, nor even measures against adult anopheles in the general environment, as being direct antimalarial measures In our view, there are only two direct antimalarial measures, namely, killing the malaria parasite in man and killing the malaria parasite in mosquitoes. The first is to be done by treating malaria-infected persons with quinine, the second by killing malaria-infected mosquitoes in the houses. In comparison with these two measures, anything else that can be done to control malaria is necessarily very indirect. For example, no one who thinks seriously on the matter can doubt that general antilarval measures in the field are a very indirect method of trying to deal with the disease — that they are a line of action which takes us very far away from the rather exact knowledge of the ætiology and epidemiology of malaria which we are fortunate enough to possess at the present day. They were rightly regarded as a direct measure twenty-five years ago, when it was believed that what was called the epidemiological chain could be expressed in the simple formula:

mosquito + malarial patient = malaria.

But we have long known that the formula, even in its simplest form, must be represented figuratively by at least three chainlets, each consisting of links of different shapes and sizes to indicate various circumstances and conditions of unequal influence, joined together rather loosely by larger and stronger links, which, as we now know, are almost unbreakable with the means and materials usually available in malarious places.

Adopting this restricted definition of direct and indirect means of controlling malaria, we may begin our recommendations as to direct methods by referring to the "brief conclusions" with which we prefaced our former general report on malaria in Europe (C.H.273). In those conclusions, we stated the general considerations of which account should be taken in framing suggestions for dealing with the disease, and

we indicated in general terms the line of policy which we thought should be adopted. This was to the effect that, in the malarious countries of Europe, certain "primary measures" for dealing with the disease are practicable, and give prospects of very favourable results, without it being necessary to undertake those comprehensive antimosquito measures which are so closely associated in the public mind with malaria prevention, but are impossible of employment, save in quite exceptional cases, on account of their enormous expense. We defined primary measures as being measures which are limited to malaria-infected individuals and the interior of the houses in which they live, and we stated that, in the opinion of the Commission, these measures are always indispensable, whether or not any other direct or indirect means of controlling malaria are employed.

Conclusion. — The Commission defines what it understands by the terms "direct" and "indirect" measures, and suggests that in every malarious locality certain direct methods, called "primary measures", which have to do with malaria-infected individuals and the interior of the houses in which they live, are indispensable.

8. First let us consider the measures relating to malaria-infected individuals.

We think that, whatever else it may be possible to do in malarious localities, the first and most important thing to do is to arrange for the treatment of the disease by quinine. In certain parts of Europe the gratuitous distribution of quinine is the only antimalarial measure which the countries concerned can afford to carry out. We are persuaded that the wide distribution of quinine is a public duty which, whenever and wherever necessary, should be organised and paid for by the State. Without going into detail, we would merely state that in this measure, as in others, the plan which succeeds best will usually be the plan which is best suited to the ideas, customs and prejudices of the people.

In organised communities something more than the gratuitous distribution of quinine to all who appear to be suffering from malaria must be attempted. In communities which have attained the status of a town or municipality, there will usually be at least one resident or visiting private medical practitioner, and the Commission is of opinion that in such localities it is advisable to appoint and pay him for the specific duty of treating malaria patients in their own homes and of discovering and treating new cases and carriers. A further advance consists in the organisation of a definite system for the satisfactory diagnosis and efficient treatment of the disease. In our opinion, this duty is one which, wherever possible, should be in the hands of private medical practitioners who can visit patients in their own homes; but it is essential that the practitioner (who will be appointed "part-time special malaria officer") should undergo a post-graduate course of malarial study. In the investigation of malaria in Europe, nothing is more striking than the difference between the manifestations of malaria in a locality where the practising medical men have full knowledge of its diagnosis, clinical course and treatment (and where, consequently, patients are properly treated) and the manifestations in a similar locality which is without that expert medical aid. The difference may be so great that, in places in the

former category (as the Commission was able to observe personally on several occasions during its tour in Europe), modern methods of enquiry for ascertaining the "splenic index" or the "parasite index", as a test of the incidence and endemicity of the disease, may give entirely negative results. We have observed in North Holland some excellent instances of what private practitioners, working entirely on their own initiative, can do to keep the effects of malaria in check and to provide information of its incidence and epidemiology. We refer particularly to the work of Dr. Korteweg in the Zaan district, Dr. Honig at Nieuwendam, Dr. Horst at Zaandyk and Dr. Faber at Sloten. These private practitioners have made it their rule to take and examine thin and thick blood preparations from any of their patients in whom malaria is suspected, and to keep a card-system record of the positive cases, separately for primary occurrences and relapses, with details of age, sex, residence, parasite and splenic findings, symptoms and effects of treatment. In this way there has become available for four or five separate communities, each of about 3,000 inhabitants, an epidemiological and clinical record which, for accuracy and fullness of information, appears to the Commission to be of great value. It is understood, of course, that these practitioners did not intentionally take any steps to control malaria; their action was limited to the diagnosis and treatment of cases as they arose among patients who sought their advice. The good which they did is chiefly evident from a study of the clinical records. These show, in the first place, that the discovered cases were cured within a few days and seldom or never suffered from enlarged spleens or other appreciable after-effects of the illness, and, secondly, in marked contrast, that there were found, from time to time, persons who had never been treated and in consequence were in a cachectic condition and with greatly enlarged spleens, so that they presented an appearance quite similar to that of untreated patients in the Tropics and in some parts of Eastern Europe. No one who was cognisant of the existence of such cases could fail to appreciate what might be the condition of a large number of the inhabitants of those malarious districts in North Holland if early diagnosis and effective treatment were not readily available.

We should like also to point out that the Commission during its tour in Spain observed, notably in the province of Caceres, a system being developed whereby medical practitioners were entrusted with the duties of official malaria doctors.

Conclusion. — The Commission considers the treatment of malaria-infected persons to be one of the most important measures even from the point of view of prevention. It considers that, in rural areas and localities under primitive conditions, the State must make arrangements for the treatment of patients according to the means available, and that at least an arrangement for the gratuitous supply and distribution of quinine in such areas is indispensable. In organised communities in which the sanitary authorities consider it expedient, the Commission considers that satisfactory diagnosis as well as treatment should be arranged for, and recommends that, wherever possible, private medical practitioners already established in the locality, and having undergone a special training with this end in view, should be appointed to undertake the work.

9. The part which a private practitioner can take in controlling the manifestations of malaria is greatly enhanced by an arrangement for inducing persons who, ordinarily, do not consult a doctor until they are seriously ill to do so at an earlier stage. That there are many sufferers from malaria in that class of people was clearly shown in a small town in England which experienced an outbreak of locally contracted malaria in 1917-18. At the beginning of 1918, it was known that the doctor in the town had been consulted by eleven residents who had contracted malaria in 1917. It was decided to appoint and pay him as a "part-time special malaria officer" and to announce that persons suffering from malaria would be provided with medical attendance and treatment free of cost. When this became known, several persons whose cases had not previously come to notice consulted him, thus bringing the number of known cases in the town to eighteen. Systematic house-to-house enquiry for cases was then made, with the result that the number of known cases was brought to thirty-two. According to these small figures, the number of malaria patients who suffered sufficiently to induce them to go to the expense of consulting a doctor was only one-third of the total cases in the town. The arrangement referred to now forms part of the English Public Health (Malaria, etc.) Regulations, 1919, in the following terms:

> "*Article* 11. — On the occurrence within a district of two or more cases of malaria in which the infection has, in the opinion of the Medical Officer of Health, been contracted within the district, the Local Authority may and if required by the Ministry of Health must appoint and pay a Medical Practitioner approved by the Ministry of Health, who shall make systematic visits to houses where malaria has occurred, or where risk of malaria infection arises, and shall offer to examine persons therein who are suspected of being infected with malaria, and shall endeavour to obtain material for microscopic examination in order to determine whether malarial infection is present."

We think that some plan of this kind for the discovery and treatment by a private medical practitioner of patients in their own homes, and for keeping an accurate record of malaria occurrences, should be arranged in every malarious locality in which one or more practitioners are already established. In countries with a satisfactory system of medical education, all private practitioners, whether they hold a part-time State appointment or not, should be prepared to collaborate by working in this way for the health of the community as well as of the individual, but it is right and proper, whenever possible, to organise various plans for inducing them to do so, such as the institution of health-insurance systems, sick-benefit clubs, the appointment of practitioners as part-time medical officers of health, poor law medical officers, special malaria officers, school medical officers, etc.

Conclusion. — The Commission describes an arrangement by which a private medical practitioner is appointed and paid by the State as "part-time special malaria officer", with the specific duty of discovering and treating cases and carriers and of carrying out the other "primary measures" recommended.

10. Obviously, no useful purpose would be served by magnifying unduly the part which the private medical practitioner can play in the control of malaria. We do not desire to do so, but we wish to insist (as we did in our former report) on the fact

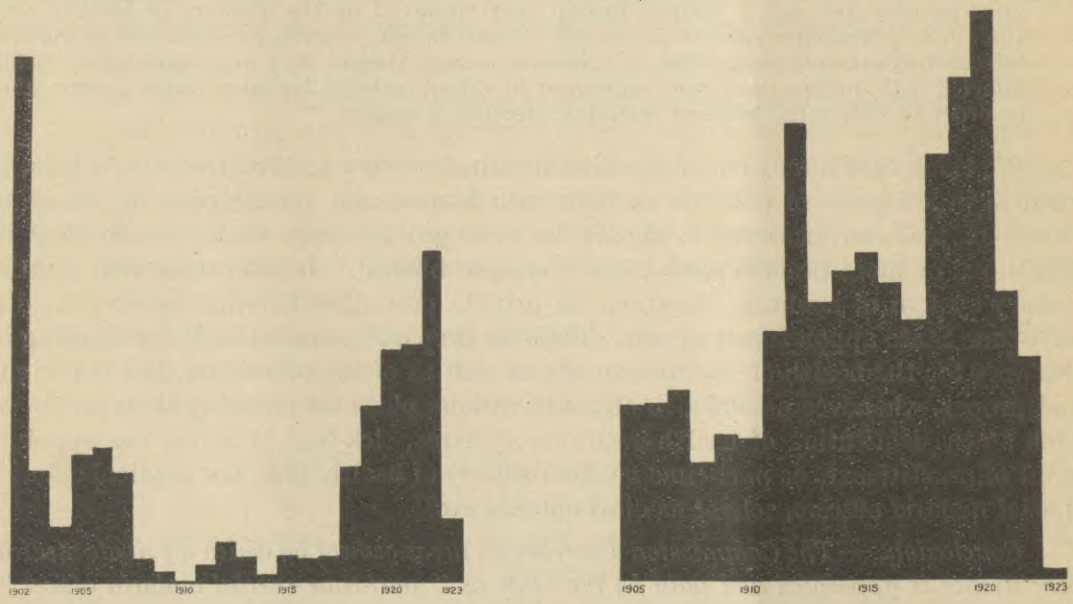
that at present there is no royal road and no short cut to the control of malaria, and that for this reason we must continue for the present to travel along the old and well-tried roads, improving and adapting them as our knowledge and experience grows.

It is a useful corrective to any undue reliance upon what can be effected by private practitioners, whose work is limited to diagnosing and treating patients who seek their advice, to glance for a moment at the following figures of the incidence of cases of malaria in the practices of Dr. Korteweg and Dr. Honig in North Holland. The statistics are reproduced in graphic form:

Cases of Malaria in Private Practice.

Locality	1902	1903	1904	1905	1906	1907	1908	1909	1910	1911	1912	1913
Wormerveer (3,000 inhab.)	540	111	56	126	*134*	109	25	12	3	19	41	27
Nieuwendam (id.)	—	—	—	152	151	165	103	127	124	215	*392*	240

Locality (*contd.*)	1914	1915	1916	1917	1918	1919	1920	1921	1922	1923	1924	1925
Wormerveer	10	28	25	27	117	173	229	234	326	64	12	13
Nieuwendam	266	282	256	225	366	430	*489*	248	192	10	12	7



Cases of Malaria in the Practice of a Medical Practitioner at Wormerveer (Netherlands) at Nieuwendam
1902-23 1905-23

It will be seen at once that there is no indication that these doctors, though very fully equipped as to the diagnosis and treatment of malaria, and very keenly interested

in the subject, achieved any success in reducing the annual incidence of the disease. What they did achieve we have already recorded, but evidently there was no cessation of the periodic rises of prevalence which, everywhere in Europe, are such an important character in the epidemiology of malaria. It is doubtless justifiable to assume that the yearly prevalence would be greater in the absence of the very thorough medical attention which patients who sought advice received, but we cannot tell by how much it would be greater. It will, we are sure, occur at once to the reader that in the early discovery and treatment of cases (just as in antimosquito and other methods of control) a "minimal degree of perfection" in the execution of the measure must be reached if such efforts to control the incidence of malaria are to attain the desired end.

Conclusion. — The good results of early diagnosis and efficient treatment are more apparent in the reduction of the severity of the disease than in the reduction of its incidence. The execution of the measures must reach a certain rather high degree of efficiency ("minimal effective degree of perfection") before its effects on incidence will become appreciable.

11. From this we are led to conclude that it is very desirable, if not essential, that whoever may be appointed for the discovery and treatment of cases should be well equipped for his task. Unfortunately, according to our experience, only a small proportion of medical men now in general practice in Europe possess sufficient knowledge of malaria to enable them to take their rightful place and to play the most useful part in its control. We feel that this is a difficulty which, as soon as possible, should be removed. We suggest that in future every candidate for a medical qualification in European countries where malaria occurs should be required to show that the clinical study of malaria has been included in his curriculum and that he has been instructed concerning the life history of the parasite and the diagnosis of the disease by microscopic methods. Nowadays there should be little difficulty in complying with this requirement. The establishment of the laboratory which we have suggested as being essential to the use of malaria as a form of treatment of certain diseases would enable medical schools and hospitals to obtain material necessary for teaching the subject in a practical way.

Conclusion. — The Commission, realising that doctors who practise in European countries where malaria occurs no less than those who practise in the Tropics should know how to diagnose and to treat malaria, suggests to the authorities responsible for the organisation of medical education in the different European countries that, when this subject is not already included in the curriculum of candidates for a medical qualification, specific arrangements for its inclusion should be made.

12. Although this Section of our report is intended to deal with principles rather than with detailed arrangements, one or two further points relating to the discovery and treatment of cases must be mentioned. Regular inspection of school-children, factory workers and other organised classes of the population must be part of the

system, and an endeavour must be made to follow up all patients in their homes. The practitioner who is in charge of the measures ("part-time special malaria officer") will need assistants, especially for house-to-house enquiries. Duly qualified female "health visitors" who have received the necessary training are, in our view, the most helpful assistants in this work. In small districts the office can be combined with kindred duties relating to health, such as school nurse, tuberculosis visitor, etc. Records should be kept on cards, a separate series of cards being used for dwellings and for cases.

13. The other primary measure which we recommend was described in our former report as follows: "The instruction of the inhabitants, in their homes and in the schools, as to how malaria is spread from member to member of the same family by the agency of particular mosquitoes, which find the house a safe resting-place, and how to catch and kill these mosquitoes daily; teaching the use of mosquito nets and other means of personal and house protection against mosquitoes, the advantages of cleaning and whitewashing rooms, ceilings, etc."

In Europe, the majority of infected anophelines are found inside houses; their destruction is a measure the importance of which it is impossible to exaggerate. We think that it should be a duty of the special malaria officer and his assistants at each visit to a household to explain this matter to the occupants, and to demonstrate to them how to find and to kill the adult anopheles mosquitoes which are present in the house. He should explain also how to make a house inhospitable to anopheles by removing cobwebs and dirt, clearing out cupboards, recesses and other dark corners likely to harbour mosquitoes, as well as by whitewashing, etc., wherever suitable. He should try to persuade the occupants to search for and to kill anopheles mosquitoes in their houses every day. At each periodical visit he should ascertain to what extent the occupants carry out his advice. The aim should be to teach them to have the same dislike and objection to the presence of these gorged and sluggish mosquitoes in their houses as cultured people already have to the presence of bed bugs, lice and other harmful and disgusting vermin. The measure has the advantage of costing nothing. It has also the merit derived from the results of experimental laboratory work showing that one infected mosquito can give malaria to as many as from twelve to thirty persons. Therefore it is difficult to praise too highly any person who succeeds in killing even one of these infected mosquitoes. We are aware, of course, that organised arrangements can be made by local authorities for killing mosquitoes in houses by periodic fumigation or other means, but we think it preferable from the beginning to place the responsibility for the work upon the householder and particularly upon the housewife and children. Thus we hope that in time it will become a part of the housewife's daily task, just as much as sweeping, brushing and tidying the living-rooms and bedrooms. Female health visitors and health nurses, who have been properly instructed and trained to deal with the particular items of house-cleaning which are important from the point of view of preventing infectious diseases, can do a very great deal of good by instructing house-

wives on those matters. Effective help can also be given by school-teachers who are in a position to interest the children in the destruction of mosquitoes in houses and in schools.

Conclusion. — The Commission strongly recommends that, in addition to making the best arrangements possible for the discovery and effective treatment of cases and carriers, an active and energetic endeavour should be made, wherever possible, to induce householders, especially housewives, to make the killing of adult mosquitoes found within the house a part of the daily cleaning task. The Commission is convinced that that measure, if it could be effectively carried out, would have very remarkable results.

14. *Indirect Measures.* — The Commission has carefully considered in what circumstances any other measures than those dealt with should be recommended, and what those measures should be. As a result of this consideration, we desire, in the first place, to refer to the problem of what should be done in certain regions where the conditions in which the people live and work are so primitive, and their economic position and social status and culture are so poor, that it is not possible in practice to apply direct measures in a manner which enables them to be brought to the standard which we call "minimal effective degree of perfection". In several European countries there are large or small areas in this class and, like similar regions in the Tropics, they are very malarious. We are of opinion that, except the free distribution of quinine, no direct antimalarial measure can be applied to them until the land has been brought into such a condition that it is worth the while of the inhabitants to settle permanently upon it and until those permanent settlers have reached a fair standard of housing and living. Nothing is more favourable to a high incidence and severity of malaria than frequent movements of a population hither and thither in search of a bare living, or of a place where the conditions of life are less hard; and very few things have a greater effect in reducing malaria than the stability of the population which comes when such a place is found. Agricultural reclamation of the land, so that people may be settled permanently upon it with a fair prospect of gaining a livelihood and perhaps a decent house and moderate comfort, is, therefore, a measure which tends indirectly to produce a great reduction of malaria incidence and severity. In general, the better the agricultural reclamation is carried out from the point of view of increasing its productiveness, the quicker will malaria seem to disappear as an important cause of sickness and death — provided always, of course, that the people themselves share in the improved prosperity by being able to adopt a higher standard of housing and living. It is hardly necessary to say that when — as sometimes happens — reclaimed land is worked by hired labourers, who receive only a small fixed wage and live a life of great hardship in temporary huts and hovels, there is no improvement of malaria among them. Indeed, in the Tropics, highly cultivated areas where these conditions obtain continue to be among the most malarious in the world. This proves that the actual measures necessary for reclamation (drainage, etc.) are not the factor which causes the health

of the people to improve, but that the good result is due to the better conditions of living and housing which the increased productiveness of the soil enables the people to obtain. The Netherlands is the country where the people as a whole have benefited most from land reclamation, but, among the countries of Central and Eastern Europe, Italy is in the forefront as an exponent of schemes and systems of "bonification" as an antimalarial and general sanitary measure.

On a smaller scale, Palestine has recently provided some excellent examples of the benefits which have followed the general scheme of "bonification", which is gradually being applied as far as possible throughout the country. There the scheme begins with arrangements for rectifying the existing confusion in regard to the land system of the country and the state of undetermined or scattered ownership to which the bad cultivation of much of the land was due. Various departments of the Government are concerned with the matter, and (as in Italy) the Department of Health takes an important share by urging the claims of bonification as an anti-malarial measure, by collaborating with the engineers during the progress of the work and by seeing that the work is accompanied and followed by measures of housing, education, general welfare and higher standard of living which are rightly regarded as the primary aim and purpose of the scheme.

Conclusion. — Of all indirect methods of reducing malaria, the Commission attaches most importance to general schemes of bonification which aim at improving the economic and social condition of the people and their general well-being and standard of life.

The stabilisation of the population, following on its settlement on the land, may not only improve its economic conditions but may also influence favourably its educational standard — and consequently its sanitary conditions — by making school attendance more general and more regular.

15. We have already pointed out that terms like bonification and *assainissement* are almost universally misunderstood and misinterpreted except in the particular countries where the terms originated. We have also noted that the belief prevails in some countries that the actual measures which are necessary for making the land more suitable for cultivation and more fertile are the means by which the reduction of malaria is effected. In particular, the drainage which is necessary for agricultural land reclamation has been credited with being the chief agent concerned. It is assumed that the drainage acts by reducing the breeding-places of anopheles mosquitoes and therefore by reducing the numbers of these insects in the area. In support of these beliefs, it is often said that even the ancients knew that drainage reduced malaria, and that no further enquiry into the matter is necessary. We are not desirous of saying anything in this report which will prevent useful public works being done, but, having regard to the financial aspect of the Commission's mandate, we are equally unwilling that countries should continue to believe that the kind of drainage which is necessary for agricultural reclamation of the soil is an important anti-mosquito measure. For it is now known, quite definitely, that the open ditches and canals by which swamps and marshy areas are drained for agricultural purposes

are often more prolific breeding-places of anopheles than were the original swamps themselves. The Italians are well aware of this. They do not regard the "large bonifications" as an antimosquito measure, and they know that such a bonification may increase the abundance of anopheles in the area reclaimed. But they also know that, in an area where bonification has been completed, and where in consequence the inhabitants settle permanently in better houses and in all the other circumstances of a moderately good standard of life, malaria tends more or less quickly to lose its importance as a cause of sickness and death. This good result more than compensates for an increase in the abundance of anopheles in the general environment. Thus it appears that the measures themselves are only a means to a definite end, which is to be pursued despite the knowledge that some of the measures are of a kind which favour the incidence and spread of malaria. Therefore, what we learn from the Italian example is that we must not take each of the actual bonification measures (such as drainage) separately and utilise it as a single antimalarial measure in another country. When we utilise bonifiation, we must do so as a whole; our plan must include particularly the arrangements for raising the standard of life, for better housing, education and general welfare which are an integral part of a complete bonification in Italy and (as we saw from the Palestine example recorded) in other countries where schemes of that kind have been successful. The importance of these last items in the scheme is brought home to us by the knowledge that, when the inhabitants of reclaimed and highly cultivated land are not permitted themselves to reap the advantages of the increased productiveness of the soil, no improvement in malaria results. Obviously, therefore, the sphere of the public health officer and the malariologist in connection with schemes of agricultural land reclamation consists particularly in seeing that the agricultural bonification has been accompanied and followed by an equal improvement in the conditions of life of all the people who inhabit the reclaimed area.

It should be added that all work of *assainissement*, drainage or construction of dams should be carried out under the control of a malariologist or of a health officer who should have under his supervision all prophylactic measures.

Conclusion. — The Commission points out that the antimalarial factor in general schemes of bonification is the change in the conditions of life of the inhabitants. The actual measures employed are only a means to that end and hardly one of them, taken separately, can be utilised as a useful antimalarial or antimosquito measure. The most useful sphere of the hygienist and malariologist in connection with bonification schemes is defined in the text.

16. It is interesting to know that the changed conditions of life just referred to, and the consequent reduction of malarial incidence and severity, have often been brought about in the absence of any measures intentionally based on modern knowledge of the ætiology and epidemiology of malaria. We may illustrate this by describing briefly the following small scheme of bonification which was demonstrated to the Commission during its recent tour in Sicily. The locality was a dairy farm

comprising 50 hectares of land near Simeto, on the plain of Catania. The situation was described to the Commission as being so malarious that it was uninhabitable. At the time of our visit, there was no village nearer to the estate than 20 kilometres. The proprietor commenced his project of bonification by building a road to the area, by bringing from 8 kilometres' distance the electric current which was required for lighting and power at the farm, and by constructing the necessary buildings, including a house for himself and houses for the staff and farm workers. The land was gradually brought under cultivation, irrigation being used where required. The slopes were planted with fruit-trees, but the greater part of the land was used for growing lucerne and cereals. During the first year, the labourers and farm hands slept in tents and temporary shelters. They suffered so much from malaria that the proprietor feared it would be necessary to abandon the enterprise. They were treated regularly with quinine, but no antimosquito measures were taken. By the end of the second year the malaria situation had ameliorated considerably and it continued to do so year by year. At the end of six years the community comprised about 100 persons, and, according to the information given us, the amount of malaria among them was inappreciable. We found considerable numbers of *A. maculipennis* and *A. superpictus* in the stables, but none in the living-room of the only labourers' house which we examined. Many anopheles larvæ were present in an irrigation canal near the buildings. We found no enlarged spleens among the few children whom we saw, and the people generally looked strong and well.

The interest of this example is that no antilarval or other methods of mosquito destruction were tried and that both larvæ and adult insects are still present in the area in quite sufficient numbers for malaria to spread; the place is now an instance of "anophelism without malaria".

Conclusion. — An example is given which shows that bonification as defined in this Section may be effective without expert measures based on modern knowledge. It illustrates the importance of the auxiliary factors in the epidemiology of malaria.

17. We have already said that the kind of drainage in open canals and ditches which is a necessary item in the agricultural reclamation and development of the soil (drainage of swamps, marches, etc.) is a measure which, unavoidably sometimes, creates more and better breeding-places than existed in the original area. This observation, coupled with the absence of recommendations for general antimosquito work, may make it appear that our Commission has not taken due note of the many successful "antilarval campaigns" which have been reported in different parts of the world. Therefore we should like to say at once that we recognise and appreciate fully those successes, and that we should have been very glad if we could have recommended work on similar lines in Europe. We are also very much impressed with the remarkable success in killing anopheles larvæ by the use of Paris green, which we had an opportunity of seeing in Palestine and of studying more carefully at the Antimalaria Demonstration Stations created by the International Health Board of the Rockefeller Foundation in collaboration with the Italian Public Health Adminis-

tration in Sardinia, Italy and Sicily. We shall not deal here with other antilarval measures, such as the use of larvicides, of larvicidal fish (*Gambusia*), etc. These methods, all of which have proved their efficacity in suitable conditions, will be dealt with in a special chapter. But the truth is that, in all the malarious districts of Europe which we visited, we found only a very few localities in which it could reasonably be hoped that measures against anopheles in the general environment could be prosecuted with any hope of obtaining sufficient success to warrant the large staff and great expense that would be necessary even for a limited campaign. We do not doubt that the present abundance of *A. maculipennis* in some localities in Europe can be materially reduced by antilarval measures persistently carried on in accordance with the most modern methods, but, generally speaking, it would seem that in Europe, as in the Tropics, the serious objection to antilarval measures is their difficulty and expense. Therefore we hope that, at any rate in most malarious localities in Europe, the cheaper and less difficult antimalarial measures which we suggest will suffice to bring about the limited result towards which, in our opinion, the malarious countries of Europe should aim.

SECTION II.

ARRANGEMENTS FOR STUDYING MALARIA.

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I. THE STUDY OF ARTIFICIAL INFECTION OF MOSQUITOES AND MAN.

In the preceding Section, we stated the Commission's opinion that the scientific study of malaria in all its aspects must be continuously pursued. To this end we recommended: (1) The establishment in each country of a laboratory for the provision of infected mosquitoes, which could be used, under expert supervision, for the malaria treatment of certain diseases; (2) the establishment in one or two malarious areas in each country of an "observational station", where certain routine epidemiological enquiries should be made at regular short intervals.

We hope that co-ordinated study along these two lines will be pursued continuously in every European country where the necessary arrangements can be made. As a guide to those arrangements, we shall describe in this Section two or three of the laboratories and observational stations which members of the Commission visited during their European tours.

We shall begin by giving a brief account of the arrangements which have been made in England for the continuous provision of a supply of mosquitoes for inducing a pure infection of benign tertian malaria in patients to be treated. The work provides an opportunity of studying the clinical and parasitological features of malaria contracted in the natural way, as well as the circumstances governing the infection of mosquitoes and the factors which influence the persistence of the infective virus in those insects. The first results of a study on these lines were the subject of a special report to the Commission, which was published in 1926 as C.H./Malaria/57(1).

The hospital in which the arrangements are installed is the Horton Mental Hospital at Epsom, near London. It is a hospital accommodating about 1,500 patients, and there are several other hospitals of the same size in the near neighbourhood. Therefore a considerable number of cases of general paralysis and other mental diseases which are to be treated with malaria are always available.

In the grounds of the hospital there is an isolated villa which has been allotted exclusively for the malarial treatment of patients. Fig. 4 is a photograph of this villa.

Figure 4. — Pavilion used for Malaria Treatment.

It contains two wards, each with seven beds, and several small rooms each with one or two beds. The total accommodation is for twenty patients. Fig. 5 is a photograph of one of the larger rooms.

Figure 5. — One of the Larger Wards.

Each ward and small room is completely mosquito-proofed with double doors, as shown in Fig. 6, and with removable mosquito-proof window frames.

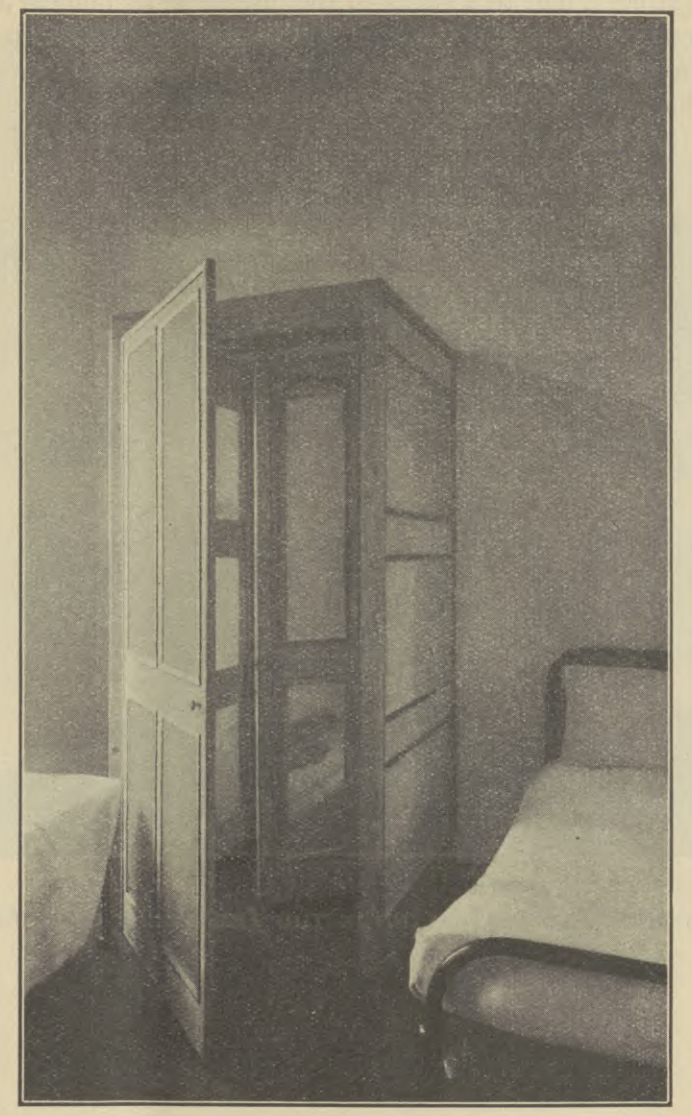


Figure 6. — Doors protected against Mosquitoes.

One of the medical officers of the hospital (Dr. Nicol), who is a psychiatrist, with considerable experience in the clinical and pathological study of malaria and in its treatment, devotes himself to the clinical care of the patients who pass through the course of treatment, and to a study of the disease in its clinical aspect and in its effect upon general paralysis and other mental conditions. He has under him a staff of nurses who have been specially trained in the nursing of malaria patients and the manner in which observations relating to the degree of fever and other clinical symptoms should be taken and recorded. Fig. 7 is a photograph of this staff.

Figure 7. — Nurses specially trained in the Treatment of Malaria Patients.

Two small rooms in the building are equipped for the necessary laboratory work (Fig. 8), which is done by a senior laboratory assistant (Mr. P. G. Shute) who has been specially trained for the duty.

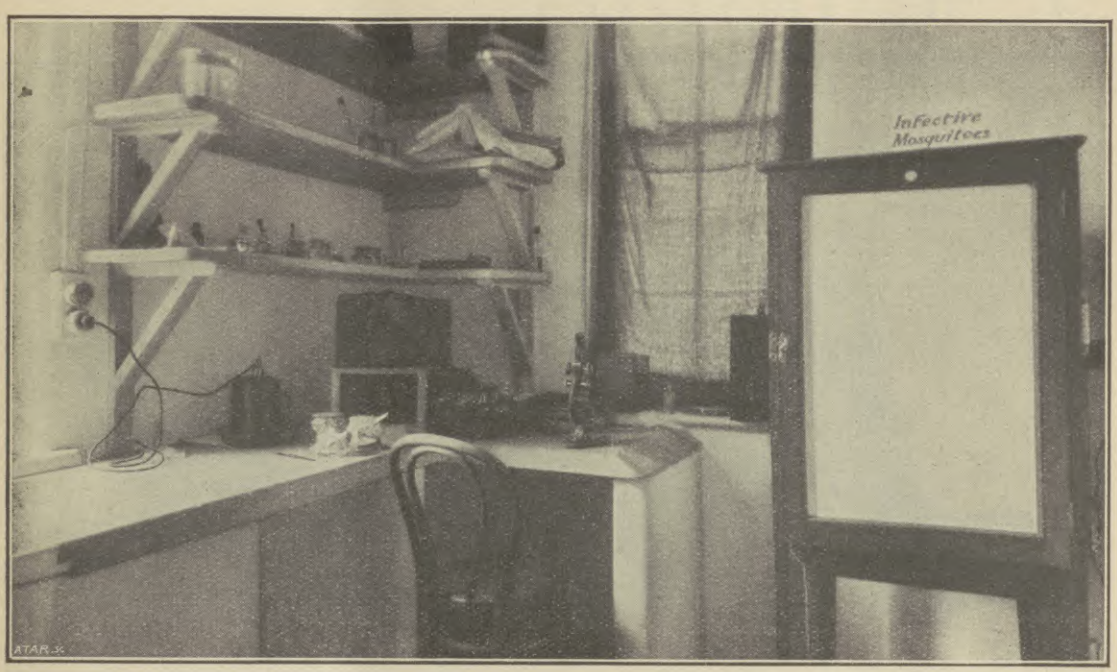


Figure 8. — LABORATORY.

The work is concerned only with the benign tertian malaria parasite (*P. vivax*) and with *A. maculipennis*.

The strain of *P. vivax*, which has been in use since May 1925, was obtained from an otherwise healthy patient who contracted malaria in Madagascar. Before it was used for the infection of mosquitoes, it was proved to be an unmixed strain by direct blood inoculation into two patients.

The mosquitoes (females of *maculipennis*) which are used are not bred from larvæ but are collected in the adult stage from stables and other buildings in a country district where malaria does not occur. They are collected one by one in test-tubes, from which they are transferred to the mosquito cage shown in Fig. 9.

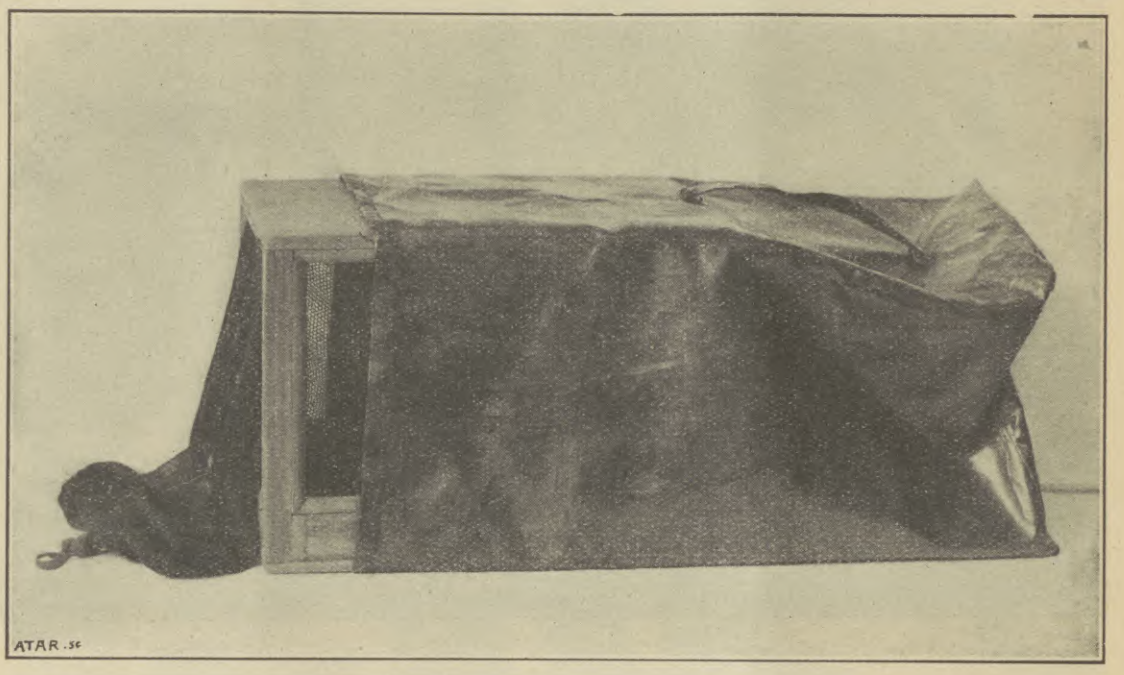
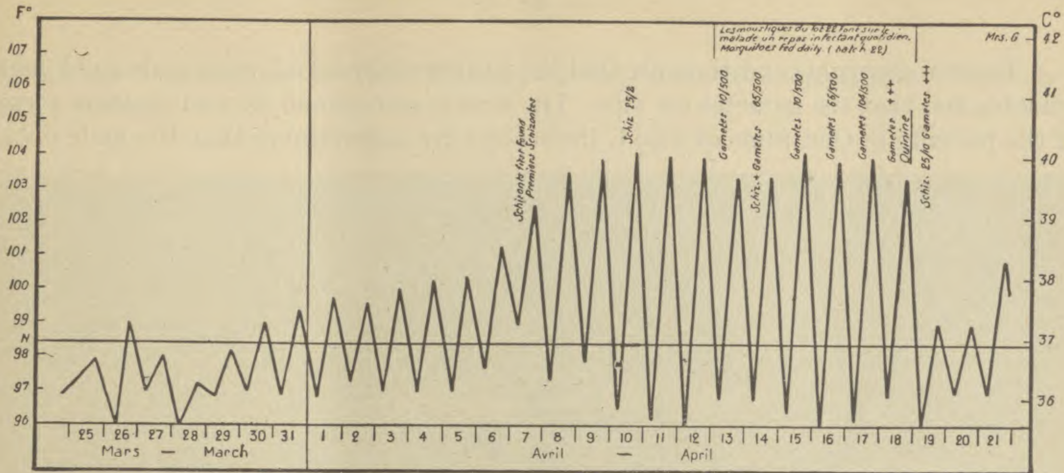


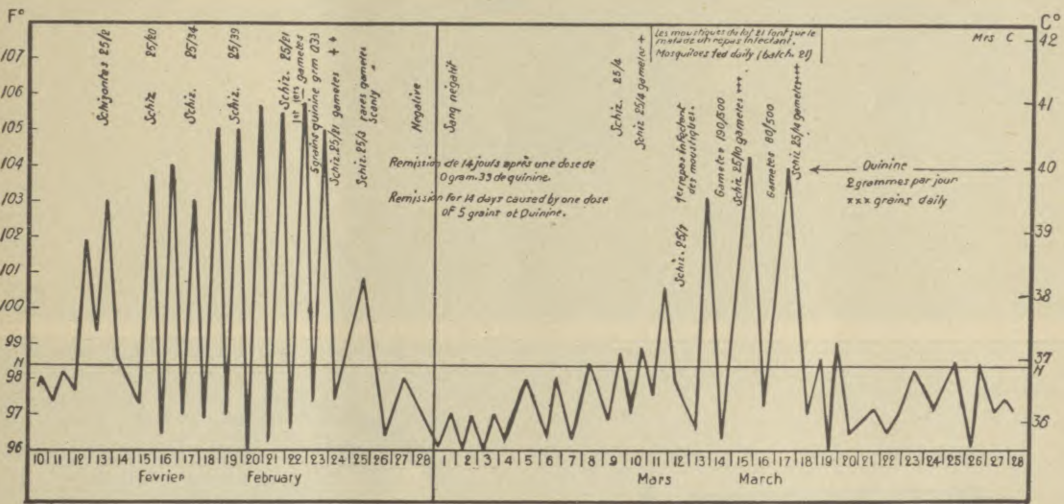
Figure 9. — Mosquito Cage with Waterproof Cover.

When about 300 have been caught, the waterproof cover shown in the photograph is drawn over the cage, which is then taken to the laboratory. After removing the waterproof cover, the cage is placed in the incubator at 23° C. for 24 or 48 hours, in order that the blood in the stomachs of the mosquitoes may be digested quickly and that they may be ready to feed upon the infecting case.

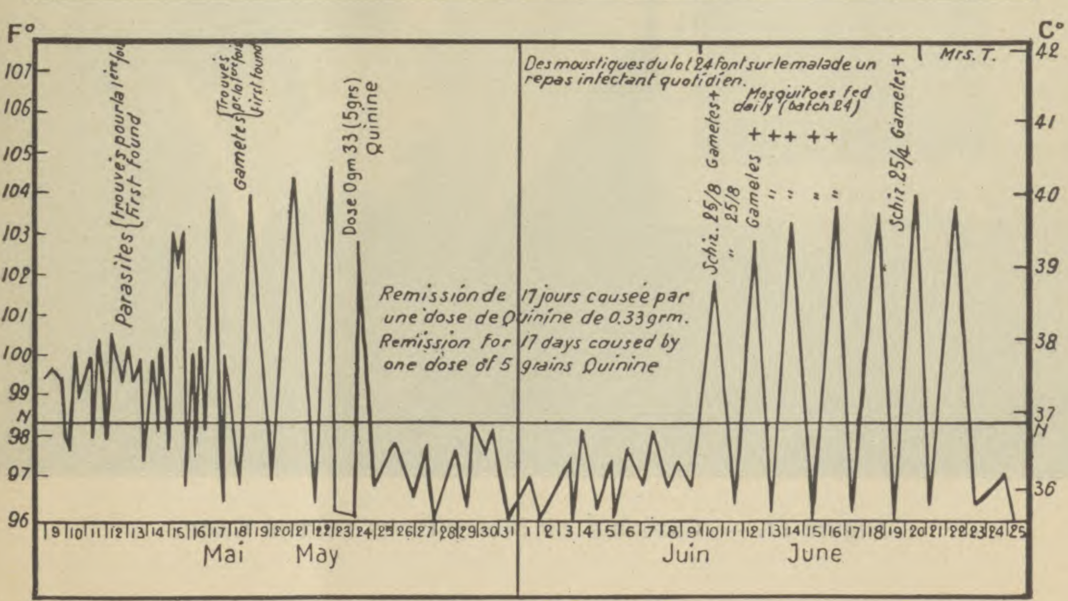
The infecting case must be in the stage of the attack which is represented by the words "mosquitoes fed daily" in the following graphs :



Les moustiques du lot 22 font sur le malade un repas infectant quotidien.
Mosquitoes fed daily (batch 22)
Mrs. G
Schizontes first found
Premiers Schizontes
Schiz. 25/2
Gametes
Quinine
Mars — March
Avril — April



Mrs C
Schizontes 25/2
Schiz.
Negative
Sang négatif
Remission de 14 jours après une dose de 0 gram. 33 de quinine.
Remission for 14 days caused by one dose of 5 grains of Quinine.
Quinine
2 grammes par jour
xxx grains daily
Fevrier February
Mars March



Des moustiques du lot 24 font sur le malade un repas infectant quotidien.
Mosquitoes fed daily (batch 24)
Mrs. T.
Parasites {trouvés pour la 1ère fois / First found
Dose 0gm 33 (5grs) Quinine
Remission de 17 jours causée par une dose de Quinine de 0.33grm.
Remission for 17 days caused by one dose of 5 grains Quinine
Schiz. 25/4 Gametes +
Mai May
Juin June

The two essential conditions are that the peripheral blood contains male and female gametes and that the gametes are ripe. The first is ascertained by finding these forms of the parasite in thin films of blood, the second by ascertaining that the male forms

Figure 10. — Flagellated Male Parasite partially absorbed by a Polymorphonuclear Leucocyte.

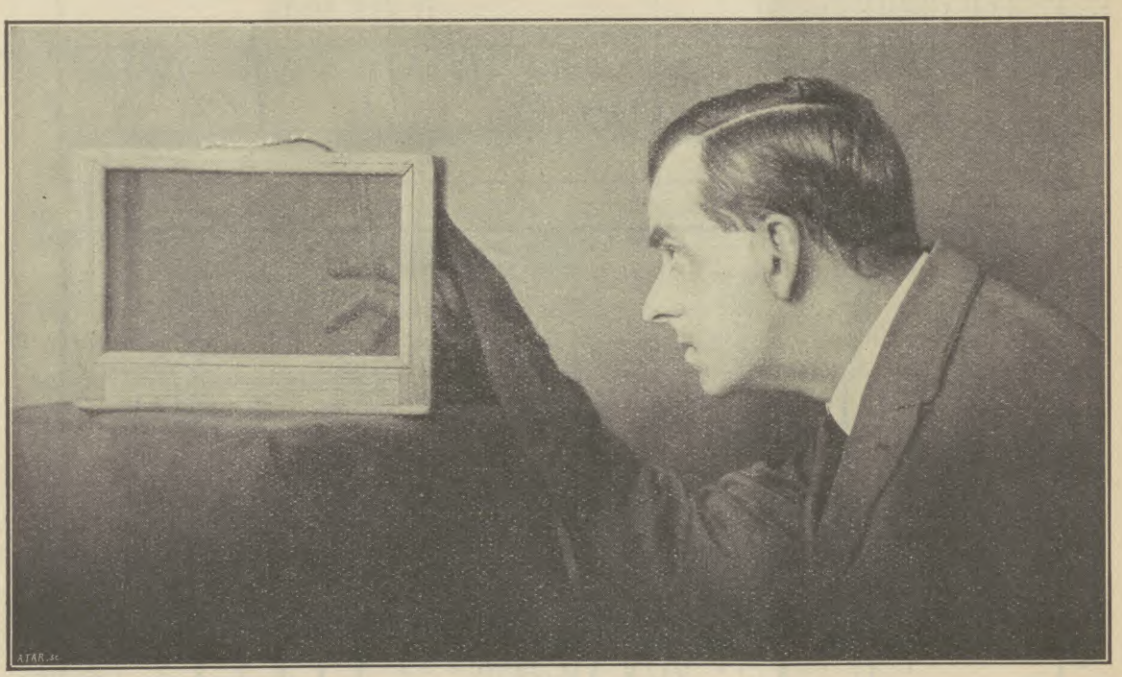


Figure 11. — Capture of Mosquitoes in the Cage.

"flagellate" readily (as in Fig. 10) in a "moist-chamber preparation" of freshly drawn blood.

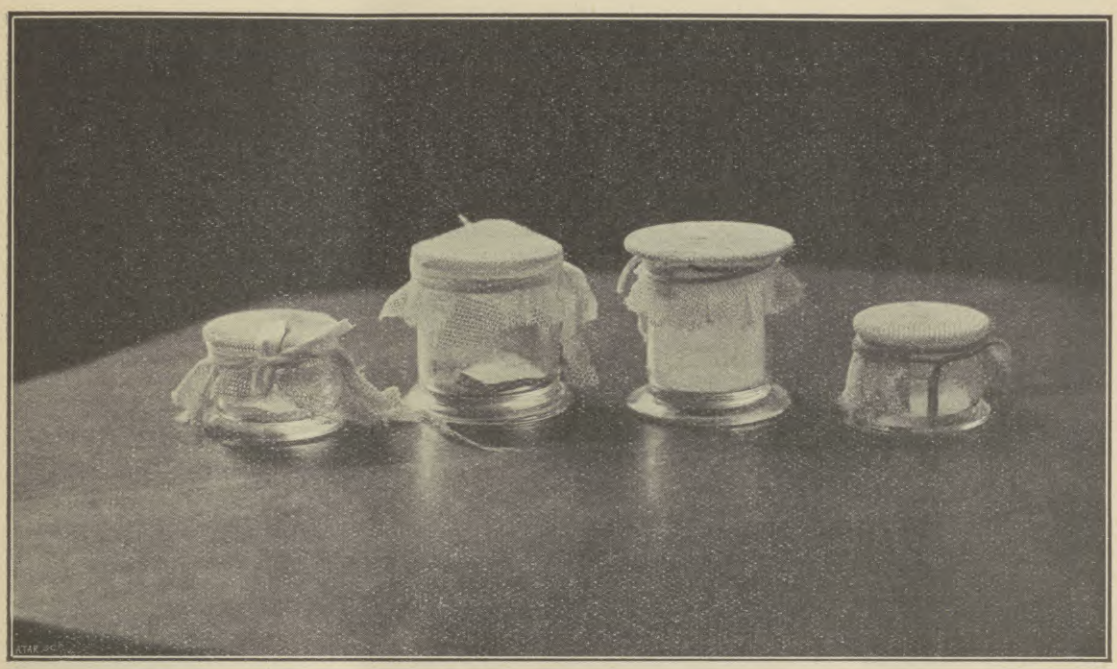


Figure 12. — Glass Jars used for feeding Mosquitoes.

When the mosquitoes are to be fed on the infecting case, they are taken from the cage by catching them in a test-tube in the manner shown in Fig. 11. Then they are transferred from the test-tube to the glass jars shown in Fig. 12.

This is done in the following way: Tie a piece of paper over the open mouth of the jar. In this cover cut a half-circle valve of the same size as the mouth of a test-tube. Take the test tube that contains the mosquito and put its cotton-wool plug over the paper valve. Draw away the cotton-wool and at the same time push the mouth of the tube through the valve into the bottle. When the mosquito has flown into the bottle, draw out the tube and at the same time plug the valve with the cotton-wool. Transfer twenty mosquitoes in this way to each of four or five bottles. Then lay a piece of cotton mosquito-netting over the paper which closes the mouth of the bottle. Keep the mosquito-netting in place by laying the palm of the hand over it and carefully draw away the paper, thus leaving the netting as a cover to the mouth of the bottle. Tie the netting on tightly as in Fig. 12.

The jars containing the mosquitoes are then placed on the leg of the patient in the manner shown in Fig. 13. A nurse keeps the mouths of the jars pressed closely against the skin during the period allowed for feeding, which is usually about twenty minutes. The mosquitoes bite readily through the netting which covers the mouths of the bottles.

Figure 13. — Mosquitoes biting the Patient.

When the mosquitoes have fed, the jars are placed inside the mosquito cage and the mosquito-netting covers removed. The mosquitoes escape into the cage and the jars are taken out.

The cage is then placed in the incubator. The temperature at which the incubator is kept is 23° C. By keeping a bowl of water in the incubator and by hanging wet cloths in it, the air is kept as nearly saturated with moisture as possible.

The procedure described is repeated daily, the mosquitoes being fed for at least five days on the infecting case. Afterwards they are fed every day or every other day on a patient who is awaiting treatment.

Some mosquitoes die every day. They are dissected to ascertain the progress of the malaria infection. When sporozoites are present in the salivary glands (which is usually between the tenth and fifteen day after the first infective feed, but may be as long as the eighteenth or twentieth day) incubation at 23° C. is discontinued, the group being kept instead either at room temperature or in an ice-box at 5° or

6° C. during the periods when the mosquitoes are not required for infecting patients.

In order to infect a patient, four or five mosquitoes are transferred from the cage to one of the glass jars and are allowed to bite the patient in the same manner as was described for the procedure of infecting the mosquitoes. Usually two or three of the mosquitoes bite within a few minutes.

If an infected batch of mosquitoes is kept in an ice-box during the intervals between successive feedings, some individuals will usually remain alive and infective for at least a month and occasionally much longer.

II. OBSERVATIONAL STATIONS.

Although in Europe there are several stations for "experimental malaria control", it is rare to find a strictly "observational station" which is concerned solely with enquiring into the natural rise and fall of malaria in human beings and in mosquitoes respectively from month to month and year to year, and into the factors to which those monthly and annual changes of incidence may be due. The absence of such stations makes it difficult, or even impossible, to evaluate the results of the measures that are being taken in the "control stations".

The Commission observed in certain countries that, in spite of the energy with which the antimalaria campaign has been carried out, and despite the special care and even enthusiasm with which the campaign has been carried on in different stations, it is extremely difficult, if not impossible, to form any exact idea, — from the statistics drawn up so far, — of the situation in regard to malaria and of the results of the campaign. Existing statistical data generally give only the number of persons examined in the stations and in different localities — that is to say, the number of persons who have voluntarily submitted themselves for examination or who have been treated at home.

It is true that the facts thus elicited are duly registered (positive and negative blood findings, kind of parasite found, state of the spleen), but they give an idea only of the work accomplished and not of its results. Such statistics can give no certain indication as to whether malaria has decreased spontaneously during the last few years in certain given areas, or whether this diminution can be attributed to the antimalaria measures that have been applied. Such statistics as are now being collected are certainly necessary to control the work carried out and, consequently, useful when considering the cost of such work; but it is essential that a second and independent system of statistics should be established. Such statistics should take account of the total population of certain specified localities, however few, and include sick and healthy alike. The examinations necessary to collect this statistical information should be

carried out in the season of maximum malaria prevalence. It is not necessary that such examinations should be carried out everywhere at the same time; it is only necessary that the examination in any given locality should be carried out at the same season of each year. It would be sufficient, in the circumstances, to establish the spleen index of the population, by confining one's attention to children less than 15 years of age.

It is useless and obviously impossible to undertake such examinations over a widespread area. The selection, in the sphere of activity of the antimalaria station, of a village where no antimalaria measures are to be carried out and of another where a general campaign is to be undertaken (including the search for and treatment of patients, and the distribution of quinine), and a third where attention is to be paid only to small measures of *assainissement* of the soil or where special antilarval measures are designed, would enable one to determine whether subsequent diminution of malaria is spontaneous or not and what measures are the most effective for bringing about such diminution. In similar fashion, one should be able to ascertain whether or not it is necessary to carry out antimalaria measures over a more or less extended area around the villages it is desired to protect. Such observations would enable one to avoid in the future all expenditure not absolutely justified by the results achieved.

The Commission is acquainted with observation stations in various parts of Europe (notably in Italy and Spain). That of Amsterdam is here described as an example.

It was established by the Director of the Municipal Sanitary Service. The work was begun primarily with the object of studying the distribution of *A. maculipennis* in the town and suburbs and the methods of destroying adult mosquitoes in stables, but it was soon extended, with the collaboration of medical practitioners, to include the notification of cases of malaria, the taking of blood-slides and the catching and dissection of anopheles mosquitoes caught in infected houses. When it was organised for these purposes, it was placed under the direction of the Medical Officer of Health of the municipality, and became part of the routine duties of dealing with infectious diseases. The following special staff was provided, but, when necessary, it is also employed for disinfection work in connection with other infectious diseases:

1 sanitary inspector;
2 assistants;
1 laboratory assistant (a trained microscopist).

Microscope slides in a portable cardboard case are distributed to the medical practitioners, with copies of the following form:

Slide Number	Patient's Name	Sex	Age	Address	Has the patient had malaria before? If so, when?
.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....

Doctor's name and address:

.....

The sanitary inspector collects the slides and forms from the houses of the doctors and takes them to the laboratory. The slides are examined at once, the result being recorded on the back of the form, which is returned to the doctor after the particulars of the notification have been recorded. When the result is positive, the house is visited by the sanitary inspector, who catches the mosquitoes found in it and takes them to the laboratory for dissection. These visits are repeated as long as any mosquitoes can be found in the house. From these observations an account is drawn up each year of the numbers of mosquitoes found in malarious houses during each month of the year and the numbers found infected with zygotes and with sporozoites respectively. The remaining observational work relates to a monthly survey of anopheles larvæ in a number of selected breeding-places and a monthly survey of adult anopheles in a number of selected stables. The number of larvæ present in an area of known size is estimated from the number caught by dipping with a shallow pan of known size. When adult anopheles are few, their number is estimated by counting, but when the number is large, the following procedure is adopted: (1) Spray a known area with an insecticide solution and weigh the mosquitoes which have been killed; (2) collect the mosquitoes from an area of known size by passing a vacuum-cleaning machine over it and, after killing them in the bag, weigh them in the same way. As a rule, 1,000 anopheles (*maculipennis*) weigh 2 grammes.

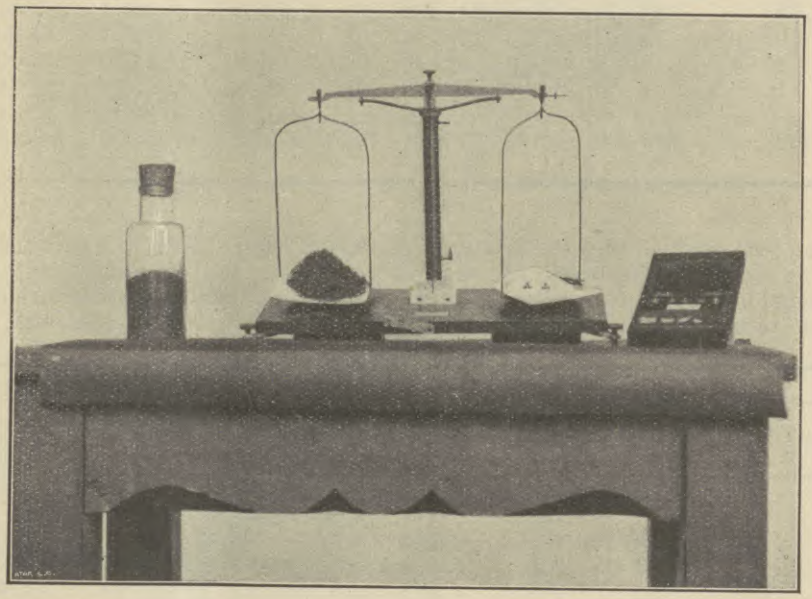


Figure 14.

ESTIMATION BY WEIGHING OF THE NUMBER OF MOSQUITOES CAUGHT.

Recording Results. — The diagnosis of malaria is always confirmed by blood examination. Each case is registered and is marked on a map, as shown in the inset (Figure 15).

The malaria cases recorded during the last seven years and the seasonal incidence are shown in the following statement:

Month	1920			1921			1922			1923			1924			1925			1926		
	Nieuwendam	Sloten	Amsterdam	Nieuwendam	Sloten	Amsterdam	Nieuwendam	Sloten	Amsterdam	Nieuwendam	Sloten	Amsterdam	Nieuwendam	Sloten	Amsterdam	Nieuwendam	Sloten	Amsterdam	Nieuwendam	Sloten	Amsterdam
January .	4	—	—	10	0	—	4	0	20	0	0	14	0	1	3	0	0	2	0	1	3
February .	5	—	—	11	4	—	0	2	30	1	2	11	0	0	4	0	0	4	0	0	2
March . .	16	—	—	17	16	—	8	14	46	3	15	32	0	1	4	0	1	7	0	2	8
April . .	31	—	—	34	18	—	20	38	216	1	19	91	3	11	28	0	8	33	0	10	30
May . . .	60	—	—	39	41	—	35	87	412	2	21	112	0	14	69	0	19	95	3	19	97
June . . .	94	—	—	46	30	—	58	95	559	0	31	132	4	17	146	2	13	86	1	18	104
July . . .	178	—	—	31	11	—	35	62	407	3	23	102	5	22	98	1	11	63	0	12	55
August . .	62	—	—	20	19	—	20	31	349	0	10	61	0	17	81	2	8	48	0	6	38
September	25	—	—	17	21	—	9	21	199	0	9	66	0	4	48	1	10	41	2	6	31
October .	9	—	—	15	34	—	2	10	91	0	6	31	0	6	22	1	4	20	0	6	22
November	4	—	—	6	6	—	1	2	40	0	0	14	0	1	14	0	0	5	0	0	9
December	1	—	—	2	0	—	0	0	22	0	0	6	0	0	8	0	0	8	0	0	4
Total .	489	—	—	248	200	—	193	362	2391	10	136	672	12	94	525	7	74	412	6	80	403

It will be seen that, during the last four years, the annual total of cases has been about the same. The seasonal incidence in the town as a whole has its peak in May of each year.

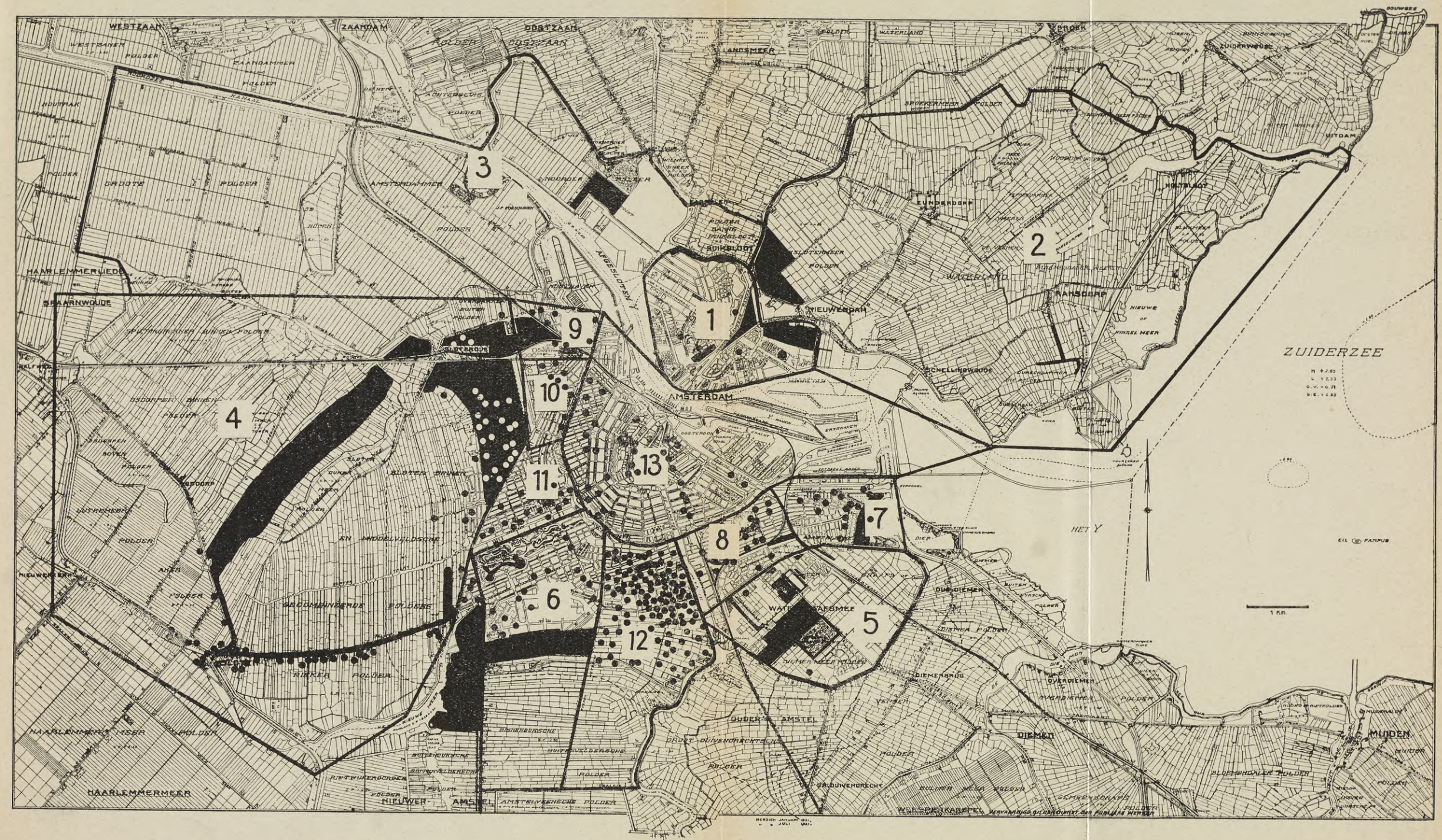
The seasonal incidence of larvæ and the average number of adult anopheles caught per house and per stable respectively in some of the years of the enquiry were as follows:

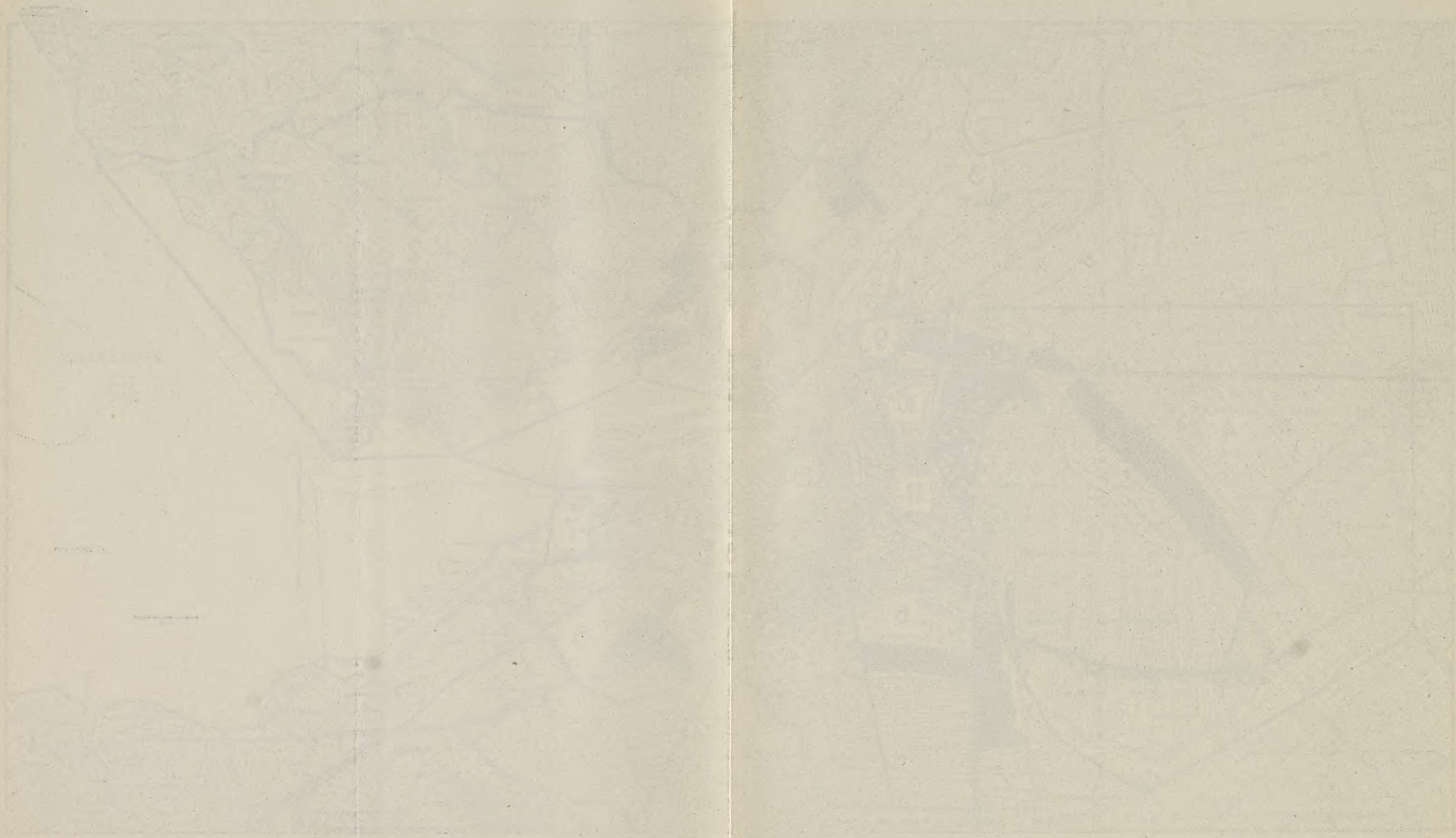
Month	Survey of larvæ: Larvæ per dip					Survey of adult anophelines		
	1920	1921	1924	1925	1926	Year	Number of anophelines: Per stable	Per house
April	0	0.2	0	0.02	0.3			
May	0.6	0.1	0.5	1.0	0.5	1920 . . .	1,789	21
June	0.4	2.2	0.9	0.6	0.7	1921 . . .	2,572	23
July	2.1	?	4.3	1.5	2.1	1922 . . .	1,782	10
August	3.8	?	3.1	1.4	1.4	1923 . . .	2,759	26
September . . .	0.5	?	0.3	0.3	0.9	1924 . . .	2,418	12
October	0.1	0	—	—	0.2	1925 . . .	2,197	11
November. . . .	0	—	—	—	—	1926 . . .	1,938	11

It will be seen that from year to year there is not a great change in the average numbers of adult anopheles that are caught in stables but that the average number caught in houses is more variable. Apparently, 1923 was a year in which anopheles were unusually abundant. The available results of the dissection of anopheles caught in houses in different years at this station will be found correlated with the incidence of malaria in the next chapter (Measurement of Malaria in Mosquitoes).

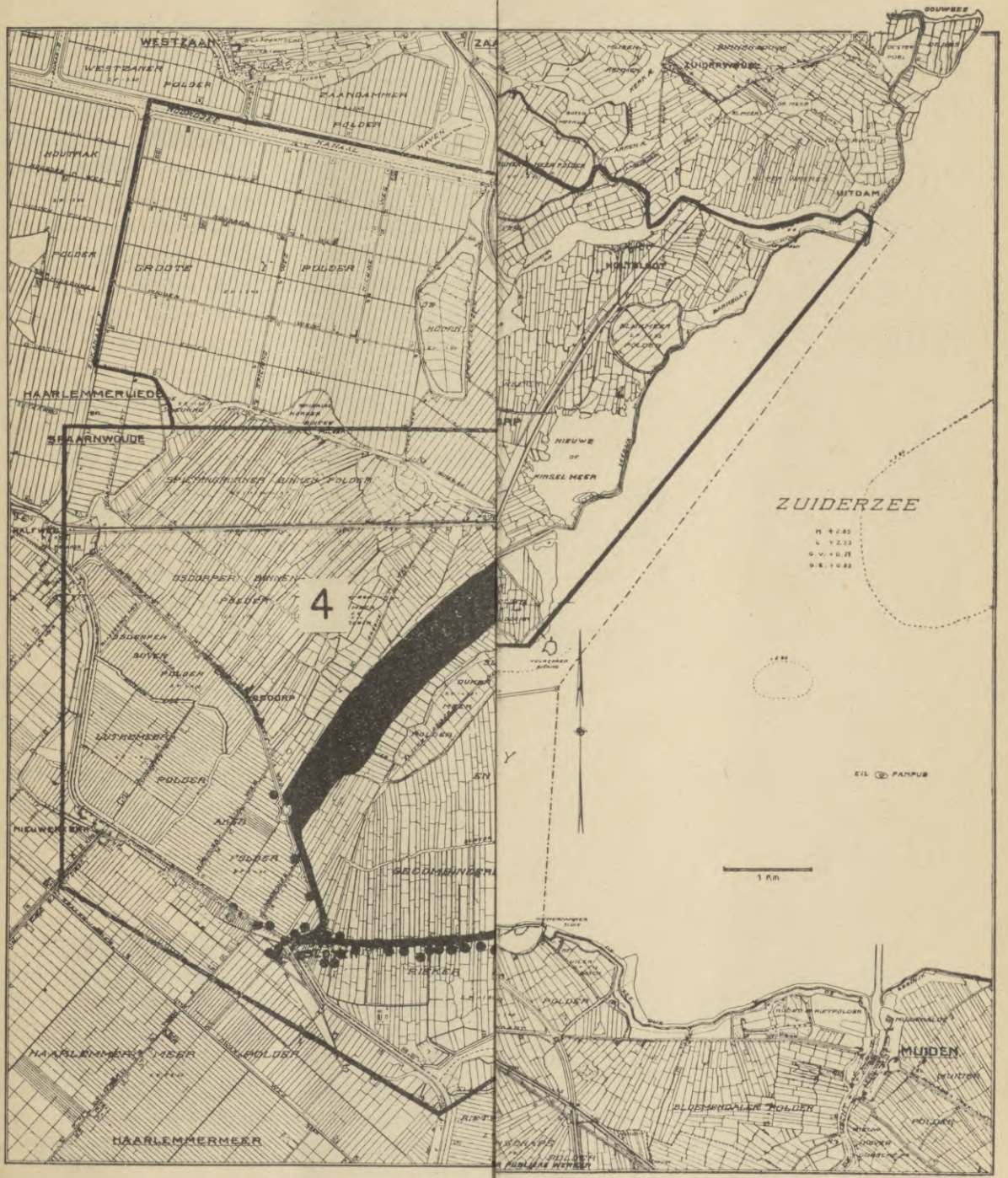
Figure 15. — MAP SHOWING THE MALARIA CASES IN AMSTERDAM.

The figures indicate the districts into which the town has been divided to facilitate the registration of malaria cases. The dots represent the malaria cases.





The figures indicate the sent the malaria cases.



III. MEASUREMENT OF MALARIA IN MAN AND MOSQUITOES.

The steps that are justifiable or necessary for dealing with malaria cannot be considered usefully without adequate knowledge of the distribution and character of the disease. Unfortunately, it is much more difficult to ascertain the distribution and amount of malaria than of any other of the common infectious diseases. The distribution of smallpox can be mapped by an illiterate agency, but no one would pretend that even fully qualified medical men, until they have received a special training in the work, can do the same for malaria. Malaria may be very prevalent in places where its presence is little obvious. In such places nearly all the local inhabitants up to a certain age have the disease, but typical clinical "cases" may not be seen. Again, in localities where malaria rarely occurs, the illness which it causes is sometimes so mild that those affected with it carry on their occupation as usual, or at any rate are not so ill that they go to the expense of consulting a doctor; and, when they do so, the doctor is often at a loss to know what illness they have. Primary cases in an early stage are particularly difficult to diagnose. During the investigation of an outbreak of indigenous malaria in England in 1917, it was found that cases had been occurring in the locality for three months without the nature of the illness being discovered.

On account of these diagnostic difficulties and the fact that in most countries only a very small proportion of general medical practitioners, and even medical officers of health, have received the special training necessary to overcome them, there is not as yet a definitely standardised plan of enquiry into and of recording the distribution and character of malaria.

In the following outline of procedures which are commonly employed, we shall begin with those that are applicable to countries in which there are only a few medical men who are adequately instructed and practised in the diagnosis of the disease. A first requirement in each country is a central expert organisation for collecting and recording results, for giving technical advice and instruction when necessary, and for carrying out local enquiries in selected areas as a guide to be followed in the more general scheme.

1. Declaration of Malarious Zones.

This is the simplest method: Government medical officers stationed in provinces, communes, counties or districts are required to report to the central Government the occurrence simultaneously, or at brief intervals, of two or more first attacks of malaria contracted locally in their district. Areas in which this finding is reported are generally declared to be "malarious zones". In defining them, consideration is also given to the presence of malaria-carrying mosquitoes and breeding-places. The method does not indicate the relative incidence of the disease in the different zones nor the type and character of infection. It indicates only that the resident population

of the locality or district are liable to contract malaria. In Italy, this plan serves as the basis for deciding to what districts the State antimalarial legislation (particularly as regards the gratuitous supply of quinine) shall be applicable.

The declaration of malarious zones likewise forms the basis of antimalarial legislation in Spain.

In England, a somewhat similar plan was adopted in 1917 for the application of special preventive measures to a few "malaria-suspected" or "dangerous" localities selected on the ground either that cases of indigenous malaria had already occurred in them or that they were places in which a considerable concentration of human malaria carriers coincided with an exceptional abundance of anopheles mosquitoes.

The organisation of arrangements for dealing with malaria in Bulgaria is also based on the declaration of malarious zones. (Fig. 16, page 51.)

2. Use of Mortality Statistics.

In Europe, the statistics of which most use is made in describing the distribution and character of malaria are the statistics of deaths attributed to the disease. The belief is almost universal that the diagnosis of an illness which terminates fatally is more to be relied upon than is the diagnosis of an illness from which the patient recovers. Therefore it is usual to quote malaria mortality statistics as giving an exact picture of the extent and severity of the disease, even in countries where little reliance is placed on the accuracy of the diagnosis of malaria in non-fatal cases. It is known that in tropical countries, where the causes of death are recorded by a non-medical agency, the analysis of mortality statistics attributed to malaria leads to absurd conclusions, but, so far as we are aware, no one hitherto has seriously questioned the accuracy of the malaria mortality statistics of European countries. As the subject is clearly of importance, the Commission has given some attention to it, particularly in relation to statistical diagrams, which show the annual mortality rates attributed to malaria over a long series of years. Such diagrams are sometimes used to demonstrate that a great diminution of malaria mortality has occurred, and that the diminution is correlated with certain antimalarial measures that have been taken. Diagrams of this kind for England and the Netherlands are reproduced in Figs. 17 and 18 (page 53); we have endeavoured to ascertain how to interpret them correctly and how far it may be justifiable to utilise them for demonstrating the trend of malarial mortality in the countries concerned. Our study includes a detailed enquiry into 250 of the deaths registered as due to malaria in England and Wales during a few recent years and an enquiry into the history of "malarial diseases" in the Netherlands and England from the pre-statistical period to the present day.

A glance at the diagrams will show that they resemble each other very closely. It will be seen that they comprise a modern period, during which the curve is nearly flat, and a more remote period, during which the curve falls abruptly from a great height. A correct interpretation of the more recent flat part of the curve will, of

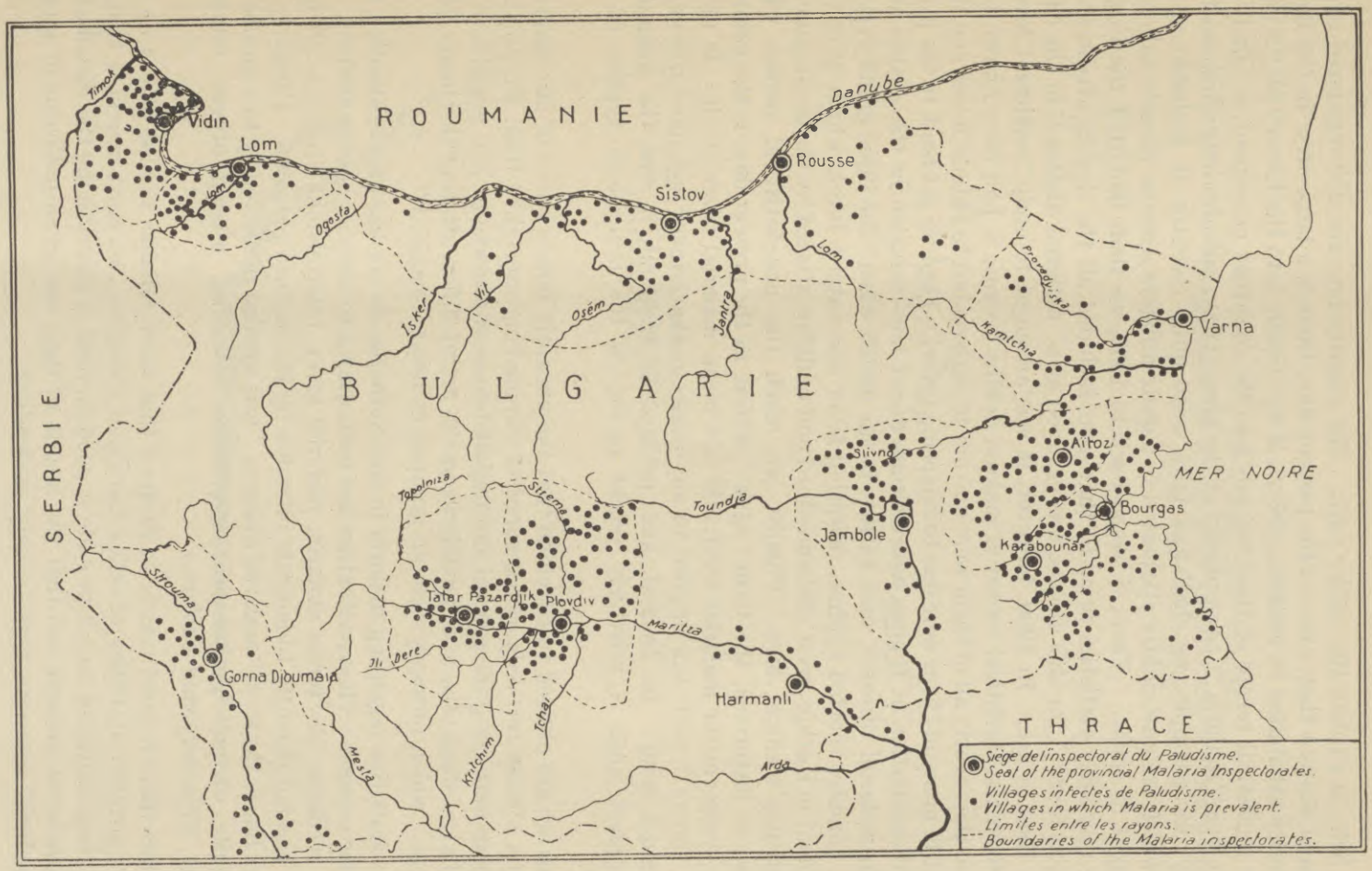


Figure 16. — Map of Malaria in Bulgaria.

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course, help to explain the earlier part. The enquiry into the 250 registered deaths in England showed that, even at the present day, there is a large error in the figures of mortality attributed to malaria. Next, if we enquire into the history of "fevers" and the statistical record of their mortality in the countries concerned, we shall find that the term "malaria", as employed at the present day, includes fewer diseases than formerly; for example, we shall find that, until quite recently, it included all the deaths which are now rightly attributed to a quite different disease, namely kala-azar, so frequent in India. Then, if we go back to 1900, we shall find that the English malaria mortality statistics prior to that year included all the deaths attributed to "remittent fever", for this disease was grouped as a "malarial disease" in the classification then in use. In 1900, however, it was arranged to omit "remittent fever" deaths from the statistical record of malaria deaths because it had been known for a long time that nearly all of them were due not to malaria but to enteric fever, and that, earlier still, many of them were due to relapsing fever. Then we get back to the period of the differentiation of typhus and its consequent non-inclusion in the deaths attributed to malarial diseases, and, earlier, to the period when "the three grand types of fever", namely, spotted typhus, relapsing fever and enteric fever, which were then so prevalent in Europe, were still undefined and undifferentiated by the great majority of practising medical men. Finally, we reach the pre-statistical period when, according to historians, the term "ague", which, at the present day, is the common English synonym for malarial fever, did not mean malarial fever at all. It meant simply "acuta" and was applied to any acute or sharp fever and most commonly a continued fever. In Ireland, and perhaps in Scotland, it was the diagnostic term applied until a relatively recent period to the indigenous typhus of the country.

Thus we are obliged to conclude that the abruptly falling curve of our diagrams represents almost certainly not a curve of diminishing mortality from true malaria but a curve indicating the general and rapid advance of knowledge and practice in the art of clinical diagnosis, and particlarly in the art of differentiating the many kinds of "fevers" which formerly were all grouped as being "malarial".

The statistics regarding malaria in the Netherlands are likewise misleading and for similar reasons. There, attention has been drawn to another source of error. In modern medicine the terms malaria, malarial fever, intermittent fever are all used more or less indifferently to indicate infection by the malaria parasite. Formerly, on the other hand, the term "malarial diseases" was applied indifferently to a number of other quite distinct pathological conditions, including, among others, infantile diarrhœa, dysentery and cholera.

Unless there is good reason to suppose that more reliance can be placed on the malaria mortality statistics of other European countries, we must conclude that, in general, these statistics do not provide a good method of ascertaining the distribution and character of malaria and that the results of their use as an indicator of success in antimalarial measures may be very misleading.

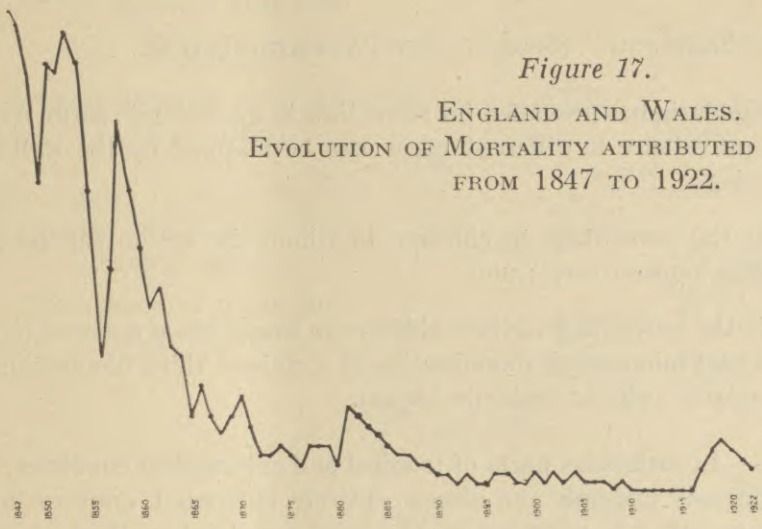


Figure 17.

ENGLAND AND WALES.
EVOLUTION OF MORTALITY ATTRIBUTED TO MALARIA
FROM 1847 TO 1922.

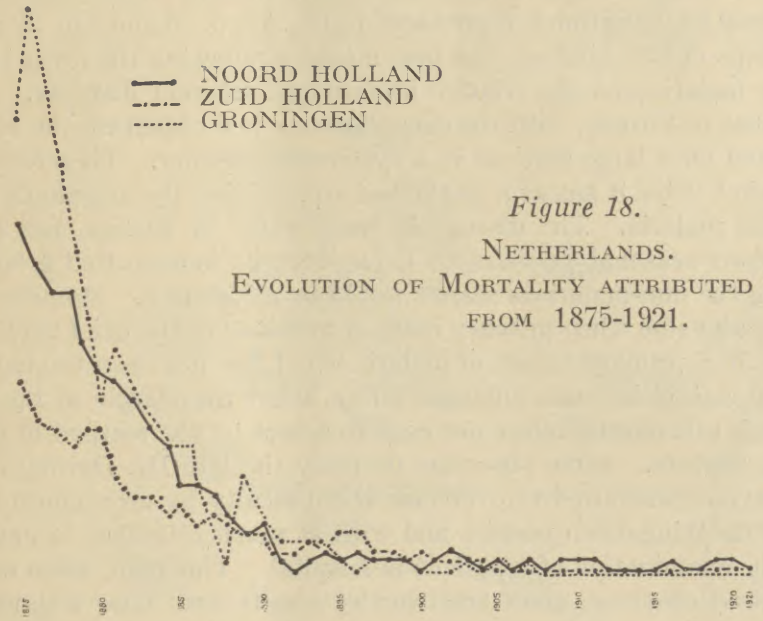


Figure 18.

NETHERLANDS.
EVOLUTION OF MORTALITY ATTRIBUTED TO MALARIA
FROM 1875-1921.

3. "Sampling" (Spleen and Parasite Rates).

In places where malaria has prevailed for some time in an endemic form, its distribution and relative prevalence in different areas can be mapped by the well-known methods of ascertaining:

(*a*) What is the percentage of children in whom the spleen can be felt by ordinary palpation (spleen rate); and

(*b*) What is the percentage of these children in whose blood malarial parasites are found by a short microscopic examination of a stained thick blood-film taken in the field (parasite rate or endemic index).

Spleen Index [1]. — In malarious parts of tropical and subtropical countries, where the disease is continuously endemic and almost entirely untreated, enquiry into the spleen index of communities is regarded as the most practical method at present available for rapidly ascertaining the distribution and, to some degree, the intensity of malaria. In such countries one of the first tasks of an expert staff is to collect data from which a map indicating the spleen indices in a large number of localities can be prepared. Such a map for Palestine is reproduced in Fig. 19, p. 55 and Fig. 20, p. 56, map of Oltenia. Maps of this kind are the best means of showing the areas chiefly affected by endemic malaria and the relative intensity in different districts.

It can be said that in Europe, with the exception of a few countries, the method has not been practised on a large scale or in a systematic manner. Therefore, it is not easy to decide what value it has as a method of ascertaining the distribution and intensity of European malaria. The disease in most parts of Europe has a low endemicity and a short seasonal prevalence; it might easily happen that a "splenic index" taken during the non-malarious season would be misleading. Moreover, the method is of little or no value when primary cases of malaria are the chief manifestation of the disease. In a primary attack of malaria which has not been treated with quinine, the spleen certainly becomes enlarged (often below the margin of the ribs), but the enlargement is soft and therefore not easy to detect by the method of palpation in the standing posture. Some observers (notably the late Dr. Darling of our own Commission) have endeavoured to overcome the difficulty by arranging to examine the children in the lying-down posture and with as much attention to detail as would be taken in the examination of a patient in hospital. This plan, when carried out by a well-practised observer, gives trustworthy results and more instances of slightly enlarged spleens (group I, "palpable") are found, but it is tedious and can seldom be carried out on a large scale. It was tried rather extensively in 1920 in some parts of the Netherlands. The localities chosen were those in which a considerable

[1] Spleen index indicates the percentage of enlarged spleens among children less than 12 years of age. The spleen rate indicates the percentage of enlarged spleens among any given population.

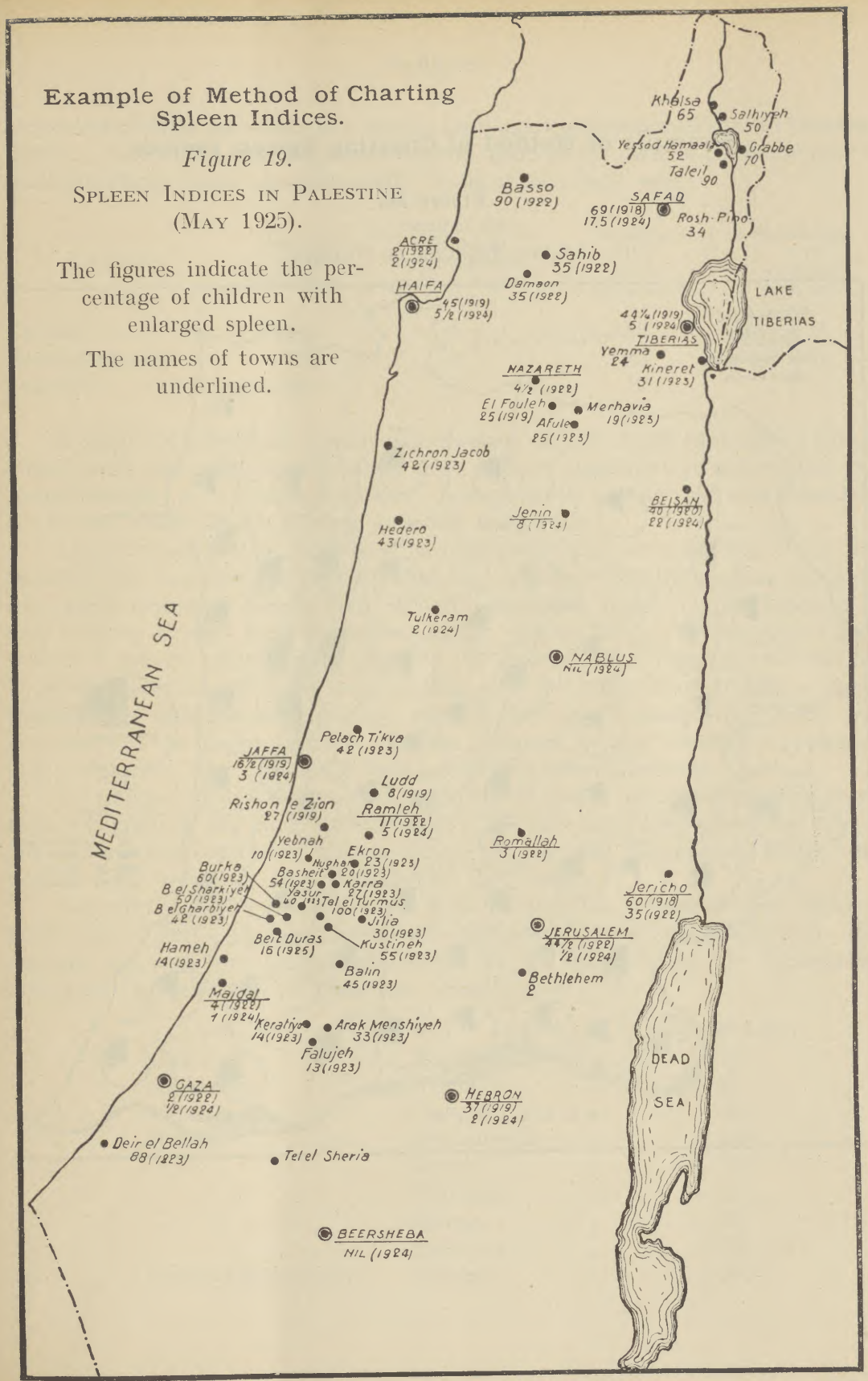
Example of Method of Charting Spleen Indices.

Figure 19.

SPLEEN INDICES IN PALESTINE (MAY 1925).

The figures indicate the percentage of children with enlarged spleen.

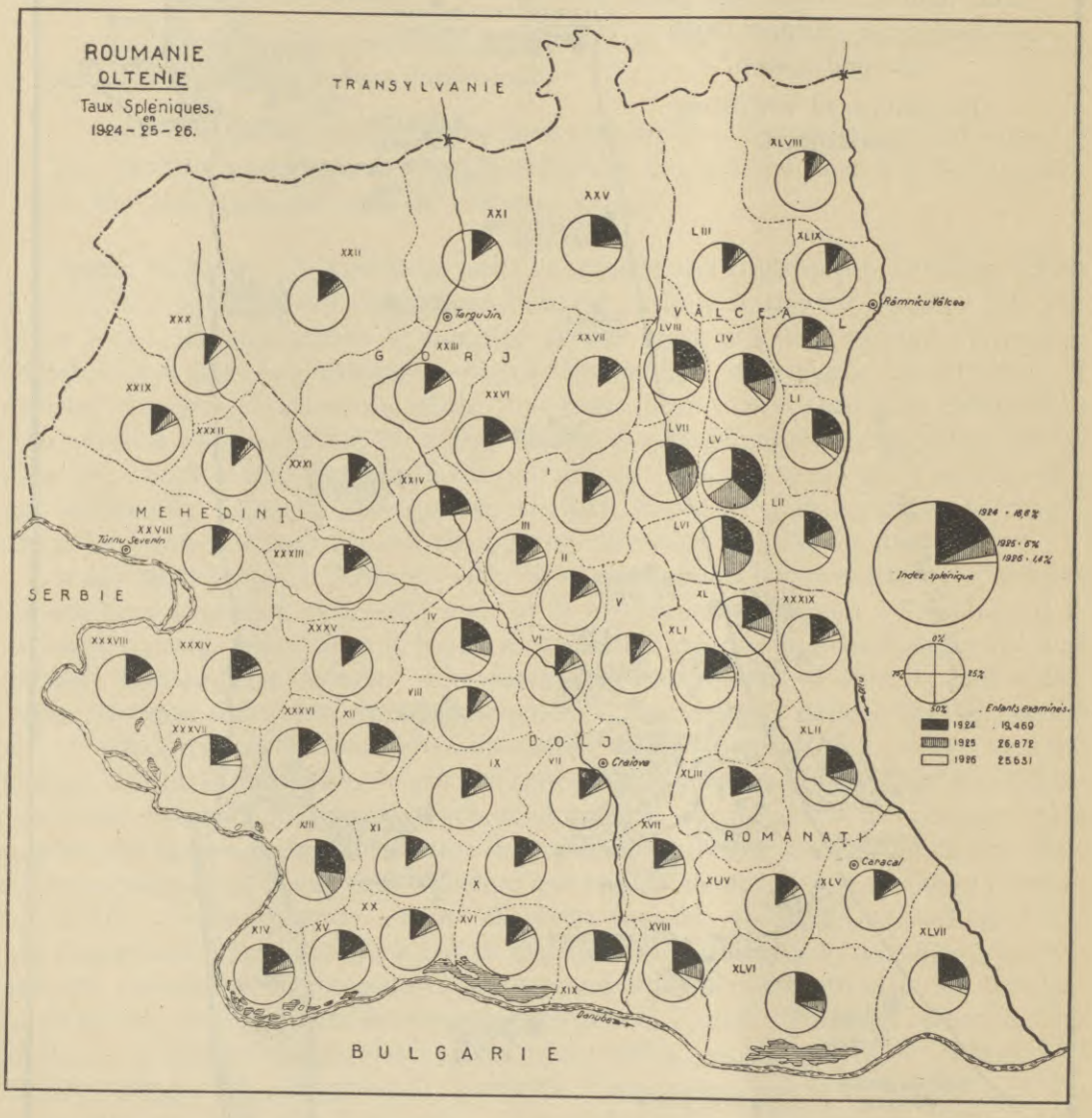
The names of towns are underlined.



Example of Method of Charting Spleen Indices.

Figure 20.

SPLEEN INDICES IN OLTENIA.



amount of malaria prevailed, but, after a thorough examination of several thousand children, the method was abandoned because, good as the method is, the number of enlarged spleens found was very small. Some of the results were:

Locality	Number of children examined	Number with spleen one finger's-breath or more below ribs	Number with spleen "palpable"	Percentage with enlarged spleens
Alkmaar.	2,926	6	150	5.3
Heerhugowaard . . .	728	4	23	3.8
Zaandam	1,000	—	17	1.7

It should be noted that erroneous deductions may be drawn from spleen indices as low as the above in countries where other diseases in addition to malaria give rise to splenomegaly — for example, rickets. It need hardly be said that such difficulties are all the greater in areas where kala-azar is endemic.

Another disadvantage in the use of spleen indices as an indication of the distribution and character of malaria is that they are misleading in countries and localities where quinine is largely used. Even in malarious places in the Tropics it is easy to bring about a great diminution in the "splenic index" by adopting a good system of quinine distribution in schools. In Europe, the Commission ascertained on several occasions that the examination of school-children in malarious places where school distribution of quinine was practised gave no indication of the true prevalence of the disease and was therefore a plan of enquiry which, for epidemiological purposes, was not worth the considerable labour involved.

In the same connection, we may remark that almost continuous quinine treatment was probably the cause of the low rate of splenic enlargement among the numerous soldiers who contracted malaria during the war and continued to suffer from relapses for a long time after returning to their homes.

Nevertheless, there are in Europe, as in the Tropics, certain areas in which it is the rule to find a high rate of splenic enlargement among the inhabitants. For example, some of the spleen rates among children examined by the Commission during its European tour in 1924 were as follows:

Country	Locality	Splenic Index
Italy:	Termine (Venetia) . . .	83
Dalmatia:	Vrana	95
	Opuzen	50
Russia:	Persianovka	69
	Kazan	36
	Tzaritzine	36
	Idzium	30
	Sederovka.	30
Greece (Macedonia):	Yanitza	57

Country	Locality	Splenic Index
Roumania:	Sadova	66
	Gurbanesti	38
	Dabuleni	30
Bulgaria:	Athanaskeny	52

Figures of this kind (and the list could be greatly extended) show that a wide field of enquiry into spleen rates is available. What is required is that in some of these localities the matter should be enquired into continuously and in a detailed manner. For this purpose it would probably be best to adopt the system of splenic measurement according to Schuffner's method, which is described below and which the Commission has used during its study tours.

This method enables a rapid examination to be made of patients and carriers.

The degree of enlargement of the spleen is determined by the point reached by the lower border of the spleen on a line drawn from the costal margin to another line joining the umbilicus with the anterior superior iliac spine.

Procedure. — The examiner sits in front of his patient, who stands at first slightly bent forward and subsequently bent almost double. The lower edge of the spleen is felt for while the patient is made to breathe deeply. Enlarged spleens are classified as follows:

1. Spleens which extend beyond the costal margin and reach as far as the upper fourth of the line.
2. Those which reach the middle of the line.
3. Those which extend as far as the third quarter of the line.
4. Those which reach the umbilicus.
5. Those which extend beyond the umbilicus towards the right.

This method enables one to ascertain first whether differences in size can be correlated with age and length of residence, and what differences occur in natural circumstances from month to month throughout the year and from year to year throughout a considerable period. In the absence of this knowledge relating to areas of high endemicity, the use of spleen rates as a measure of the success of antimalarial measures may be very misleading.

In this connection, the Commission has been asked how long a condition of high spleen index might be expected to persist in a community where the sources of new infection were suddenly cut off or materially reduced.

There are places where, in natural circumstances, the spleen rate fluctuates considerably from year to year and others where it remains fairly constant over a long period. In areas which are subject to periodic autumnal epidemics, there is always a steady fall of the spleen rate during each post-epidemic period; it has been shown by Gill that in malarious villages of the Punjab in India this reduction in the spleen rates during the five years following an epidemic may be as much as from 80 to 10 per cent. In places where a seasonal (winter) interruption of infection occurs, there is also a seasonal fall of the spleen index, as, for example, from 82 per cent in October to 25 per cent in April or May.

Parasite Rates. — This method of ascertaining the distribution, character and intensity of malaria is most to be relied upon and it is the method from which most can be learned of the true situation with regard to the incidence and course of malaria from month to month and year to year. A central expert organisation should be able to arrange to carry it out over a wide area, because the necessary blood-slides can be taken by instructed health visitors or health nurses and forwarded to a central laboratory for examination. It is desirable that such examinations be repeated. In the province of Caceres (Spain), 80,000 examinations have been carried out among a population of 200,000. The practical advantage which the method possesses in comparison with the method of "spleen rates" is that the latter must be taken personally by an expert in the localities concerned.

To study more thoroughly the parasitology of communities severely infected with malaria, several methods of estimation of the number of parasites present in the blood of infected children have been advised; these might perhaps be profitably used in one or two severely infected regions of Europe.

4. Notification of Cases.

Malaria is among the infectious diseases which are compulsorily notifiable in the following European countries:

Czechoslovakia (*i.e.*, Bohemia, Moravia and Silesia),
Denmark,
England and Wales,
Estonia,
Greece,
Hungary,
Irish Free State,
Italy (under certain conditions),
Latvia,
Lithuania,
Lower Austria,
Malta,
Northern Ireland,
Norway,
Poland,
Scotland,
Switzerland,
U.S.S.R.

Notification of cases is not a method which gives sufficiently accurate information for demographic statistical purposes. It is obviously extremely difficult to enforce

in localities where the disease is very prevalent. In endemic areas much more accurate results are obtained by the determination of spleen and parasite indices. Compulsory notification of cases finds its most useful application in countries where primary cases of malaria are rare. In England, for example, the notification of suspected cases has proved useful because the notification is followed by expert enquiry into the accuracy of the diagnosis and into the origin of the case and by advice as to the steps which should be taken to prevent further spread. The adoption of the measure has shown that the primary disease, as it presents itself to doctors in general practice, is difficult to diagnose, and that notifications based on clinical signs alone are of little value. If these findings are equally applicable in other European countries, it would seem that, unless enquiry into suspected cases is undertaken by a central expert agency, it would not be useful to adopt notification until the general practitioners of the country had been specially instructed in diagnosis and were accustomed to utilise microscopic blood examination as a routine diagnostic method.

Records of admissions to hospital and of attendances at dispensaries are a modified form of notification, which also provides useful information if there are approved arrangements for confirming the diagnosis by blood examination.

5. Discovery of Patients by House-to-house Visits.

The best method of carrying out an exact and complete epidemiological study is by means of systematic visits to every house, school, hospital and other institutions in the area concerned. By verbal enquiry and by clinical examination, all persons infected with malaria can be discovered. A special form is drawn up for each house, on which are inscribed the names of all the inmates, and opposite each name all available information connected with malaria, more especially the results of blood examination.

Such household forms furnish a very complete record of the cases of malaria at the time of the enquiry.

Subsequently, the locality of houses in which cases have been discovered can be marked on a map, a special sign indicating fresh infections.

Having obtained such first information regarding the malaria condition of the locality, all houses should be periodically re-visited, so that any new development may be noted (new cases, relapses, recoveries, etc.).

Conclusions.

It seems to the Commission that for practical purposes the notification of malaria zones constitutes the first step towards the determination of the distribution

of malaria in the country. The second step consists in verifying the accuracy of such notifications and the determination of the parasite index at least. The latter is indeed the only measure to employ in countries with inadequate medical organisation, and, in order that dispersion of effort may be avoided, the Commission is of the opinion that it is well to choose one or two localities in each malaria zone which can be submitted to a thorough scientific investigation and to a careful house-to-house search to obtain information on the distribution and character of the disease.

This method of enquiry should be considered as an indispensable preliminary to the application of measures if, as we believe, only such antimalarial measures should be applied as are appropriate to the special conditions existing in each town, village or other communities as the case may be.

It should be understood that these suggestions of the Commission are in no sense absolute or categorical, above all in so far as they concern the order in which the different methods should be applied.

6. Measurement of Malaria in Mosquitoes.

In malarious localities, the amount and seasonal incidence of malaria must be measured in anopheles mosquitoes as well as in man. The Commission suggests that in future it should be studied systematically wherever the means and materials are available. A knowledge of the seasonal incidence of malaria in mosquitoes caught in houses is essential to the satisfactory prosecution of the primary antimalarial measures which the Commission has recommended; it indicates the months during which infection is most likely to occur and, consequently, the months when the killing of mosquitoes in houses is most important. This will be clear from the following examples:

1. In North Holland, in villages near Amsterdam, the monthly amount of malaria in mosquitoes (*maculipennis*) caught in houses was measured from January 1920 to July 1922. The results compared with the monthly incidence of cases of malaria in the same localities are shown in Fig. 21 (page 62).

It will be seen that the seasonal incidence of malaria in mosquitoes caught in houses is quite different from the seasonal incidence of malaria in man: the former is a phenomenon of autumn and winter, chiefly from September to March, with a maximum in November or December; the latter is a phenomenon of spring and summer, with a maximum in June or July.

2. In Italy, at Fiumicino and neighbouring villages, an examination of specimens of *maculipennis* caught in houses and stables was made (under the direction of

Professor Grassi) from October 1918 to September 1919. The monthly percentage found infected was as follows:

Jan.	Feb.	March.	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
0.8	3.2	0.8	—	—	0.2	1.2	0.48	1.8	2.2	1.8	4.4

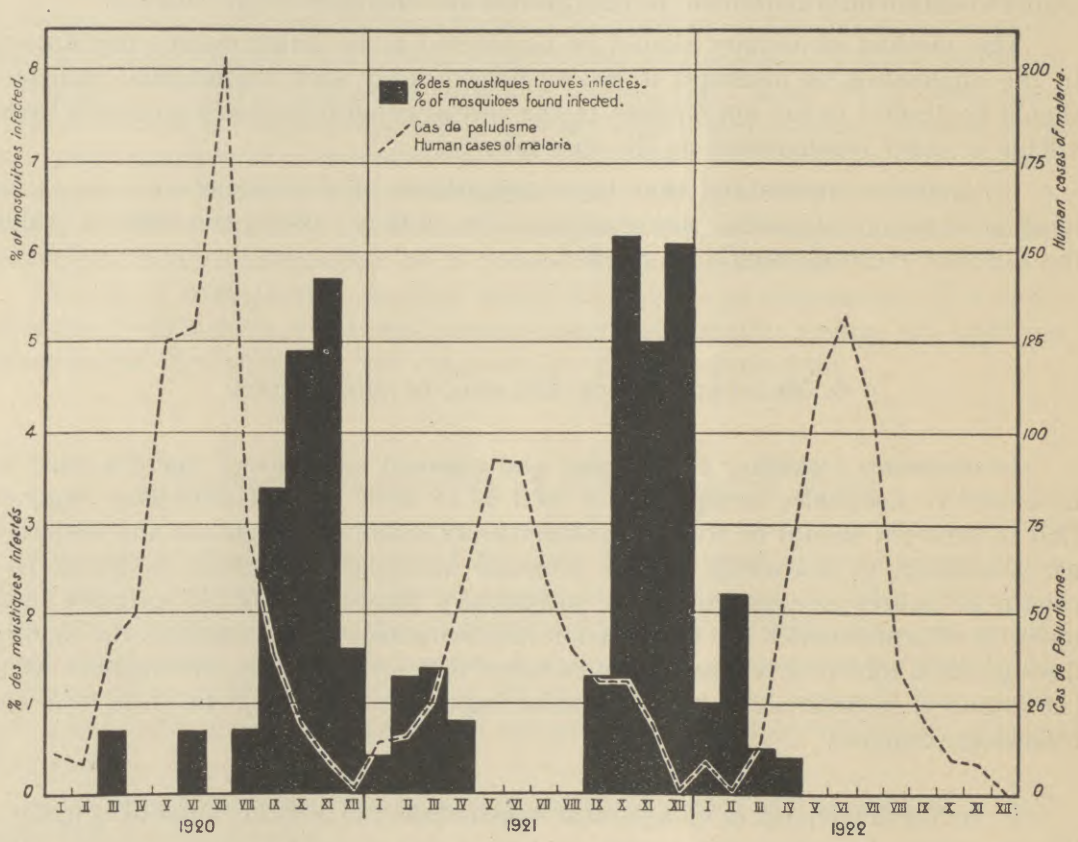


Figure 21. — Seasonal Incidence of Malaria in Mosquitoes and Clinical Cases of Malaria in Man.

It will be seen that in this locality, as in North Holland, the incidence of malaria in mosquitoes caught in houses is highest during the winter, particularly from October to February. The monthly incidence of cases of human malaria in the locality is quite different: it is highest in August and lowest in January.

The statements appear to show that, in the particular localities referred to, arrangements for searching out and treating human cases are chiefly required during the spring and summer, but that arrangements for killing infected mosquitoes in houses are most important during the autumn and winter. Other localities and

countries may show quite different results in this respect, particularly if *P. falciparum* instead of *P. vivax* is the malaria parasite chiefly concerned.

The Commission hopes also that malarial infection in mosquitoes will be studied systematically in every laboratory which may be established in connection with arrangements for the malarial treatment of mental patients. This study provides valuable information on the conditions necessary for the infection of mosquitoes, on the length of life of infected insects, on the persistence of the virus in those insects and on other matters of epidemiological interest.

SECTION III.

PREVENTION AND CONTROL OF MALARIA.

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I. ORGANISATION.

In our former report (C.H. 273) we described the different plans on which administrative and medical arrangements for dealing with malaria were organised in 1924 in various European countries. In Eastern Europe, at that time, the disease prevailed in epidemic form and the arrangements for dealing with it were complicated by problems relating to the movement and settlement of refugees and by a lack of trained personnel. Conditions are now more stable, and emergency schemes are gradually being replaced by a continuous public health policy and the development of medical and public health services on a permanent basis. In this reconstruction, antimalarial arrangements must take their rightful place according to the rank which the disease holds among the various causes of sickness and death in the different countries concerned. Our Commission has suggested in Section 1 that, to obtain further information on this subject and to add to present knowledge of the epidemiology of the disease, its pathological effects and the most suitable methods of treatment and prevention, arrangements for continuous research should bulk largely in any permanent antimalarial organisation which is being created or extended in the malarious countries of Europe.

To arrange for this need and generally to organise and co-ordinate official and unofficial antimalarial work, it is advisable to establish at the headquarters of the Government a central official organisation similar to that which is usual for other social diseases, such as tuberculosis or venereal diseases. This organisation should be a subsection of the general department of health and should be composed of one or more expert medical officers who act (through the Director of Health) as the technical advisers on malaria to the Government. To assist this section and to secure the collaboration of other Governmental departments and of voluntary agencies, it may be advisable in some countries to establish an "Antimalaria Advisory Committee", composed of representatives from the Agricultural, Engineering, Financial, War and other Departments of Government, as well as representatives of official and unofficial agencies engaged in antimalarial work in different parts of the country.

The chief duties of the central executive organisation will be: (1) to advise the Government on antimalarial policy and measures; (2) to arrange for malaria

research; (3) to arrange for training medical officers and subordinate personnel in malariology; (4) to conduct malaria surveys; (5) to give general advice and assistance in the conduct of local measures.

For the purposes of research, we suggested in Section 1 the establishment of: (1) an observational field station for routine enquiry into the natural history of malaria; (2) a laboratory for the artificial infection of anopheles mosquitoes.

Each of these stations should be in charge of an experienced malariologist with a sufficient subordinate staff.

In addition, one or more field research malariologists will be required for malaria survey work in localities where antimalarial measures are being undertaken, and the central research staff should also include a field entomologist, an agricultural expert and, if possible, an engineer who has made a special study of antimalarial engineering work, etc.

The arrangements for training medical officers and personnel in malariology should be made at the observational field station, which should therefore be provided with a library of malaria literature and a museum of specimens, charts, diagrams and models.

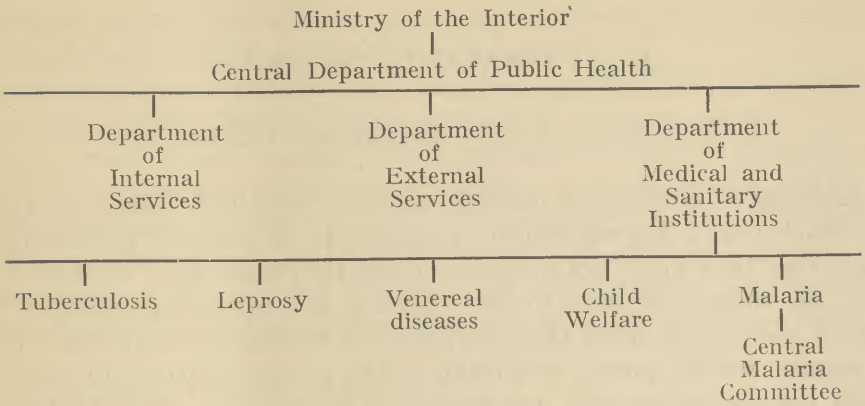
The laboratory for the artificial infection of mosquitoes should be established either in or within easy reach of a hospital where the clinical and pathological study of the disease can be pursued.

As regards the form of organisation which is to be preferred for practical antimalarial measures in the field, the Commission does not consider it advisable to lay down any hard-and-fast rule. In some areas visited by the Commission a service of full-time malaria officers is clearly necessary; in others, the antimalarial work that is required can be allocated to the ordinary district sanitary officers in addition to their other duties; in others, it is practicable to employ private medical practitioners in part-time antimalarial work. Voluntary unofficial organisations must also be utilised wherever possible. Local conditions largely affect the problem, and during the early years of the campaign a wide latitude in respect of organisation is usually the best policy, provided always that there is effective inspection and supervision. In areas where full-time malaria officers must be employed it is desirable, as time goes on, to aim at developing their activities and extending their duties so that they come to be in effect health officers in the general sense of the term.

On the occasion of its tour in 1925, the Commission had the opportunity of studying the antimalaria organisation in Spain (C.H./Malaria/58 (1)). It would be useful to give, as an example, a short description of the system which has been established there comparatively recently; in its establishment, experience acquired by the health administrations of other countries (Italy among others) was turned to good account.

In Spain, the direction and superintendence of all antimalaria measures are entrusted to a Section of the Central Health Organisation (Ministry of the Interior).

The position which the Central Malaria Committee occupies in the general plan of the central administration is indicated in the following table:



The technical medical personnel of the Central Malaria Committee consists of: (1) Experienced technical experts selected from among the personnel of the Institute of Malariology and Tropical Medicine of the University of Madrid; (2) of medical experts (malariologists) who have taken a special course of three months' duration at the Laboratory of Parasitology of the University and at the National Hygiene Institute and have undergone practical instruction in the dispensary of Navalmoral de la Mata, in the province of Caceres, which is used as a school of malariology; (3) of municipal medical officers who have followed a course in one of the institutes just referred to or at the provincial health institute and who have subsequently worked voluntarily for a certain time for the Central Malaria Committee in the dispensary functioning in their respective districts; (4) of resident medical officers and medical students — most frequently students attending the course of parasitology in Madrid, who devote their holidays to the antimalaria campaign.

In addition to this medical personnel, mention should be made of: (1) "praticantes", subordinate health officers; (2) persons employed in the distribution of quinine and workmen specially experienced in the practical application of antimalaria measures; (3) sick-attendants or district nurses who are trained at the Navalmoral School (Caceres) under the direction of an Italian Red Cross nurse specially trained in malaria treatment.

The duties of the Central Malaria Committee include: (1) the collection of information which will permit the declaration of malaria zones; (2) proposals for the formation of provincial committees to carry out antimalaria measures: (3) the creation of the necessary dispensaries and the nomination of their personnel as circumstances demand; (4) the purchase of quinine and its distribution either free or at cost price.

The Central Malaria Committee has adopted a general principle of undertaking antimalaria measures only in such areas where there is a possibility of obtaining a positive result. The certainty of obtaining financial and moral collaboration on the part of the local authorities (administrative as well as technical) is an essential preliminary consideration when deciding on the extension of its activity to any given region. This in no way hinders provincial health inspectors from carrying out independently, and with the means at their disposal, any or all antimalaria measures.

II. ANTIMALARIA METHODS.

1. Treatment as an Antimalarial Measure.

The problem of controlling malaria would be relatively simple if a drug were available which would kill all malaria parasites in an infected person quickly and definitely so that they would not re-appear unless the person were reinfected. No drug which will do so has yet been found. Quinine is a specific remedy for a clinical attack and it also brings about the destruction of most of the parasites, but it is less effective against certain phases and forms of the parasite (sporozoites and gametes) and it does not always prevent new infections or relapses. Nevertheless, it is unsurpassed among available remedies, and therefore quinine treatment is a principal item in the antimalarial programme of every country. Unfortunately, as the Commission had occasion to confirm more than once during its tour in Europe, the high price and the insufficient available supplies of quinine are a serious obstacle to its widespread use.

On this subject the Commission was asked to consider: (1) the world requirements of quinine; (2) the measures for increasing production; (3) the practicability of extension of cultivation to new countries; (4) cost of production and price of sale; (5) distribution by State agencies and sale by private firms.

The Commission has decided that most of these subjects were more properly matters for consideration by an International Conference on Quinine. A proposal for such a conference was made by the Government of the Kingdom of the Serbs, Croats and Slovenes and was adopted by the League Health Committee, but no decision was arrived at as to convocation or date. In the meantime, a Sub-Committee, consisting of Professor Giemsa (Germany), Sir David Prain (Great Britain), Professor Schüffner (Netherlands), Professor Martinotti (Italy) and Professor Marchoux (France), was appointed to report on special aspects of the industrial production problem from the botanical, chemical and pharmaceutical points of view. Reports by each of these experts, except Professor Schüffner, are available. Sir David Prain's report describes cinchona from the botanical and historical point of view, with a note by Colonel Gage on the cost price of sulphate of quinine in British India (12 shillings per pound of 16 ounces). Professor Giemsa's report explains the chemical and therapeutic properties of cinchona alkaloids. He placed quino-ethylene, quino-propylene and the more refined ethers of cupreine in the first rank for activity as antimalarial agents. The alkaloids of cinchona came next. He emphasised the small advantage there is in isolating the different alkaloids, and recommended the employment of the total alkaloids, which, in his opinion, are free from all toxicity and are profitable from a commercial point of view. Amongst synthetic preparations, he gave details of hydro-quinine as well as of quino-ethylene, which would be an ideal remedy were it not for the fact that the cultivation of *Remijia pedunculata*, which contains cupreine, had been almost entirely abandoned.

With regard to the advisability of employing total alkaloids, Professor Marchoux arrived at the same conclusions as Professor Giemsa.

At a meeting of the Health Committee held in April 1925, it was decided to organise an experimental trial in several countries of the relative efficacy of the total alkaloids and of cinchonine in comparison with quinine on the lines of the comparative trial of quinidine and quinine which had already been made by the Cinchona Committee of the English Medical Research Council [1]. That enquiry showed that quinidine is not inferior to quinine in malarial treatment; it was hoped that, if a similar finding should result from a trial of total alkaloids and of cinchonine, an important step towards lowering the cost of the treatment of malaria would have been taken.

The plan of enquiry was briefly as follows:

The chemical analysis of the substances used was carried out at the National Institute for Medical Research before they were distributed to the countries where the experiments were to be carried out (Algeria, Spain, Italy, Roumania, Kingdom of the Serbs, Croats and Slovenes). With supplies of the drugs was sent a number of treatment forms to be filled in by the medical officers and laboratory workers who had been entrusted with this study (C.H./Malaria/45 (*e*). (1)).

The study was carried out as follows: Patients are treated with one or other of the substances to be tested, without any selection, but merely in accordance with the order in which they are admitted to hospital. The patients treated all exhibit schizonts in their blood at the commencement of treatment. After having been weighed, they are given, during five days consecutively, one of the preparations (cinchonine, kinetum, or hydrochlorate of quinine) in doses equivalent to 1 gramme a day for a man weighing 70 kilogrammes. The daily dose, dissolved in feebly acidulated water, is given in two parts, morning and evening, by the doctor in charge of the observations. A drop of blood taken after each dose enables the evolution of the parasites to be observed twice a day. The temperature is taken at the same time, at a fixed hour morning and evening, and a note is made of symptoms (nausea, albuminuria, buzzing of the ears).

The results of the blood examination enable a comparison of the therapeutic action of the different preparations as shown by the time taken for the total disappearance of schizonts from the blood. This examination is made throughout by the same observer, using the same technique on all occasions.

A minimum number of thirty patients for each substance to be tested is considered necessary for any opinion to be formed regarding the therapeutic value in the different forms of malaria (primary attacks, relapses, etc.), and according to whether they had received previous treatment or not.

The Commission is in possession of results relating to 670 cases of malaria which were treated strictly according to the above method and of 86 cases in which the amount of the drug and the period of treatment were modified with a view to obtaining supplementary knowledge. The results of an independent enquiry with cinchonine carried out on behalf of the English Medical Research Council by Dr. William Fletcher, at Kuala Lumpur, in the Federated Malay States, are also available, and the results of experimental work relating to cases intentionally infected as a method of treating general paralysis. Needless to say, the Commission has paid attention to the results obtained by other workers.

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[1] Kinetum is a preparation of residual alkaloids consisting almost entirely of alkaloid bases. The composition of the samples used in the clinical tests was as follows: quinine 15%, cinchonidine 35%, cinchonine 25%, quinidine 5% and quinoidine 20%.

The Commission considers that the following general conclusions may be drawn from these enquiries:

Relative Value of the Different Alkaloids.

Numerous investigations have definitely shown that the value of quinine among the cinchona alkaloids is not unique. The experiments described on the preceding page have shown that:

1. Quinine, quinidine and kinetum are practically of equal value as antimalarial agents in the same doses. Cinchonine is equally effective in larger doses (1.50 grammes as compared with 1 gramme quinine), if the duration of treatment is prolonged.

2. As regards toxicity for the patient, there is no appreciable difference between quinine and the other alkaloids when the latter are freed from impurities; but quinidine has a more potent depressant action on the heart muscle than quinine or cinchonine.

3. All available evidence strongly suggests that a standard preparation consisting of a mixture of the principal alkaloids, and purified only so far as to be free from the more toxic constituents, would serve for the treatment of malaria equally as well as quinine.

Treatment and Prophylaxis.

New knowledge concerning the limited action of quinine as an antimalarial remedy is not yet sufficient to enable hard-and-fast rules to be prescribed for the use of the drug in the most effective way in the antimalarial campaign. Enquiry in the laboratory and experimental trials in hospitals and in the field must be continuously pursued. The lesson which we draw from the new knowledge already gained is that, while quinine (and allied alkaloids) can be used more economically than seemed advisable a few years ago, they must certainly be used with stricter attention to detail and with a closer regard to individual conditions and to the particular purpose in view.

A. *Therapeutic Use of Quinine.*

In considering the use of quinine, it is necessary to distinguish two sets of conditions: (*a*) quinine is distributed by a personnel not highly qualified and incapable of ensuring that each patient carefully follows the course of treatment. Such a state of affairs exists in communities where medical assistance is inadequate — conditions which are most important from our point of view.

Persons charged with the distribution of quinine should, if possible, personally administer to each patient suffering from fever sufficient of the drug. The daily

dose should be from 1 to 1.5 grammes (estimated in terms of hydrochloride) of some salt of quinine: this daily dose should be continued till the cessation of the febrile attack.

Without any desire to make a pronouncement in favour of any particular treatment to be followed after the febrile attack, the Commission insists on the necessity of prolonging the administration of quinine either by continuing to give a daily dose of 1 gramme or giving a similar dose on two consecutive days of each week (Saturday and Sunday, for example).

Moreover, the Commission considers it desirable to reinforce the action of the treatment, both during and after the febrile attack, by appropriate means — good food and such other measures as are needed to improve the general state of health.

(*b*) In cases in which patients in hospitals are concerned, or well-to-do people living in conditions as favourable as those offered by the hospital, the following considerations are of importance:

1. Throughout the treatment, reinfection should be avoided by wire-gauze, mosquito-nets and the destruction of mosquitoes.

2. The results of treatment should be controlled by the microscopic examination of the blood and the treatment should be modified according to the results of such examinations.

3. Patients should be kept in bed throughout the treatment of the acute attack, even if relapses are numerous.

Needless to say, the remarks made above regarding general care of the patient apply to this class of cases also.

The Commission considers that the details of treatment should be left to the discretion of the treating physician. It considers that too prolonged a treatment and excessive dosage should be avoided, as they not only entail a waste of quinine but possible damage to the patient.

B. *Prophylactic Use of Quinine.*

Quinine does not prevent infection, but, taken over a sufficient period of time and in appropriate doses, it can often prevent the appearance of symptoms of infection and enables the organism to rid itself of the parasites. Such is the *guiding principle of the prophylactic use of quinine*; consequently, there is no advantage whatever in giving quinine as a prophylactic to people going to malaria countries before they arrive. It must not be forgotten that this form of prophylaxis often implies waste of the drug, if it is not carried out in a methodical manner, among people insufficiently disciplined and insufficiently taught regarding the manner of protecting themselves, as far as possible, from repeated infection.

2. Measures against Mosquitoes.

The Capture of Mosquitoes.

In Palestine and in Italy, the Commission was favourably impressed with the following simple method of catching adult mosquitoes in rooms and stables where infected mosquitoes hide.

1. The person who is to catch the mosquitoes enters the room and prepares it so that daylight is admitted through only one opening, preferably the door. This is done very quickly by using sacks and straw for darkening windows and for filling holes and other small openings.

2. A white sheet is tacked over the open door through which light is being admitted. The sheet is stretched tightly so that it remains flat and smooth; there must be no open space left between the lower end of the sheet and the ground through which mosquitoes would escape.

3. The operator who remains in the room places two or three small bundles of straw on the ground or in tin buckets in different parts of the room and lights them, then sprinkling water on them or covering them with damp straw to make as much smoke as possible.

4. The room is soon filled with dense smoke and shortly afterwards the mosquitoes begin to fly to the white sheet, which is the only light area. The operator squats on the floor near the sheet and catches the mosquitoes in a test tube as they alight on the sheet. The smoke, of course, is troublesome to the operator, but, by sitting on the floor near the sheet, he is able to support it long enough to catch all the mosquitoes. Care must be taken to avoid the use of substances capable of injuring furniture and fittings.

Larvicides. — The Commission does not consider it necessary to make any special mention of oil applied to breeding-places. The efficacy of this antilarval measure is generally recognised. Among more recent methods, attention is directed to the use of Paris green, trioxymethylene, and of liquid paraffin. The chemical known as Paris green or Schweinfurt green is a double salt of copper arsenite and copper acetate. For larvicidal use it should contain at least 50 per cent arsenious oxide; a chemical analysis and a field test should be made with a sample of each consignment before employing it on a large scale. For use, it is mixed with dry road dust in the proportion of 1 part of Paris green to 100 parts of dust by volume. If dust is not available, wood ashes, magnesia, spoiled flour, lime or fine sand may be used. Mixing is done mechanically in a revolving box provided with a wire sieve. The mixture is distributed over the surface of breeding-places either by throwing it in the air by hand so that it falls on the water as a cloud, or by means of a hand-blower or bellows similar to that used by farmers for dusting vines. Distribution should be done sparingly; a very small quantity suffices to kill anopheles larvæ. One litre of the mixture is sufficient for 100 square metres of water surface.

Liquid paraffin as a larvicide has been largely tried in the Netherlands. It is applied by spraying in quantities of from 2 cc. to 5 cc. per square metre. It kills anopheles larvæ and pupæ by blocking the tracheal system. It is not necessary that the paraffin should form an unbroken film on the surface of the water.

In comparison with petroleum, both Paris green and liquid paraffin have many advantages.

A comparative study of Paris green and liquid paraffin in the Netherlands has been reported to the Commission by Professor Swellengrebel and Dr. H. de Rook. (C.H./Malaria/75.) The chief differences as regards effectiveness were found to be:

(1) Paris green is effective in running water, but paraffin is not; (2) the efficacy of Paris green is seriously lessened by wind and rain, but paraffin is not affected by them; (3) liquid paraffin has a more continuous and lasting action than Paris green; (4) paraffin kills pupæ as well as larvæ; (5) paraffin is more expensive than Paris green but can be applied more quickly, so that the cost of labour is less.

On the whole, the conclusion was drawn that in the Netherlands paraffin is preferable except for the larger canals, but that in a country of rivers and running streams the preference is with Paris green.

Experimental Antimalaria Stations.

The Commission considers it useful to publish the following paragraphs by way of an example: they are extracted from a report kindly supplied by the Director of the Experimental Antimalaria Station (Stazione Sperimentale per la Lotta Antimalarica), with the approval of the Central Public Health Department of Italy. This report deals with one of the six experimental antimalaria stations established in Italy by the International Health Board of the Rockefeller Foundation with the cordial approval of the Italian Government and in very close collaboration with the Health Administration so that the best possible results might be obtained.

Establishment of the Stations.

Towards the end of 1924 six field centres were established consecutively in different parts of Italy and, later, a Central Office, a library and a laboratory were established in Rome (168, Corso Vittorio Emanuele). The first of these centres was opened at Portotorres, a town with about 6,000 inhabitants, which had the reputation of being one of the most malarious places in Sardinia. The municipal authorities were approached and undertook to furnish rent-free a large well-lit room to serve as a laboratory, provided with water and electric light, as well as a storehouse and a workshop near the river.

Before arriving at a decision, a local survey was carried out during the winter of 1924-25, both of the population and of the area concerned.

Preliminary Survey.

1. *Character and Resources of the Town.* — The village is compact; the rural population on the outskirts is small. Information was collected regarding the budget of the commune, demographic and health statistics, as well as the principal agricultural and industrial activities.

2. *Prevalence and Endemicity of Malaria.* — At the beginning of spring, a time of the year when the prevalence of malaria is at its lowest, all school-children below the age of 12 years were examined to ascertain the spleen index, the parasite index and the proportion of hæmoglobin in the blood. This examination was carried out on more than 600 children, that is to say, more than 10 per cent of the total population. Each of the children was examined lying down with the abdomen uncovered.

The degree of the enlargement of the spleen was described by the following symbols: P (palpable during inspiration only); 1, 2, 3 (extending into the upper part of the abdomen); I, II, III (extending below the umbilicus). The enlargement of the spleen was expressed neither in "finger-breadths" nor in centimetres, to avoid the necessity of using correction tables in the calculation of averages according to the height of the children examined.

To obtain the parasite index, the thick film method was adopted, the drop of blood being obtained either from the ear or the finger: fifty such drops were stained at one time on a special slide which was immersed in a receptacle containing dilute Giemsa stain. Each of these thick films was examined for at least five minutes. The hæmoglobin was estimated with Dare's electric-light hæmoglobinometer. This is a costly apparatus, but it can be used in broad daylight and with great rapidity. For each child examined, the following information was collected: the name, name of the father, address, length of residence at Portotorres, sex, age, medical history of the previous year from the point of view of chills and of fever, date of the last attack of fever.

Special pocket-books were provided for this survey, each book being sufficient to record observations on 250 individuals. The medical field director always carried one of these pocket-books so that he might eventually obtain data regarding all the children in the town. The spleen and parasite indices, however, were only estimated between November 1st and April 30th. The visiting nurse keeps track of all the newly born infants so that they might be examined when they reach the age of 1 year.

Adults were not examined, but approximately accurate information was obtained as to the amount of quinine used each year, and the percentage of cases diagnosed as malaria at the local dispensary during each month during the three previous years (fever rate) and the number of deaths attributed to malaria during recent years.

This survey of Portotorres disclosed a spleen index of 46.8 per cent. Of the enlarged spleens, 72.6 per cent were below the costal margin and 4.8 per cent extended beyond the umbilicus. The parasite rate was 34.2 per cent. The variety of parasites found was as follows:

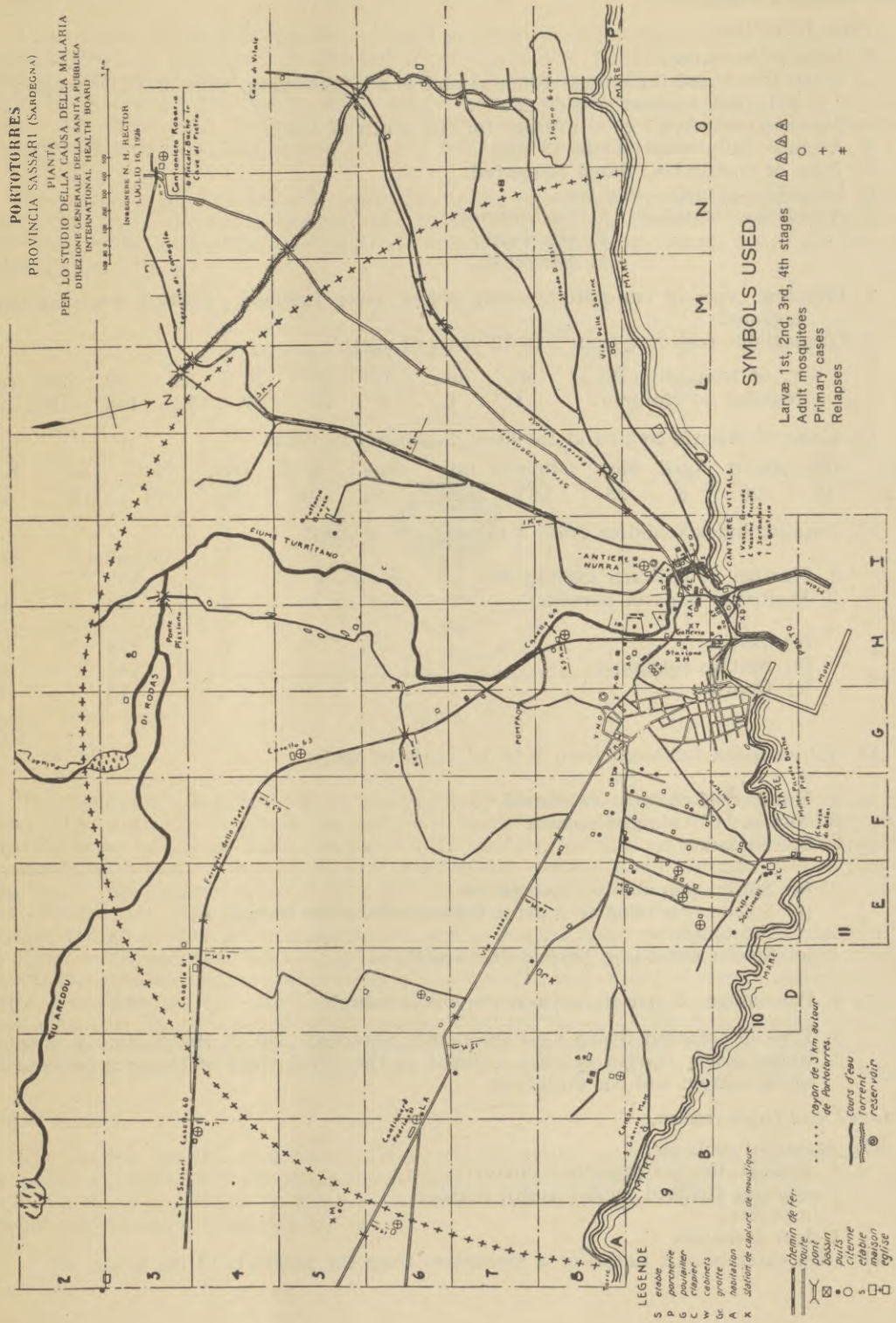
	%
Tertian	43.1
Aestivo-autumnal	51.4
Quartan	5.5
	100.0

3. *Prevalence of Anopheles.* — Investigations were carried out throughout the summer of 1924 with the object of obtaining information concerning the number and species of anopheles existing at Portotorres; several stables on the outskirts of the town were noted as containing a very large number. For example, on July 21st, more than 1,000 *A. maculipennis* were caught by a single individual in fifteen minutes in a stable situated near a fresh-water lagoon at the mouth of the river.

4. *Anopheline Breeding-places: Survey Maps.* — During the winter, the engineer attached to the experimental station made a careful examination of the country contained within a radius of 3 kilometres from the outskirts of the town; he then prepared the survey map. This map showed all the localities in which there were accumulations of water, either natural or artificial, at the time of maximum rainfall — that is to say, wells, cisterns, irrigation and other reservoirs, ditches, streams, marshes, ponds, borrow-pits, springs and seepage areas capable of containing water for at least a week. This survey occupied the engineer for ten days. It showed that the river, throughout its length, was an important breeding-place for anopheles, 12 kilometres of its course being within mosquito-flying distance of the town. The same thing was true of a certain number of irrigation channels and borrow-pits along the railway line and of several collections of water. In making the map, the engineer made use of an existing map which he reduced to the desired scale of 1 in 10,000; on this he inserted all important details from the malaria point of view after a careful personal examination of every part of the zone. The map was transferred to tracing paper to enable direct reproduction of large wall-maps. A plate some 45 centimetres square was also made; between two and three hundred copies of the map were reproduced, which were used to illustrate the progress of work.

Figure 22.

MAP OF PORTOTORRES.



Data regarding Portotorres.

First Inspection.

1. Population: 6,000.
2. Occupations and industries: tomato- and peach-preserving, wine and oil; seaport and potential summer seaside resort.
3. Average prosperity: good average for the south of Italy.
4. Average daily wage: 14 to 18 lire.
5. Type of population: much congested.
6. Domestic animals: very few.
7. Anopheles identified: *A. maculipennis*;
   A. bifurcatus;
   A. algeriensis.
8. Principal types of mosquito-breeding places; river Turitano ; flooded low-lying lands; lagoons.
9. Hæmoglobin (children from 2 to 12 years of age);

% of hæmoglobin:	30	40	50	60	70	80	90	100	Total
Number of children:	1	1	6	20	47	112	163	125	475

10. Cases of malaria treated at the local dispensary in 1925:

Janv.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total
32	18	20	6	35	54	246	135	96	30	14	13	699

11. Parasite index (children from 2 to 12 years of age):

	Number	%
1. Number of children examined	802	
2. Positives: malaria parasites	274	34.2
(*a*) Tertian	118	43.1
(*b*) Aestivo-autumnal	141	51.4
(*c*) Quartan	15	5.5
		100.0

12. Spleen index (children from 2 to 12 years of age):

1. Number of children examined	312	
2. Number of enlarged spleens	146	
3. Spleen index	—	46.8
(*a*) Spleen palpable on inspiration	40	27.4
(*b*) Spleen extending to a point between the costal margin and the umbilicus	99	67.8
(*c*) Spleen extending beyond the umbilicus	7	4.8
4. Percentage of spleens beyond the costal margin	106	72.6

5. Type of enlarged spleen most frequently observed: No. 1, that is to say, a spleen whose lower margin reaches a point in the upper third of the area between the costal margin and the umbilicus.

Personnel and Organisation.

The personnel includes:
1 medical director (qualified doctor);
1 assistant (trained public health nurse);
1 inspector;
1 field assistant.
The area extends to a radius of 3 kilometres from the outskirts of the town.

Scientific Work.

Examination of Breeding-places. — Their description, measurement and enumeration are made by the field assistant and checked by the inspector. Dipping for larvæ is done by the inspector, who is provided with a special "dipper", a thermometer and a number of bottles. The inspector records the results of his search on a special form. A complete list of breeding-places, with their number, classification and size, is entered on wall-charts in the laboratory. The assistant puts in a daily report, which is submitted to the inspector.

The capture of adult anopheles is carried out by the inspector in certain fixed places of capture (usually 15 or so), selected at the beginning of the year. Among these are stables, pigsties and bedrooms. As far as possible, these places of mosquito-capture were situated as in the following diagram (Fig. 23):

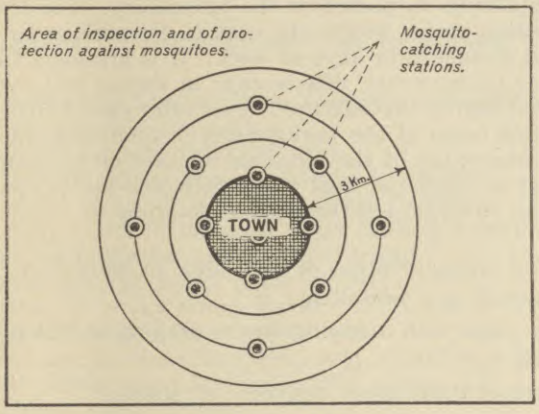


Figure 23.

The inspector is furnished with a catching tube labelled for each station as well as an aspirating tube or bulb to facilitate the capture of mosquitoes. The results of the morning catch are noted on an anopheles chart. Bearing in mind the fact that the inspector pays a fixed number of visits to each station each week, the total weekly catches made throughout the year are comparable. Two graphs are kept up to date in the laboratory showing the total weekly catches in the central zone (1 kilometre) and in the peripheral zone, respectively.

The inspector also keeps a register of meteorological observations and obtains from the municipal authorities each week a report on the number of births and of deaths. House-to-house visits to discover the sick, to take samples of blood and to find chronic malaria-carriers are made by the trained nurse. She and the medical director undertake the microscopic examination of blood-films, the classification of larvæ brought in by the inspector, the classification of mosquitoes that have been caught and their dissection. The annual measurement of malaria is done by the medical director. This demands a complete survey comparable to the preliminary survey.

Special Studies.

The medical director undertakes certain special studies each year. At the present time, the special study which is occupying the attention of the Portotorres station and the five other provincial stations consists in trying to estimate scientifically the results and cost of a local antimalaria campaign consisting of:

1. The destruction of larvæ by:

(*a*) Stocking suitable waters with *Gambusia*;
(*b*) Filling and draining, where these measures are economically realisable for the complete suppression of breeding-places;
(*c*) The application of Paris green as a larvicide.

2. The administration of quinine to chronic cases, that is to say, persons (especially children) who have enlarged spleens or who have suffered from an attack of malaria within a year.

. . . . . .

The measure on which most reliance is placed is the systematic application of Paris green at regular intervals to all breeding-places within a radius of 3 kilometres from the edge of the town. This work is done by one or more "field-agents". Each breeding-place is numbered clearly with paint on some nearby object. A list of the breeding-places with their numbers, classification and measurements is posted in the laboratory. The time required to distribute the larvicide on all breeding-places within the area is determined by the director in company with the field-agent, and divided into days of work. It is arranged that the field agents make the round of all breeding-places every fifteen days in spring and every ten days in summer. The Paris green is applied during the daytime, never later than three hours before sunset. The agent spends the remaining hours of the working day in preparing the larvicide mixture for the next day's work. The preparation of the larvicide requires large quantities of a cheap diluent. In Portotorres, road-dust is used, the dust being collected and screened by day labour. The cost of a hectolitre of the larvicide mixture was as follows:

	Lire
1. Collection and transportation of road-dust to workshop, per hectolitre .	3.15
2. Sifting road-dust, per hectolitre	3.75
3. Mixing Paris green with road-dust in the proportion of 1 to 100 by volume, per hectolitre	5.20
4. Cost of 1 litre of Paris green delivered at station	11.—
Cost of 1 hectolitre of prepared larvicide	23.10
Cost per litre (sufficient for 100 square metres)	0.23

The preparation of the larvicide requires two pieces of apparatus: a *rotary sieve*, enclosed in a box to protect the operator from dust; and a mixer, which is a tight box revolving diagonally on an axle.

It is necessary only once a year to *cut the vegetation* which grows in the ditches and along the banks of the river at Portotorres. This clearing is necessary to give access to the water and is economical because it speeds up the work of the field agent. It is contracted for at a price of 42 lire per 100 metres of ditch or river-bank.

In 1926, the cost per 100 metres of distributing Paris green was 11 lire before clearing and 3.50 after.

The budget of the laboratory at Portotorres is as follows (period: one year):

	Lire
1. Medical director.	36,000
2. Assistant	10,800
3. Inspector	6,600
4. Field agent	6,200
5. Labour and service	8,000
6. Transportation	3,000
7. Annual replacement of equipment	1,500
8. Material (Paris green, etc.) and current expenses	5,400
Total	77,500

The actual expenses of the first year's work at Portotorres were as follows:

	Amount Lire	Proportion item bears to total expenditure %	*Per capita* cost Lire
1. Installation [1]	16,643.70	14.3	2.77
2. Inspection, scientific study and control	52,198.55	44.7	8.70
3. Paris green work	5,490.50	4.7	0.92
4. Other antilarval work, including permanent measurements [1]	12,675,90	10.8	2.11
5. Quininisation	29,846.65	25.5	4.97
	116,855.30	100.0	19.47

The field equipment required for antilarval work and its cost was:

	Price in Italy Lire
3 small cloth haversacks, hanging from shoulder, for field use of doctor, inspector and agent (65 lire each)	195
2 electric two-call flash-lamps (each 35 lire)	70
2 pocket lenses, folding, magnification 10 × (each 50 lire)	100
2 bath thermometers, range 0° to 50° C. (each 10 lire)	20
24 mosquito-catching tubes of resistant glass (special funnel design)	120
2 aspirating tubes or bulbs for above (each 8 lire)	16
4 dippers for larvæ, special design (each 15 lire)	60
Spoons and pipettes for transferring larvæ	10
1 bucket-trap, special design, for dipping wells	70
1 rotary cylindrical screener for sifting road-dust, complete with box and stand	325
1 rotary mixer for Paris green larvicide, with stand	135
4 hand bellows-blower (each 35 lire)	140
1 knapsack duster	80
2 canvas sacks with sleeve outlets for transporting Paris green larvicide and filling blowers (each 40 lire)	80
1 galvanised-iron litre measure for road-dust	8
1 galvanised 100 cm. measure for Paris green	5
Total	1,434

Applicability of Antilarval Measures.

During all the journeys of the Commission in different countries, only two regions were found in which antilarval measures had been carried out on a considerable scale with definitely successful results. The first was in the Karst Mountains of Dalmatia, where there are bare, dry, waterless hills, sparsely inhabited and built on. Wherever the rainwater does not trickle away into the crevices of the chalk formation, it is carefully husbanded by the inhabitants, as in many places it forms the only water supply. These pools are chiefly used for watering cattle. As a rule, they are shallow ponds about 10 to 20 metres in diameter, in hollows which are lined

[1] Mainly expenditure not necessary in subsequent years.

with an impermeable clay. They generally contain plenty of vegetation suitable for anopheles, and are often the only breeding-places for these insects. There are no anopheles in the underground cisterns in which rainwater is collected and stored for human consumption. These "lokwas", where they were not absolutely required, were done away with and the remainder were cleaned, lined with masonry and petrolised or treated regularly with Paris green. In two years these antilarval measures have (in conjuction with quinine treatment of the sick people) been practically successful in stamping out anopheles and malaria in places where these "lokwas" were the only breeding-places of the anopheles.

The second place in which antilarval measures have been carried out on a large scale with very satisfactory and sometimes even perfect results is Palestine. The larger towns, especially Jerusalem, are entirely dependent on the water in the cisterns. *A. bifurcatus* breeds in the cisterns and the large water vessels in the houses, and is the only malaria transmitter; there are no other breeding-places. If the cisterns are not completely closed and provided with a pump under proper control, they are ruthlessly petrolised by the sanitary authorities at regular short intervals. The people drink this water without complaint. Pumps and well-fitting covers are provided at a very low price. Malaria in Jerusalem is now far below the pre-war index (spleen index 50 per cent, parasite index 23-27 per cent: Mühlens, Brünn, Goldberg, etc.), almost entirely as the result of these measures alone. The spleen index was still 47 per cent in 1919; in 1921, it was still at 19 per cent among 851 children in the Government schools; in 1924, it was 0 per cent among 829 children examined, and at another examination it was 1.9 per cent. The malaria mortality in Jerusalem in 1918 was still 113 out of 70,000 inhabitants. In 1923 there were 5 and in 1924 2 deaths. The conditions in the rural districts are very interesting, especially in the Jewish colonies. While in other countries the cry is "Colonisation means *assainissement*", here they work on the principle "First *assainissement*, then colonisation". In the newly purchased land the small watercourses, which only contain running water in winter and are dried up in summer, are properly regulated; the small tributary streams and marshes are eliminated by subsoil drainage, all open breeding-places destroyed or petrolised and the irrigation canals regulated or put in order. The colonists are not allowed to settle until this is done. The expense of these works of *assainissement* is sometimes considerable.

The conditions in Palestine are especially good for antilarval measures. The hilly country has very permeable ground, the mountains are dry, the valleys easy to drain and the mountain streams are either quite dry in summer or, if there are pools of stagnant water or marshy places, these are generally easy to regulate. The rainfall is negligible during the malaria season.

It is not to be supposed that the example of Palestine can be followed in Italy, in the Balkans or in Russia to any great extent. Quite apart from the expense, the geological, hydrological and climatic conditions would prevent any such thing (great rivers, numerous and often large tributaries, wide inundated districts, many marshes and innumerable small pools and ponds, rainfall lasting right into the summer

and many other unfavourable conditions). We are reminded of a saying of Robert Koch, who once remarked: " It is beyond human power to destroy or even considerably to reduce a species of insect like the anopheles in large districts ". This remark has been fully justified, and certainly such methods of malaria control are impracticable, with few exceptions, in the malarial districts of Europe.

The Commission, therefore, can recommend antilarval measures in only a few isolated and carefully selected districts, after they have previously been thoroughly tested from a technical and financial point of view.

There are, for instance, isolated places in the dry plateaux of Macedonia, in Ovepolje, between Stip and Veles, or on the slopes of the mountains, which have only one or two collections of water suitable for breeding anopheles (small mountain brooks with marshy banks and stagnant water in their creeks, springs and streams, in marshy surroundings, small badly kept irrigation canals, etc.). The prospects for antilarval measures are quite favourable in such places, and it would be easy and not too expensive to carry out and keep up such measures. The Commission is of opinion that, in one or two carefully selected places of this kind, subsoil drainage and other antilarval measures might be done at the expense of the State, to serve as a test example and as a model and stimulus to local communities.

References should also be made to the success obtained with *Gambusia* in the destruction of anopheline larvæ in pools used by cattle (balzas) in Estramadura (Spain). These pools, before the measure had been adopted, presented a difficult problem in the cattle-raising districts of the province.

A careful local survey occasionally reveals a situation in which strictly "peri-domestic " antilarval measures have a good prospect of being successful. An example of this kind is shown in the following diagram, in which M represents

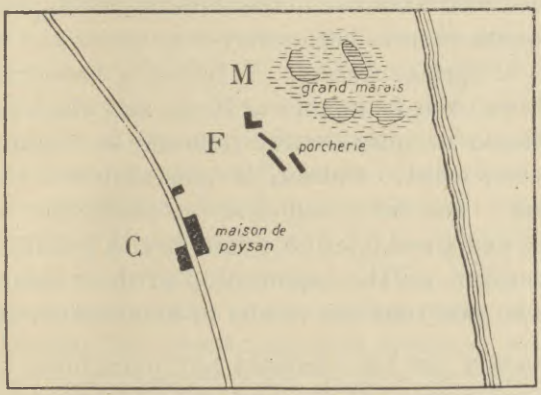


Figure 24.

a large marsh (which is a prolific breeding-place of *A. maculipennis*), F is a pig-breeding farm and C is a group of labourers' cottages. Many specimens of *maculipennis* could always be found in the bedrooms of these cottages. It was thought

that they came from the marsh, but numerous larvæ were also found in a small weed-grown ditch at the roadside in front of the cottages and in some small pools in the gardens. The ditch was piped underground and the pools filled. The result was that anopheles could no longer be found in the cottages. In this example the pigsties which were between the marsh and the cottages intercepted the mosquitoes from the marsh and the presence of *maculipennis* in the cottages was due entirely to the small "peridomestic" ditch and garden pools. The Commission has observed other instances in which a row of pigsties or cowsheds situated between a large breeding-ground and a group of houses has served to keep the latter free from anopheles mosquitoes when the small breeding-places which immediately surround the houses have been eliminated.

3. Bonification as an Antimalarial Measure.

The term "bonification" generally signifies all work carried out with the object of making regions that are periodically or permanently marshy more healthy and more suitable for agriculture. It is understood that, if this land is below the level of the watercourses or of the sea, and if it is irregularly flooded, it can only be exploited after the surface waters have been controlled, even if the land be transformed into rice-fields, as frequently happens. The problem is generally complicated because the regularisation of surface waters must extend sometimes even as far as the sources of rivers and torrents, and obstacles to the free discharge of water into the sea may have to be removed. On the other hand, it is frequently necessary to undertake costly measures to drain, wherever it is possible, damp and marshy land and to arrange for the irrigation of dried lands if these are to be made fit for cultivation.

In accordance with the nomenclature used in Italy, where these questions have been extensively studied and have been considerably developed, "hydraulic bonification" indicates such works as have been referred to above and which have needed the rational regularisation of surface waters. "Hydraulic bonification", according to a rule which has come down to us from ancient Rome and which has been shown to have capital importance, should be immediately followed by "agricultural bonification" and by permanent settlement. Indeed, if one excludes certain cases in which "hydraulic bonification" has been sufficient in itself, the economic results and, consequently, as will be explained later on, public health results are equally dependent, and in a very large measure, on the exploitation of these drained lands.

In general, it can be said that the results of bonification are direct and indirect.

The direct consequences are the changed hydrographical conditions: lakes, sea-inlets and swamps are converted into dry land and protected against repeated inundation, the level of the subsoil water is lowered as a consequence of drainage or is raised as a consequence of irrigation. It should be noted that desiccation does not always mean a complete removal of the surface water. It does so if the submerged area to be desiccated is situated on a high level so that the water can be let off immediately or can be collected in subsoil drains. But if the area is situated in a low-lying district,

the bonification can only be completed economically by drainage with open ditches. Irrigation also implies the construction of open ditches, but the majority of them hold water only temporarily.

The indirect consequences are the changed economic conditions: building of towns and villages, agriculture, new roads, etc. They may lead to a rise of the economic status of the indigenous population, and in that case the indirect consequences are social as well as economic. But it happens sometimes that only the landowners or shareholders, not necessarily belonging to this indigenous population, reap the benefit; then there is an economic but not a social improvement.

There is no difference of opinion on the good influence of agricultural bonification in decreasing the incidence or, at least, the gravity of malaria. Difficulties only arise when endeavouring to explain this beneficent influence. Two main kinds of explanations may be distinguished, the one dependent on the anopheline factor, the other on the human factor.

It is not so long ago that the nature of this influence was considered quite apparent: Ross[1] explains it as follows: "The explanation was now clear; the ancients were quite right — the disease *is* caused by an emanation from the marsh. That emanation, however, is not a gas, nor even a *contagium vivum*, but an insect ". The principal difference modern science has brought about is that "previously, we had been obliged to drain a whole area at great cost; now we should be able actually to seek out and determine the exact malaria-producing pools ... if the old method had been feasible (as it had been in many places), the new method would be still more easily feasible, and at less expense ". In this explanation, drainage of large areas and dealing with individual breeding-places are considered as measures of the same general order.

This way of looking at those bonifications which involve the removal of superfluous water considers them as an *effective but unnecessarily expensive antilarval method.* It only takes account of the direct (hydrographical) consequences of the bonification and attaches no value to the economic consequences.

To those who regard the institution of bonifications as a method of dealing with larvæ, a bonification, be it ever so successful economically and socially, must appear as a failure from a sanitary point of view if (to use Grassi's expression) the irregular original swamps are converted into straight open ditches which prove to be much more fertile breeding-places than the original swamp. They will have to insist in every bonification on a constant supervision of the surface water, to render it unsuitable for breeding-places, although they know that such measures will lay a heavy burden on the farmers, which may eventually deprive them of the greater part of their profit, thereby endangering the whole economic purpose of the bonification.

Certain authors[2] hold quite a different view. Without denying the importance of anopheline reduction, they maintain that the incidence of malaria may be reduced, even in the absence of anopheles reduction, by the "influence du bien-

[1] " Prevention of Malaria ", London 1910, page 31.
[2] Bulletin de la Société Pathologique Exotique, 1921, XIV, 658.

être ". And this " bien-être " is a consequence of improved or increased cultivation of the soil. This idea is not a new one, as SERGENT points out when citing a Tuscan proverb: "Le remède du paludisme est dans la marmite ". And, indeed, Italy is the land where the economic factor in the disappearance of malaria is particularly brought forward, and especially so in connection with bonifications.

To those who, when dealing with malaria, mainly keep in view the economic and social significance of the bonification, such an antilarval activity *à outrance* must appear absurd. Without being willing to discard antilarval measures altogether, they will insist on applying them only in a measure not detrimental to the main object they have in view and, after considering carefully the local economic and social importance of the disease and the possibility of obtaining appreciable results, in view of the extension of the breeding surface. They will be opposed to any stringent and general prescriptions which compel landowners or farmers to execute measures which have a specific antilarval rather than an agricultural purpose. Instead, they will recognise that the sanitary conditions required of the bonification are fulfilled even if nothing has been done to check the growth of anopheline larvæ, provided that the economic and social status of the population has been sufficiently improved.

These views make it necessary to consider the following questions:

(*a*) Has malaria been reduced in regions subjected to bonification ?

(*b*) Have the breeding-places been reduced ?

(*c*) How are we to explain the antimalarial action of the social and economic improvements brought about by bonifications ?

(a) *Reduction of Malaria by Bonification.*

To avoid confusion, a sharp distinction should be made between reduction of mortality and morbidity, two results of antimalarial activity which need by no means run a parallel course.

When consulting the literature, we note that malarial reduction by bonification (whether reduction of mortality or morbidity is seldom made clear) is a fact accepted without any doubt. Remarks like the following are of common occurrence: "Holland, with its flat and marshy coasts, was formerly one of the chief centres of malaria infection in Europe . . . The magnificent work that has been carried out to protect the coast-line against the sea, drainage and culture of the soil have greatly reduced the extent of endemic malaria"[1]. Or: "Malaria fevers were once common in London . . . marshes in the neighbourhood were dried up and their disappearance was accompanied by the disappearance of the fevers. . . . In Ireland . . . drainage rid the country of endemic malaria "[2].

Such examples as those cited of complete disappearance of malaria from a region formerly infested have been rare in modern times. It should be stated that the statistics relating to malaria are for the greater part confined to mortality figures, and

[1] LAVERAN. *Traité du paludisme*, 1907, pages 36 and 37.
[2] *Idem*, page 37.

it is well known that such mortality data are not sufficient to give an exact idea of the amount of endemic malaria. If one relies on such statistical data, no conclusions can be drawn as to the results achieved by or the character of the bonifications.

Nevertheless, there is no doubt that, in several places which have been subjected to such bonifications, very appreciable diminution of malaria has been observed, although no convincing statistics can be produced in support of such a contention. As has been already said, it is difficult to determine the cause of such a diminution.

(b) *Reduction of Breeding-places by Bonification.*

There can be no doubt that the work of bonification may lead to a reduction or even complete abolition of breeding-places, as is sometimes the case with hydraulic filling and always with complete subsoil drainage. If the area treated in this way is sufficiently large, we can readily believe, even without statistics, that malaria disappears.

But there are other bonifications — the *polders*, for example — which provide an actual increase in the number of breeding-places. If a marked reduction of the breeding-places in areas subjected to bonification had been a general rule, this fact would have gone a long way to fill the gap in our knowledge expressed in the preceding paragraph. As it is, we cannot admit that the diminution of malaria caused by bonifications is attributable to a reduction in the number of breeding-places.

(c) *Social and Economic Consequences of Bonifications as a Means of Malaria Reduction.*

Bonifications have consequences of a social and economic order which can explain at least a notable reduction of malarial mortality and, to a certain extent, of morbidity, without leaving the foundation of well-ascertained facts.

A bonification changes a swampy region with a poor, scattered, often semi-nomadic population into a settled well-to-do one. The scattered houses are united into villages easy of access by roads or canals. To reach a whole village with hundreds of inhabitants is easier than it was to get at a single family before the work was done. In former times, not a single medical man could gain his livelihood because the inhabitants were too poor to pay him or, if they paid him, he could not make a sufficient number of daily visits because of the absence of good roads. Now perhaps three or four may make a living there because the population has increased in number and wealth and because it is easy to pay a sufficient number of visits on the daily round. Formerly, there was no kind of co-operation between the various families. Now that villages have been formed, the poor law can come into action; sick-clubs are formed to bring medical assistance to those unable to pay for it; better-class people (mayor, priest, schoolmaster, notary) come into contact with the population: the law prescribing compulsory instruction can be enforced because there is a school; hygienic propaganda finds in the school-children not only a fertile soil but also an intermediary to reach the parents; water supply and sewage disposal can be provided

for; prescriptions regarding the building of houses can be enforced; hygienic measures applicable to an instructed and accessible population can be introduced. In short, the improved social conditions bring with them, or clear the way for, improved hygienic and medical conditions.

With regard to malaria, this implies:

(1) A better treatment of the patients;

(2) A decrease of infectious diseases brought about by measures which are valued in themselves, quite apart from their hygienic value, like water supply, sewage disposal, improvement of human dwellings;

(3) Improved general sanitary conditions;

(4) More ready collaboration of the population in the treatment of cases.

In order that a bonification scheme may have an antimalarial effect it must change environmental conditions in the above manner. It would have been quite unnecessary to make this statement in former times. But as modern knowledge has induced many people to regard the execution of bonifications as a kind of antilarval measure, and has led them to suppose that the work is done when the hydrotechnical part of it is completed, it is advisable again to draw attention to it.

In no other modern document of State has this conception of the bonification as a means of social and economic improvement been brought forward more forcibly than in the recent Italian laws concerning "integral bonification" comprising the "hydrotelluric" and the "agronomic" bonification.

Although the time during which these laws have been in force is too short to judge of their results, they are so much in accordance with the Commission's views regarding the real purpose of bonification that they should certainly be recommended to the serious attention of all authorities concerned. There is only one point where some degree of circumspection seems needful.

The Royal Decree of December 30th, 1923, Tit. IV, provides for the execution of "opere di piccola bonifica", *i.e.* small antilarval measures. During the execution of bonifications of the first or second order these measures are regarded as part of the ordinary work and consequently the State contributes to the expenses. But when the work is finished the measures have to be maintained by the proprietors or the "consorzio" in the bonified area. In Italy, this point has been duly considered and the costs of these measures do not weigh too heavily on the shoulders of these proprietors. Still, we wish to emphasise, for the benefit of the authorities wanting to promulgate similar laws, that it is necessary, before enforcing antilarval measures to be paid for by the landholders, to make sure that their revenue is such that they can really pay for it. Otherwise, one runs the risk of making the bonification a failure in the most important point — the economic one. The following example will make this clear.

In 1919, compulsory cleaning of the polder-ditches in the Netherlands, as a means to control the growth of anopheline larvæ, was recommended. To ascertain whether the landowners or farmers (who would have to pay for this) could afford to do so, the malaria commission in North Holland made some experiments showing that from two to four men had to be employed 27 days per month to clean only the narrow ditches in a cattle-growing property of the usual size (20 hectares) once a month, which represents an extra expense of from 810 to 1,620 florins at the lowest estimation (for June-August only). The net revenue (deducting the rent) of such a property being 3,000 florins and often less, this means an extra taxation of from 25 to 50 per cent on the income, which will eventually lead to the absolute ruin of the landholder.

In countries where the breeding surface is small and manual labour cheap, there will be less difficulty in enforcing such compulsory cleaning of the ditches or any other antilarval measure. The Commission, therefore, is far from wishing to take this example as an illustration of a general rule but only as a warning duly to weigh the economic consequences of similar prescriptions.

General Conclusions. — Bonifications tend to reduce the gravity of malaria in a given area. As a rule, the results are not primarily due to a reduction in the number of breeding-places but to the social and economic improvements they may bring about. By judicious measures, the authorities can enhance and accelerate the realisation of these improvements and the equal repartition of their benefits among the local population. The construction and upkeep of the bonification may be combined with antilarval measures, but care should be taken that this does not jeopardise the principal, *i.e.*, the economic, aims.

Bonifications in Italy.

From ancient times, Italy has undertaken work designed to improve the health conditions of the soil. Rome, among other towns of the Peninsula, set a good example. Similar work was carried out in other localities in the Peninsula.

Unfortunately, the break-up of the Empire intervened and the long period of the Middle Ages put a stop to all antimalaria activity. The country-side was deserted and malaria spread everywhere.

In modern times, successful work was done here and there, but the new era of struggle against the marshes dates only from the constitution of the Kingdom. Even then the campaign was not waged with energy until 1900, the year when the first law against malaria was promulgated. That year marks the beginning of a larger and more systematic action against the causes of malaria.

The problem was considered in all its bearings. A beginning was made with "hydrotelluric bonification", which consists of:

(a) *Large preventive measures:* afforestation of mountain ridges, training of banks of rivers, streams, canals, etc., deepening river-beds and the removal of permanent or temporary obstacles to the free flow of water.

(b) *Large curative measures:* reclamation of land by filling or otherwise, terracing marshy depressions, draining by canals with or without pumping, reinforcing river-banks.

(c) To a certain extent, certain complementary work has been undertaken such as "agricultural bonification" or cultivation; "small bonifications" and other measures all tending to abolish local malaria conditions.

By measures such as these a large part of the marshy areas in Italy has been rendered healthy. Out of 1,772,000 hectares of marshy territory, 768,000 (approximately the half) had been improved by 1915, the year of Italy's entrance into the war.

But it must be admitted that, though these bonifications have produced satisfactory results from the economic point of view and, above all in the north of Italy, the results from the point of view of malaria prevention have not been everywhere commensurate with the very considerable financial sacrifices entailed by such bonifications. As a result, there has been a great deal of discussion as to the real value of bonifications and their purpose. Some considered that bonifications ought to have an exclusively economic aim, but others, more numerous and more reasonable, urged the importance of not losing sight of their antimalarial role. They admitted that sanitary results do not immediately follow the work of bonification and that such results are sometimes much delayed, being influenced, not only by the bonification itself, but by such other factors as:

(*a*) The prosperity of the population of the reclaimed zone;

(*b*) The presence of domestic animals which attract the anopheles;

(*c*) Biological modifications which may also influence the local anopheline fauna. These anophelines may become more resistant, less susceptible to contract and to transmit malarial infection.

New ideas concerning bonifications and the doubts that have been expressed as to their efficacy made it desirable to undertake research with regard to the efficacy of the procedure. The Malaria Commission of the League of Nations undertook to study the question thoroughly in the two countries in which the most extensive bonifications have been carried out: Italy (at the station of Ferrara) and the Netherlands (research into polders).

Among the numerous and happy undertakings of the National Government of M. Mussolini is the total revision of the existing legislation dealing with bonifications. In this revision, advantage was taken of experience acquired and new principles were adopted to render the new legislation more effective.

The new Law, dated December 30th, 1923 (No. 3256), was published in the *Journal Officiel* of March 24th, 1924 (No. 71).

Without wishing to enter into details, mention will be made here only of the principles which constitute the basis of the great reform.

1. All the different works of bonification which formerly were the concern of many have been united under the direction of a single administration. Each administration doing whatever came to mind, there was formerly neither cohesion nor correlation of effort.

2. An exact definition has been made of what constitutes "large bonifications" of the first order: these should promise economic and health advantages of primary social importance.

3. Attention should no longer be confined to the final aspects of the problems but an endeavour should be made to attack primary causes; thus, attention should not be limited to the marshy areas in the plains but should be given also to the upper courses, in the mountains, of the streams which give rise to these marshes.

The problem is thus studied in all its aspects ("small bonifications", agricultural improvement and colonisation), following a systematic plan from the beginning. A comprehensive view of the whole problem, without neglecting any single detail, is indeed necessary from the commencement.

4. Very strict control has been instituted, organisations for the upkeep and exploitation of bonifications having been created.

5. An attempt has been made to obtain favourable conditions for settlement by preparing for settlers a comfortable environment, enabling them to live without danger to health on the treated land which they are to enrich by their labours.

6. Large and generous State subventions have been provided to encourage such enterprises.

These principles arise from the fundamental conception of what complete bonification should be, a work in which attention is paid to all sides of the problem, with a complete appreciation from the beginning of the plan to be followed.

The application of these guiding principles is provided for in the three sanitary laws which constitute the new legislation with regard to this matter:

(*a*) The law of bonifications, to which reference has been made above (the Law of December 1923);

(*b*) The law concerning land improvement of public interest;

(*c*) The law creating the function of "provveditore" in South Italy and in the islands, centralising in their hands the direction and control of all public works of a province.

The law distinguishes two stages in the process of bonification — the first, the actual improvement of the soil ("hydrotelluric bonification"); the second, settlement

and the starting of agricultural operations ("agricultural bonification"). During the first stages the work of the State should include:

(*a*) Work designed for the abolition of marshes in the plains: filling up; drying; regulating the edges of water courses; deepening river-beds; drainage, etc.;

(*b*) The training of watercourses among the hills, that is to say, works of afforestation, consolidation of declivities and slopes, the bunding up of springs so as to provide electric energy, water for irrigation and a drinking-water supply (an example of this is the construction of the reservoir of Alto Belice, near Palermo);

(*c*) The construction of a network of roads and canals to ensure good communications;

(*d*) Complementary works of small bonification, having as their object the suppression of small swamps and residual puddles favourable to the breeding of mosquitoes.

These works of large and small bonifications having been completed, the second stage begins, that of settlement and of agricultural development. The Decree of March 24th on land improvement supplements and completes the law concerning bonifications.

This decree gives special facilities and special encouragement to immigration into the improved areas from neighbouring localities and to agricultural exploitation of the land by intensive and remunerative cultivation. It should be noted that, when the real-estate improvement is really of general interest and on a large scale, it is the State itself which undertakes all the necessary work in accordance with a systematic plan.

Antimalaria measures constitute one of the guiding principles which govern all work of this nature. The habitations of workmen engaged on such work should satisfy all hygienic requirements.

Superintendence and Upkeep. — Bonifications of the first category (those which have an importance both sanitary and economic) are carried out by the State, or by provincial or communal administrations, or even by associations of proprietors having received a concession from the State. These associations of proprietors not only undertake constructional work, when this has been decided upon by the State, but above all they are responsible for the upkeep of the work, and as a corollary they benefit by such rates and contributions as may be attached thereto. The State, however, reserves to itself the right of inspecting the work during its execution by means of a commission created for this purpose.

State Contributions. — The amount of the State contribution varies in different cases. In Southern Italy and in the islands, the subvention has amounted to seven-tenths of the total cost of the work. The State also advances sums necessary for the

undertaking, through the agency of the national lending bank or similar institutions, under the form of loans at a low rate of interest and of long duration (fifty years). The law also makes provision for the granting of special credits:

(*a*) For bonuses to the technical personnel and to others engaged on the work;

(*b*) For rewards to landowners who undertake antimosquito measures; and

(*c*) To encourage studies and scientific researches on malaria; the establishment of courses of applied malariology (there are several schools of this kind in Italy); for propaganda, etc.

The action of the State in this matter has been still further developed during recent times, thanks to the nomination of the "provveditori", who, among other things, interest themselves in bonifications. Each district has its "provveditore", who is a representative of the central administration but ensures a large degree of decentralisation. Formerly, all questions relating to public works were dealt with in the ministries; at present, they are decentralised and dealt with by the "provveditori", who, being on the spot, are in a better position to form a just appreciation of local necessities and the best manner in which to meet them.

They are for this reason heavily endowed. The work of this nature which will be undertaken during the coming years is estimated to cost several thousand million lire.

The "provveditorato" are staffed by officials belonging to different State administrations (Public Works, National Economic, Central Health Department, Finance). Consequently, the "provveditori" are in a position to evaluate local needs in the matter of public works.

Such, in brief outline, is the nature of the new Italian legislation on "bonifications", one of the most remarkable activities which has engaged the clear-sighted attention of the National Government.

4. Housing.

The predominant rôle played by domestic infection in the endemiology of malaria in Europe makes it imperative that in every permanent antimalarial scheme the housing of the people should receive earnest consideration. The problem is immensely difficult because it is intimately connected with poverty. In some malarious areas, even of Western and Southern Europe, there are many people who, from lack of means, are obliged to live in huts which are little better than the huts of primitive man, and there are still some who have no "hut" of their own but live (as Celli has described) like modern troglodytes in caves excavated in the rocky hills. In other places where the dwellings are a little better, being constructed of rough stones, or of earth-bricks or basket-work or wattle, roofed with thatch or rough tiles, it is the usual custom for all the members of the family to live in one room, to take their meals from a dish in common, and to sleep on the earth floor with no furniture save mats. When

the family possesses a cow or a goat or other domestic animal, it is usually kept either in the same room or close alongside. Such "houses" cannot be protected against mosquitoes, nor can they be effectively treated by any of the methods recommended for the destruction of mosquitoes, as the roofs usually have many holes and there are no ceilings.

The Commission, during its tour in Europe, was greatly impressed by these primitive conditions of life in some malarious areas, and it feels strongly that a change for the better in this respect is essential to the success of any antimalarial scheme. It is a subject which should form a prominent item in the work of the Central Advisory Organisation and should be dealt with, wherever possible, by legislation after adequate local enquiry. The principles on which houses should be constructed, so that they may afford as little shelter as possible to mosquitoes, are now well known everywhere, and it ought not to be an insuperable task in Europe to design houses for the poor in accordance with them and to enforce their construction by degrees. At any rate, the Commission is of opinion that continuous efforts in this direction should be given an important place in the antimalarial and general sanitary policy of every country.

In districts where sufficient permanent houses are already in existence, much can be done to make them less favourable to mosquitoes by improving the lighting, by giving freer access to air-currents, by providing ceilings, by white-washing the walls, by doing away with dark corners and recesses and by strict attention to general cleanliness.

On the same subject, the Commission is of opinion that, wherever possible, advantage should be taken of the knowledge that anopheles mosquitoes rest in cowsheds, stables, pigsties and other outhouses in which animals are kept rather than in dwelling-houses. Therefore these buildings should be separate from the dwelling-house and, when possible, should be located between the house and the chief breeding-grounds so as to form a protective cordon. It is essential to the success of this plan that the dwelling-houses should be well lighted, white-washed, airy, dry and clean and that the stables should be relatively dark and damp; continuous occupation by animals is also necessary. It has been found in some countries that low-roofed pigsties which have no window make the best type of protective building. Failing other arrangements, a cordon of rabbit-hutches round a house is often a sufficient protection, provided that they comply with the requirements of being dark and warm and damp.

5. Propaganda and Popular Instruction.

It would be redundant to deal here with the necessity of disseminating popular instruction among the people with the object of making the inhabitants of malarial districts the chief allies of those who are carrying out antimalaria measures. All countries are fully aware of this necessity and, quite apart from lessons in hygiene given in the schools, various methods of propaganda are employed, both oral and

visual, which are capable of making an appeal even to adults. Attempts have been made to link up with travelling dispensaries a service of itinerant lecturers, who travel from village to village instructing the inhabitants, gathered together for this purpose in public places or suitable premises: practical demonstrations are also given. Results of such a method of teaching are still better if the lectures thus given are not exclusively confined to malaria, but treat also of agricultural subjects, such as diseases of cattle, questions of insurance, etc. Work on these lines has already been done in Italy. It is well known that the peasant, and mankind in general, does not worry about such intangible matters as his health; if his confidence and his co-operation are to be gained, it is necessary to interest him by talking of material possessions and giving him advice how to keep and multiply them.

This should be done in simple language and without too much technical detail. The following extract from a report by one of the members of our Commission will serve to emphasise how important it is that any teaching should direct attention primarily to a few simple concrete facts and procedure which the uneducated can understand and appreciate:

"... At the end of August, I visited six malaria patients in one day; the departure of my train prevented my seeing any more. Three children whose blood had been examined harboured *P. vivax*. One of them, who had been ill for several weeks, was very anæmic and had a spleen enlarged four fingers-breadth below the costal margin. When the children complained, the parents were worried, but in the case of quite young babies no notice was taken of even the most evident symptoms. At Franqueveau I came across an example of this. In the first house I visited I learned that ten or more cases of fever occur each year in the village, which has a population of 150 inhabitants. A pregnant woman carrying in her arms a child 5 months old came near to listen to what was said. The child had a waxy tint, transparent ears, pale lips and a distended abdomen. The spleen was to be felt below the costal margin. 'Your child is very pale', I said to her; 'he is sick.' 'Not at all', answered the woman; 'it is his colour'. As I insisted and spoke of taking a drop of blood to examine it, the mother promptly disappeared, thinking only of saving her child from the criminal design that had been proposed."

It is evident that in such communities there must be progress in general education and civilisation before propaganda relating to the prevention of particular diseases can be understood and made effective. This is partly why the Commission has always insisted that the fight against malaria must be waged not as a separate and isolated task but as part of a general social, economic and sanitary campaign directed by an enlightened public health service which is able to obtain assistance from other Government departments and from unofficial agencies and to secure continuity of action and unity of purpose.

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