attendance at a clinic or admission to hospital, where the differential diagnosis can be elucidated without detriment to the patient, and where treatment can be initiated without loss of time.²

In this respect the interrelation that exists at present between area physicians and tuberculosis surgeons is comparable to that which exists between the area physician and general practitioner, and for the same reason—not necessarily because the one has a specialist knowledge compared with the other (it is hoped that that reproach will soon be removed), but because the surgeon has at his command institutional and other facilities which are essential for prompt diagnosis and treatment.

The benefit of closer co-operation or unification would not, however, be entirely on the physician's side. The surgeon would learn to pay more than lip homage to the truth that tuberculosis is one and indivisible, and that bone and joint disease is a secondary manifestation to primary infection elsewhere. He would act more frequently upon the fact that while coincident clinical tuberculosis of these structures is admittedly uncommon, evidence of hilus involvement or of pulmonary disease can be found oftener than is generally realized, and that to treat the diseased joint only is not the whole, and may not even be the most important part, of the treatment, which should be threefold—directed towards the patient, the occult primary lesion, as well as to the obvious secondary manifestation.

It would be more generally realized that in associated pulmonary and non-pulmonary disease premature success in arresting the local lesion (especially if the former is the primary manifestation) may even activate or reactivate the trouble in the lung.³ It would be remembered also that, while the development of secondary deformities is a reproach, caution in attempts at preventing or correcting the primary deformity may not be too high a price to pay for life.

The surgeon's association with the tuberculosis officer would enable him to realize more vividly the economic repercussion in adult patients of his occasionally too conservative methods in some lesions of the lower limb. He would also realize that after-care in tuberculosis, as opposed to orthopaedics, is more than a medical problem, and connotes much more than the correct use of appliances; that failure is not necessarily due to indifference or carelessness, but to those social and economic disabilities that exert such a profound effect upon the prognosis of tuberculosis in any form.

In closing, may I express the hope that my colleagues in the tuberculosis service will realize before it is too late the need for proving themselves equal to the new and fascinating demands that are being made upon their adaptability, intelligence, and clinical knowledge.

REFERENCES.

- ¹ Stone: *Boston Med. and Surg. Journal*, March, 1923, p. 275.
- ² Girdlestone: *Diagnosis and Treatment of Tuberculosis of the Hip*.
- ³ Keller: *Med. Journ. and Record*, February, 1926, p. 170.

DISCUSSION.

Professor J. FRASER (Edinburgh) agreed as to the necessity and value of co-operation. The present-day principles underlying the successful treatment of non-pulmonary tuberculosis could be summed up as: (1) removing the local infection if reasonably possible; (2) stimulating the general resistance of the patient; (3) putting the affected part at rest; (4) attacking directly the infecting organism—by tuberculins, serums, and drugs; and (5) treating the various symptomatic disturbances. So far as treatment directed towards cure of infection was concerned, drugs had been disappointing; a specific chemo-therapeutic agent had still to be discovered. Hope lay in the further co-operation of the pharmacologist and the clinician, the laboratory and the ward. He had not been able to obtain a reasoned opinion on the real value of tuberculin in its therapeutics, its method of administration, and the technique of its dosage. He did not doubt that this treatment had some value. He was more convinced than ever of the correctness of surgical intervention in the presence of certain definite indications, such as tuberculous disease of some groups of cervical glands. This infection remained for some time a local disease, infected from a local point of lymphatic absorp-

tion. There was at present no sure method of arresting the disease by conservative and therapeutic means, and the results of surgical treatment justified this procedure. Rest was the basis of local treatment, and it should be as complete as possible; it encouraged fibrosis, which was nature's method of arresting the tuberculous focus. If the ideal result was to be attained there should be no sudden resumption of function; there the physician and surgeon could usefully co-operate in the constant vigilance of apparently cured cases. He was very sceptical of the success of any scheme for the training of a special type of individual—a physician with a surgeon's training—and preferred the collaboration of a physician interested in tuberculosis as a general disease with local manifestations, and a good general surgeon with orthopaedics as his hobby.

Mr. G. R. GIRDLESTONE (Oxford) thought that in the case of badly deformed patients the criticism should be directed against failure in orthopaedic technique during the period of active disease rather than against any excessive conservatism. The division of potential cripples into tuberculous and non-tuberculous would prove to be neither economical nor efficient. The treatment of tuberculous bones was not merely an appendage to orthopaedics. A recent census of the Wingfield Orthopaedic Hospital had shown that of the 134 cripples and potential cripples well over two-thirds were tuberculous. Adolescents and adults presented a much more serious problem than children. To deal with adult tuberculosis was difficult; the best operative facilities and a highly trained surgical team were necessary.

PROBLEMS OF MALARIA PROPHYLAXIS.

CONCLUSIONS OF THE MALARIA COMMISSION OF THE LEAGUE OF NATIONS.*

BY

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THE thirtieth anniversary of the discovery by Sir Ronald Ross that anopheles mosquitos are hosts and carriers of the malaria parasite falls within a few days of this year's meeting of the British Medical Association. Since the discovery, many antimalarial campaigns based on its teaching have been undertaken in various parts of the world. It seems appropriate, in a discussion on the prophylaxis of malaria at this meeting of the Tropical Section of the Association, to consider what practical conclusions can be drawn from the results of those campaigns, and what general recommendations or suggestions can be made as to the antimalarial measures which appear, from the experience gained, to be most suitable in different circumstances and conditions at the present time.

It happens that, as *rapporteur* to the Malaria Commission of the League of Nations, I have recently assisted in drawing up the Commission's provisional conclusions on that subject, and perhaps those conclusions may serve as a basis for the present discussion. The Commission, as everyone knows, is an international group of expert malariologists and public health officers who were appointed by the Health Committee of the League of Nations in May, 1923, with the primary object of pooling experience in order to establish what antimalarial measures are most appropriate in certain European countries which have little money for the purpose, either because of general want of resources or for the reason that the funds available must be used in accordance with the relative importance of malaria as a cause of sickness and death in comparison with the importance of other diseases and conditions which affect the public health. This financial limitation adds greatly to the interest of the subject, but also makes the task of giving advice more difficult. The Commission has studied the problem in various ways, but chiefly by undertaking collective study

* The opening paper of a discussion in the Section of Tropical Diseases at the Annual Meeting of the British Medical Association, Edinburgh, 1927. Dr. Andrew Balfour, President of the Section, was in the chair.

tours in malarious regions of Europe and neighbouring countries, where an endeavour has been made for some years to deal with malaria in the light of existing 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 judgement 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." It is believed that these 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 problems of malaria prophylaxis studied on the spot.

With this preliminary explanation I propose now to bring to your notice some of the conclusions referred to. In the time at my disposal I must limit myself to those which seem to be of most importance, and I can only summarize very briefly the information and reasons on which the conclusions are based. For further details I would ask those who will take part in the discussion to consult the printed report¹ which has been distributed.

1. One of the first and most important conclusions stated by the Commission is that at the present time, in the vast majority of the numerous regions where malaria prevails, antimalarial measures should be limited to an endeavour to reduce the severity and, so far as may be possible by the same measures, the incidence of the disease. They are of opinion that measures designed to accomplish more than that (and particularly measures aiming at "eradication") are not a wise proposition, and can be justified only in very exceptional circumstances. As regards this conclusion it is realized, of course, that the limited aim is not entirely satisfactory—that, as Professor Gosio² 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 reawakening 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. The Commission points out that 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, Holland, and Denmark, which, geographically, financially, and in every other respect, are much more favourably situated for obtaining success in the "eradication" of malaria than is any other affected country.

2. A second conclusion of general interest is that it is not always necessary to deal with malaria by a method arising directly out of the knowledge that the disease is transmitted by mosquitos. In this connexion the Commission cites various regions and localities in which, in the past, malaria was robbed of its importance as a cause of sickness and death without any knowledge of the etiology of the disease, and without any reduction of anopheles having occurred, as well as various localities in which the same result is being brought about to-day. The Commission observes that, since the advent of the knowledge that malaria is transmitted by mosquitos, 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 an attempt being made to reduce mosquitos. Therefore they are of opinion that in certain circumstances it is very desirable for antimalarial workers to throw off the tyranny resulting from the general belief that because

mosquitos carry malaria their elimination should be the chief object of concern and expenditure.

3. A result of the Commission's inquiries which is closely related to the conclusion just stated is the recognition that there is not yet any single 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 has already been 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. 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. Malaria control is a *local problem* to a much greater degree than is the case with the control of other infectious diseases. Therefore in every country, and very largely in every area, there must be preliminary examination to ascertain the local conditions before deciding what method of malaria control is best adapted to them.

4. Omitting the Commission's suggestions for ascertaining the amount and character of malaria in the locality and for ensuring that a continuous record on that subject will be kept, I turn now to the actual methods of controlling malaria which the Commission considers it desirable to recommend. First, I must say a word on the vexed question whether it is better to utilize several of the known antimalarial methods at the same time, or to concentrate all available effort on one carefully selected method. This is a specific question which was put to the Commission by the public health authorities of several countries visited. The answer given was that, in the opinion of the Commission, it is better 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 until the desired end is attained.

5. As regards the particular methods of malaria control to be adopted in any country or area, the Commission considers that there should be considerable freedom of choice. It deprecates the adoption of measures in a country on the ground that they have been successful in another, where, perhaps, circumstances and conditions are quite different. Each country, and to a more limited extent each locality, must "work out its own salvation" in this matter, and the suggestion is made that countries and localities should do so in greater degree than has hitherto been the case. On this point the Commission states that in some of the countries which they visited there was evidence of an endeavour to follow too slavishly the antimalarial policy adopted in some other countries without ascertaining its suitability to the local circumstances and conditions, and in some instances without interpreting correctly its purpose and without giving full weight to the considerations which determined its adoption. As an example, they note that, in the world generally, there is a widespread misapprehension regarding Italian antimalarial methods, and that, in some countries, money, energy, and time have been misapplied in the false belief that the Italian example was being followed.

6. It is usual to classify antimalarial measures as direct and indirect. The Commission adopts that classification but defines the terms more strictly than is usual. In the Commission's view there are only two direct antimalarial measures—namely, killing the malaria parasite in man, and killing the malaria parasite in infected mosquitos. In comparison with these two measures, anything else that can be done to control malaria is necessarily indirect. For example, no one who has made a particular study of antimalarial campaigns can doubt that general antilarval measures in the field, as usually carried out in practice, are an indirect method of trying to deal with human malaria—that this line of action is concerned with something which is remote from the particular knowledge of the etiology and epidemiology of malaria which we are fortunate enough to possess to-day.

¹ *Principes et méthodes de lutte antipaludique en Europe*. Deuxième rapport d'ensemble de la Commission du Paludisme. Published by the League of Nations at Geneva as Document C.H./Malaria/73, 1927.

² *International Journal of Public Health*, vol. i, No. 2, September, 1920, page 178.

7. Adopting this restricted definition of direct and indirect means of controlling malaria, the Commission suggests that in every malarious locality certain direct methods, which they term "primary measures" and which are concerned with malaria-infected individuals and the interior of the houses in which they live, are indispensable. As regards measures relating to malaria-infected individuals, the Commission considers 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 cases of the disease. In rural areas and localities under primitive conditions the State must make these arrangements, according to the means available, but at least an efficient arrangement for the gratuitous supply and effective distribution of quinine is indispensable. The Commission considers that in organized communities satisfactory diagnosis as well as treatment should be arranged for, and suggests that, wherever possible, the services of private medical practitioners already established in the locality should be utilized and paid for by the State for this work.

8. The Commission recognizes that no useful purpose would be served by magnifying unduly the results that may be obtained by those arrangements for ensuring early discovery and effective treatment of cases and carriers. They have ascertained that, in the countries which they visited, nothing is more striking than the mild character of the manifestations of malaria in a locality where there are practising medical men who are fully equipped as to the diagnosis and treatment of the disease, as compared with the severe and often fatal manifestations in a similar locality which is without that expert medical aid; but they realize also that the good results are more apparent in the reduction of severity and mortality than in the reduction of incidence. This is not surprising in view of the knowledge that quinine is not an effective prophylactic for new infections or relapses, and in view of the difficulty of attaining the "minimal effective standard" in the execution of the measures. Regular inspection of school children and of organized classes of the adult population must be part of the system, and an endeavour must be made to follow up all patients in their homes. The officer who is in charge of the measures will need assistants, especially for house-to-house inquiries. In some countries duly qualified female "health visitors" who have received the necessary training may be usefully employed in this work. In small districts the office can be combined with kindred health duties, such as school nurse, tuberculosis visitor, etc.

9. The other "primary measure" which the Commission recommends is the systematic killing of adult female anopheles mosquitos which can be found in the interior of dwelling-houses. It would take too long to describe in this paper the epidemiological and experimental grounds on which the Commission has arrived at the conclusion that this measure, if it could be effectively carried out, would have very remarkable results. As to the manner in which it should be done, the Commission considers that, wherever it may be practicable to persuade householders themselves to undertake it, that arrangement is preferable to an organized arrangement by the authorities for killing mosquitos in houses by periodic fumigation or other means. In the Commission's view the measure should be regarded as an important item in the sanitary education of the inhabitants of malarious areas. The Commission thinks that it should be a duty of the medical men and assistants who visit households to explain to the occupants how malaria is contracted and spread, and to demonstrate to them how to find and kill the adult anopheles mosquitos which are present in the house. It should be explained also how to make the house inhospitable to anopheles by removing cobwebs and dirt, clearing out recesses and dark corners, whitewashing, arranging for more light and air, and other simple means suitable to the particular locality and type of dwelling. Female health visitors and health nurses, who have been properly instructed and trained, can do a great deal of good by instructing householders on these matters. The aim should be to teach the inhabitants to have the same dislike and objection to the presence of gorged and sluggish mosquitos in their houses as cultured people already have to the presence of bed-bugs, lice, and

other harmful and disgusting vermin. If this educational propaganda is successful, it may be hoped that in time the killing of anopheles mosquitos in houses will become a routine part of the housewife's daily task, just as much as other more showy, but less useful, items of sweeping, brushing, and cleaning. The measure has the advantage of costing nothing. It is known, from the results of experimental laboratory work, that one infected mosquito can give malaria to as many as thirty persons; therefore it is difficult to praise too highly any person who succeeds in killing even one of these infected insects.

10. As regards these two primary or direct measures, the Commission is well aware that there is nothing particularly new or original about the idea of endeavouring to combat malaria in the houses of the people themselves rather than in the general environment. They realize also that it is often a difficult matter to get into the houses of the people, to examine all the occupants, to treat those who are found to be infected, and to teach them to catch and kill the mosquitos which may be hidden in inaccessible places. But no royal road or short cut to the prevention of malaria has yet been found. Therefore, in the opinion of the Commission, it is necessary for the present to continue to endeavour to combat the disease itself at its sources in the human and insect hosts.

11. The Commission has carefully considered in what circumstances any other measures than those dealt with should be recommended, and what those measures should be. On this subject reference is made in the first place to the problem of what should be done in 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 antimalarial measures in a manner which enables them to be brought to the "minimal effective standard." Except the free distribution of quinine, no effective antimalarial measure can be applied in these regions 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, and very few things have a greater effect in reducing malaria than the stability of the population which comes when a place where the conditions of life are tolerable 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. 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 reclaimed land is worked by hired labourers who receive only a small daily or weekly 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 (and even in some parts of Europe) highly cultivated areas where these conditions obtain continue to be among the most malarious in the world. This indicates that the actual measures necessary for agricultural reclamation or improvement of the soil (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. In this connexion the Commission notes that the changed conditions of life just referred to, and the subsequent reduction of malarial incidence and severity, have often been brought about in the absence of any measures intentionally based on modern knowledge of the etiology and epidemiology of malaria, and they illustrate this truth by describing a small scheme of "bonification" without antilarval or other antimosquito methods" which was demonstrated to them during their tour in Sicily. The

place is now an example of "anophelism without malaria." For these and other reasons the conclusion to which the Commission has come is that, of all indirect methods of reducing malaria, most importance must be attached to general schemes which aim at improving the economic and social conditions of the people and their general well-being and standard of life.

12. The Commission has ascertained that almost everywhere in the countries which they visited terms like "bonification," "assainissement," etc., are misunderstood and misinterpreted except in the particular countries where the terms originated. They find also that in some countries the false belief still prevails that the actual measures which are necessary for making land more suitable for cultivation and more fertile are the means by which the reduction of malaria is brought about. In particular the drainage which is necessary for agricultural land reclamation is often credited with being the chief agent concerned. It is assumed that the drainage acts by reducing the breeding places of anopheles mosquitos. In support of this belief it is often said that even the ancients knew that drainage reduces malaria, and that this antimalarial action of drainage was explained when the role of the mosquito was discovered. One result of the belief is that some countries have adopted drainage on a large scale as their first line of attack against malaria. The Commission does not desire to limit the output of public works of proved utility, but, having regard to the financial aspect of its mandate, they 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 antimosquito measure. For it is now known, unquestionably, 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 know also 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 may be of a kind which actually favours the incidence and spread of malaria. Therefore what we learn from the Italian example (and equally from the older and more extensive Dutch examples) is that we must not take each of the actual bonification measures (such as drainage) separately, and utilize it as a single antimalarial measure in another country. If "bonification" is the antimalarial measure which we desire to employ, it must be understood to mean a many-sided process. Our scheme for "bonification" must be comprehensive; it must include particularly the arrangements for settling the people permanently, for raising their standard of life, for better housing, better education and general welfare, for making scattered houses easy of access by good roads and canals, for better medical attendance, and, in general, for all the social and public health improvements which are an integral part of a complete bonification scheme in Holland, Italy, and other countries where such schemes have been successful. As I have already mentioned, the essential importance of these items in the scheme is brought home to us by instances in which, 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 connexion with schemes of agricultural land reclamation consists particularly, not in trying to enforce antilarval measures during the progress and after the completion of the work, but in seeing that the agricultural improvement has been

accompanied and followed by an equal improvement in the conditions of life of all the people who inhabit the reclaimed area. This change in the conditions of life of the inhabitants is the most important antimalarial factor in bonification schemes.

13. The Commission deals in separate chapters of the report with various other problems of malaria prophylaxis, particularly with the organization necessary for the work, and with different antimalarial and antimosquito methods—such as quinine treatment and prophylaxis, larvicides, the applicability of antilarval measures, housing as an antimalarial measure, and propaganda. From lack of time I cannot refer to these subjects in the present paper.

14. But there remains a subject which I must not omit to mention. For various reasons which are given in the report, the Commission is unanimously of opinion that the scientific study of malaria must be continuously pursued in the laboratory and the field. They consider that the best prospect of discovering a method of dealing with malaria which can be applied in affected localities with the small amount of money and means that can usually be provided, lies in renewed activity in the study of the disease in all its aspects. Therefore they suggest that each Government which has not already done so should establish a small central permanent organization of selected workers who would devote their whole time to malaria research. In this connexion they suggest (a) the establishment in one or two malarious areas of each country of an "observational station" where certain routine epidemiological inquiries should be made at regular short intervals for several years; (b) the establishment in each country where malaria is used therapeutically of a laboratory for the cultivation of a pure strain of malaria in mosquitos, to be used, under expert supervision, for the purposes of the treatment. The establishment of such a laboratory in a properly organized hospital automatically 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 anopheles and the persistence of the infective virus in those insects. It also enables a satisfactory study to be made of the action of quinine and other drugs which are used for the treatment of malaria. Examples of each of these institutions are described in the report, as well as an example of a station for "experimental malaria control."

DISCUSSION.

Lieut.-Colonel E. D. W. GREIG, with the aid of lantern slides, outlined the points bearing on malaria prophylaxis which emerged from his study of eighteen cases of intentionally induced malaria. He divided his cases, as regards susceptibility, into (1) refractory, and (2) ordinarily susceptible; the difference was very clearly observable, but in this series there were none which could be classed as very susceptible. He recalled that James had ascribed resistance to infection to some property of the blood or tissues of the recipient and not to an insufficient dose of sporozoites; and he discussed the views of Christophers as to immunity against malaria, expressing the opinion that some test which would differentiate good and bad infectors of mosquitos would be of service for prophylaxis. In his cases the period of latency after infection varied from six to twenty days. Sexual forms of the parasite did not appear until six or seven days after the disease declared itself, so that, allowing three days, which James held to be necessary before gametocytes could infect mosquitos, a patient in a primary attack would not be capable of infecting mosquitos until about ten days further had elapsed. Such intentional infections as those described afforded opportunity for study of the parasitocidal power of drugs.

Dr. L. W. HACKETT (Rome) described the use of Paris green in the antilarval measures undertaken by the International Health Board in Italy.

Dr. DRBOHLAV (Prague) gave an outline of the conditions of occurrence of malaria and the methods used against the disease in Czechoslovakia.

Professor E. MARTINI (Hamburg) feared that the report of the Malaria Commission would be interpreted by

Governments as meaning that by supplying free quinine they could discharge their whole duty regarding malaria. He leaned towards the preventive methods described by Dr. Hackett, but he agreed with Colonel James that there was perhaps too great a tendency to adopt mechanically for every country a measure which had anywhere produced good results. For malaria prevention there was no fixed rule; each district required individual consideration. At a place he visited near Astrakhan prophylactic quinine was the only measure applicable to local circumstances. Angora was nearly abandoned as the Turkish capital on account of malaria; quinine alone was ineffective, but when this was coupled with well considered drainage the disease was controlled, and anopheles became rare. In Anatolia it was the experience of local doctors that apparent resistance to quinine often disappeared when an ascariis infection had been eradicated. In his view the cases of so-called spring malaria were nearly always relapses of autumn infections. In Turkey he had acted on this belief as regards his personal prophylactic measures, omitting all precautions up to the end of May even in districts where malaria was endemic, and he had no reason to regret his action.

Dr. P. H. MANSON-BAHR (London) gave his experience with plasmochin and its compound with quinine in the treatment of malaria. He considered that this new drug, from its action on the gametocytes of tertian and subtertian parasites, would have considerable bearing on the prophylaxis of malaria in the future. All who had used it were agreed as to the phenomenal rapidity of its action upon the crescents of subtertian malaria, which disappeared from the circulation within three days after the exhibition of 0.24 gram of plasmochin. He quoted a striking illustrative case in which the compound was successfully employed after full doses of quinine had proved unavailing, and in which disintegration of the gametocytes was observed microscopically. The drug was well tolerated, and if it were possible to treat a malaria-stricken population daily with small doses, the transmission of infection through the anopheles would soon cease from destruction in the blood stream of the gametocytes. Under the present system of quinine prophylaxis the formation of gametocytes in peripheral blood was rather encouraged than the reverse.

Colonel S. P. JAMES briefly replied to the discussion.

ASTHMA AND TUBERCULOSIS IN RELATION TO "CLIMATE ALLERGENS."*

BY

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WE began about 1919 to investigate the action of various allergens on asthmatics, and found that only about 15 per cent. of our cases could be classified as supersensitive to the four groups of allergens known at that time—namely, pollens of various grasses and flowers, epidermal products, foodstuffs, and bacterial vaccines. We had, however, also noted those asthmatics who could not be classed under one of the four headings mentioned, but had yet to be considered supersensitive, although we were unable to identify the causative allergens. Among other things we found that more than 90 per cent. of asthmatics give a positive skin reaction to an extract of dandruff of human skin, whereas normal persons only react to such an extract in exceptional cases, proving that the skin at least of these patients is supersensitive.† Thus about 80 per cent. of our asthmatics suffered from some form of allergy, but the causative agent of their attacks was unknown.

In our endeavours to find the cause of the attacks in these 80 per cent. we utilized the known fact that the environment of the asthmatic patient is, as a rule, of primary importance in determining the intensity and frequency of his attacks. It is known that most asthmatics are free from attacks at high altitudes. Turban and Spengler, who have published statistics for Davos (about 5,000 feet), found that 68 per cent. of all asthmatics going to Davos become free from attacks within two or three days, that 25 per cent. improve considerably within two or three weeks, and that only 7 per cent. remain uninfluenced. It is also known that residence at the seaside or a sea voyage often improves the condition of asthmatics. This can be observed also in a flat country like Holland, where the health of asthmatics varies greatly in different regions. The character of the soil is also of great importance, sandy soil and a low level ground-water offering much better conditions for asthmatics than clay and peat soil and a high level ground-water. Recently these observations have been confirmed completely for Ost Preussen by Tiefensee, working in the clinic of Matthes in Königsberg, who found that from 1,100 asthmatics living in East Prussia, more than 90 per cent. had their houses on clay, moor, or peat soil, and only a very small number on sandy soil.

These observations exclude the known factors of climate, barometric pressure, temperature, humidity of the air, etc., as direct causes for the incidence of asthma, and make it clear that the conditions of the soil are of paramount importance. As will be shown later, humidity may play an important part in making a place "bad" for asthmatics, but it does this by facilitating the growth of certain micro-organisms which constitute the determining causes of the asthmatic condition in different regions.

Mainly on the basis of such observations we formulated the hypothesis that the difference between various climates is due to certain allergens in the air, the presence of which is dependent on factors of climate; they may be called climate allergens. These climate allergens must be considered as the principal causes of asthma in all flat countries with a high humidity and a moist soil.

In my monograph on allergic diseases¹ I fully described the results of experiments made to prove the validity of this hypothesis. Among other things it was shown that outside air in a place known as very bad for asthma (Rotterdam) contains water-soluble colloidal substances, which on injection into sensitive persons induce attacks of asthma, and that dust from the floors of private houses gathered in regions where asthma is very frequent contains many more allergens than dust from places which are good for asthma. In Switzerland there is a gradual diminution in the allergen content of house dust corresponding to the height of the place.

A number of allergens which may be considered representatives of groups of climate allergens have been determined. The first examples were found by us as the result of reading a paper by Ancona, who observed an epidemic of asthma in an Italian village, the cause of which was traced to a parasite occurring in grain (*Pediculoides ventricosus*) which formed allergens, to which most of the people who frequently handled this grain became sensitive. We then found that other insects—that is, the common mites which so frequently occur in grain, hay, and straw and packing material—form allergens which may be the exciting cause of asthma in about 20 per cent. of our cases. Later we found that common moulds, like *Aspergillus fumigatus*, and other aspergilli, penicillium, mucor, etc.—moulds that are abundant in moist and damp houses—form allergens to which more than 50 per cent. of our asthmatics are sensitive.

Since these allergens formed by moulds are to be considered as typical representatives of a group of allergens which is certainly most important for the entire problem of allergy, we will have to study their properties in detail.

Properties of Mould Allergens.

1. Mould allergens are soluble in water and are of colloidal nature; they are not destroyed by heating to 120° C., nor by acid, alkali, or formaldehyde. They are

* This article is a synopsis of a series of three advanced lectures given at the London University in February, 1927.

† These results have been confirmed by Professor Rost in Freiburg (Germany).