Section of Epidemiology and State Medicine.

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The Disappearance of Malaria from England.

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Abstract.—*Part I.*—An attempt to interpret the available historical and statistical evidence of the distribution, incidence and character of malaria, from the seventeenth century onwards, and to ascertain to what degree the belief is justified that the disease was formerly prevalent and severe, but that within the last fifty years its incidence and fatality have declined continuously until, at the present day, it is usually said to have "disappeared" from this country.

Part II is an examination of the causes of the decline of malarial incidence and severity during the period under consideration. Each of the factors or circumstances which from time to time has been thought to be concerned in the reduction is discussed in the light of the results of recent inquiries in the field and in the laboratory; and some factors are considered which have not received attention previously. A selection from the results of laboratory work in connection with the therapeutic use of malaria in general paralysis is included, where applicable, in the commentary.

It is universally believed that a long time ago malaria was prevalent and severe in various parts of England, but that within the last half century or so the disease has undergone a progressive and striking diminution. This reduction came about before the era of conscious preventive effort, and no satisfactory explanation of the remarkable change has yet been given. It is widely felt that accurate knowledge of the manner in which the improvement came about would give valuable indications for the prosecution of anti-malarial measures in other countries.

Obviously our first task is to decide to what degree the general belief as to former prevalence and later disappearance is justified. The history of the incidence of malaria in England prior to the era of medical statistics is chiefly of various forms of "ague" which swept over the whole country from time to time in epidemic form. But we learn from Creighton [1] that originally the term "ague," which at present is the common English synonym for malarial fever, did not mean a paroxysmal or intermittent fever, or any other illness arising from the endemic conditions now termed "malarial." It meant simply *acuta*, "the adjective of *febris acuta* made into a substantive," and was applied to any acute fever and most commonly to a continued fever. We are warned particularly against regarding the "epidemic agues," the "hot agues," the "new agues," and the "quartan agues" which were widely prevalent all over England in different years of the seventeenth and earlier centuries, as having any relation to the endemic fevers of malarious districts. In Ireland the term was applied, until a comparatively recent period, to the indigenous typhus of that country. The distinguishing character of the epidemic

fevers which prevailed during what was called the "intermittent constitution" of the period 1677 to 1781, was their obstinate resistance to treatment by Peruvian bark. This character alone, as we know now, is sufficient evidence that they were not malarial. In the midst of the great "constitution" of these epidemic fevers or "epidemic agues" as they were called, the country was swept by waves of catarrhal fevers, now, for the most part, identified as "influenza," and before the end of the century there were epidemics of what were afterwards clearly recognized as spotted typhus, enteric fever and relapsing fever. The trial of cinchona bark on a large scale during the great epidemic period of "agues" from 1780 to 1786 was of outstanding importance in the differentiation of true malaria. It gradually came to be understood that the only types of "ague" for which cinchona bark is a specific were limited in distribution to certain well-defined (usually marshy) areas and that, in all probability, this had always been the case. In comparison with England as a whole, these areas were few in number and small in extent, and we can justifiably conclude that this new epidemiological knowledge and the subsequent differentiation of typhus, relapsing fever and enteric fever, brought a realization that true malaria in England had always been less prevalent and less widespread than had been supposed. Sydenham, even as early as 1676, seems partially to have realized this, for it is said that he did not regard the "agues of the marsh" as being of the same nature and origin as the agueish or intermittent fevers which occurred in epidemics all over England. He seems to have accounted the "agues of the marsh" as being relatively unimportant, for, according to Creighton, his writings contain only one specific reference to them. On the other hand, Professor Nuttall [2], in 1901, contended that the epidemics of which Sydenham and others wrote may well have been true instances of malarial fever. His contention was based on the supposition that these "epidemic agues" were cases of malignant tertian (æstivo-autumnal or subtertian) malaria, in which the fever is often irregularly continuous and in which complications similar to those described in Sydenham's "epidemic agues" commonly occur.

The chief difficulty in accepting Professor Nuttall's view is that at the present time the malignant tertian parasite does not seem able to exist or to spread indigenously under natural conditions in this country. In 1917 the arrival of large numbers of soldiers whose blood contained numerous "crescents," rendered conditions in some potentially malarious areas in England unprecedentedly favourable for the transmission of malignant tertian malaria, but this type of the disease failed entirely to spread, although the benign tertian type did so extensively. It is also worthy of note that in laboratory experiments connected with the treatment of general paralysis by malaria, we have endeavoured on several occasions to maintain a strain of malignant tertian malaria but without success; human infection with this species of the parasite seems to die out rapidly in the English climate, and up to the present we have not succeeded in transmitting it to mosquitoes.

From these considerations, and after puzzling over many details, I have formed the impression that true indigenous malaria was never widely distributed in England, and I am doubtful if it ever spread far from the few localities near the sea-coast which are now known to be its endemic foci in this country. In effect, this impression is the same as the conclusion stated by Creighton in 1894: "The malarious parts of England have been tolerably well defined at all times; and at all times the greater part of the country was as little malarious as it is now." In 1921 Lieut.-Colonel C. A. Gill, I.M.S. [3], expressed his conclusions that the distribution of the disease in this country has not undergone any material change within historical times.

Coming now to the era of medical statistics, it is known that the first half of the nineteenth century was a period of great advance in the differentiation of fevers in this country. In particular, between 1840 and 1850, as Creighton says, "the three grand types of fever" existing during that period in Britain, namely,

spotted typhus, enteric fever and relapsing fever, were at length so clearly distinguished, defined and described, " that no one remained in doubt or confusion." Doubtless the " statistical " incidence of ague diminished at a rate corresponding to the advance and spread of knowledge in the art of diagnosing these diseases, and we know that this advance was speedy when, between 1830 and 1840, quinine began to displace cinchona bark in general practice in this country. By about the middle of the nineteenth century the art of clinical diagnosis had probably reached a stage at which an experienced observer could give a moderately accurate account of the distribution of endemic malaria in the country as a whole. In 1863 Dr. George Whitley [4], under instructions from the Privy Council, compiled such an account under the title, " The Quantity of Ague and other Malarial Diseases now Prevailing in the Principal Marsh Districts of England." The best available evidence of the general correctness of Dr. Whitley's list of places where malaria was known to be endemic is its close correspondence to the distribution of places in which cases of locally contracted malaria are known to have arisen during the ten years ending with 1926. This is shown in the following maps :—

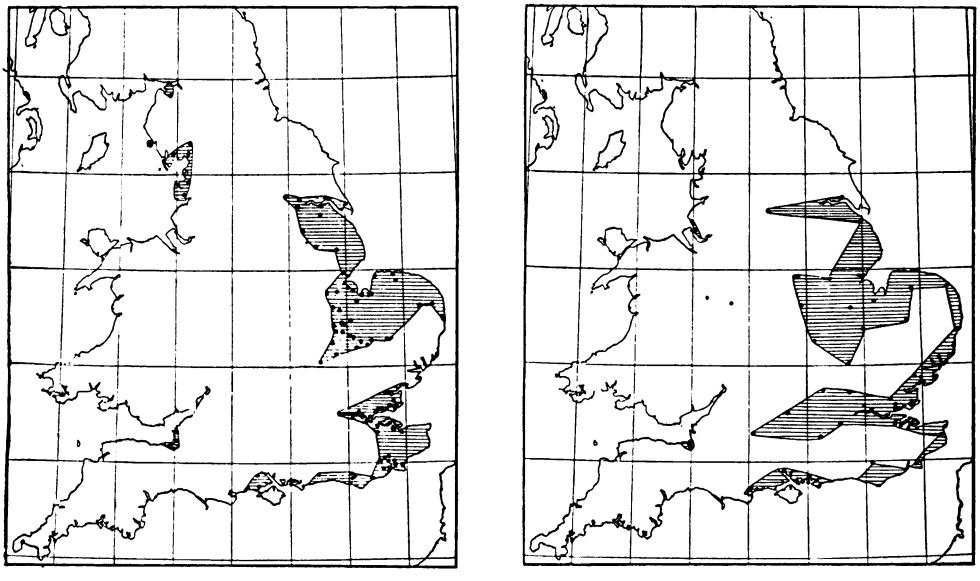


FIG. 1.—Geographical distribution of indigenous malaria.

About 1860. Between 1917 and 1926.

It is as surprising as it is important that the geographical distribution of the areas in England which are still " potentially malarious "—that is, still liable to the occurrence of locally contracted cases—is practically the same as it was seventy years ago. It means that these areas in general have not been converted from " malarious areas " into " non-malarious areas." This was proved in 1916 and subsequent years when soldiers invalided on account of malaria contracted in Macedonia and other oversea countries, began to return to England. Some of them were located in rural towns and villages in which malaria used to be a common disease, and the result was that within a few weeks there was a sharp and widespread

epidemic of new cases among the local inhabitants. Evidently in these districts all the factors in the soil and environment necessary for the spread of malaria were already present and, in order to cause an outbreak, all that was required was to add a little fuel to the smouldering embers by introducing relapsing cases of the disease.

But while the area of south-east England marked on the map, when considered as a whole, is, potentially, not less malarious than it used to be, we need not doubt that there has occurred in it a significant reduction (and in some years a complete cessation) of observed cases of the disease, and in particular a cessation of severe and fatal cases. After the epidemic year of 1917, when 235 indigenous cases came to notice, the number of locally contracted cases discovered fell rapidly until, in recent years, the number has usually varied between two and six. For a longer period the only available evidence of the decline or "disappearance" which we are considering is provided by the mortality statistics compiled by the Registrar-General for England and Wales. The following diagram shows the general trend of the figures since 1847 :—

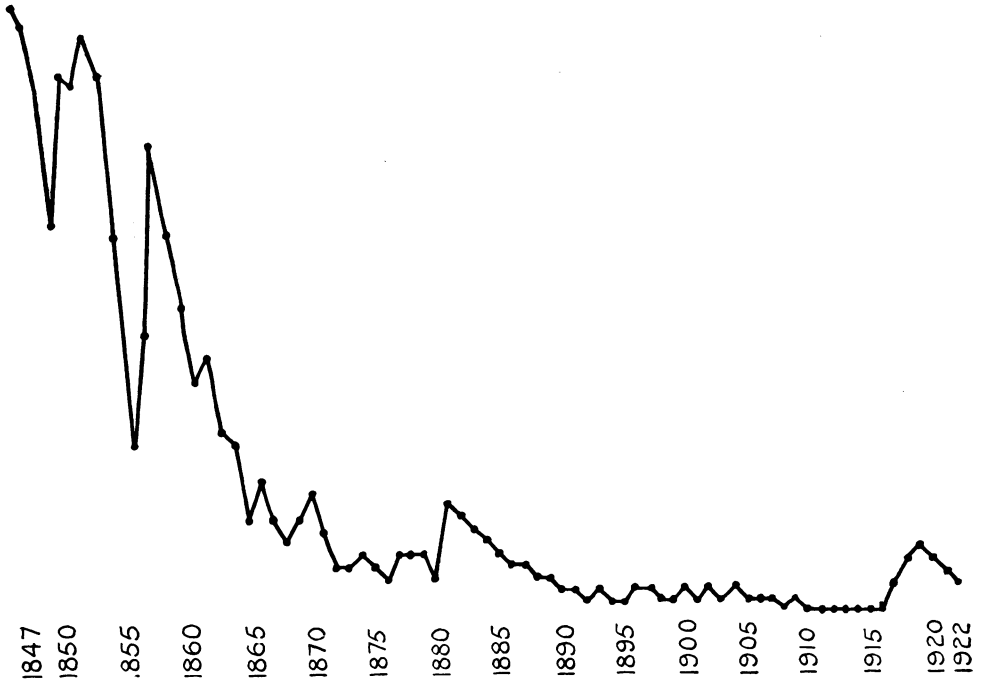


FIG. 2.—Mortality from malaria in England and Wales per 1,000 of population.

The following points should be borne in mind when drawing conclusions from this chart: (1) Two causes of death, namely, "remittent fever" and "ague," are grouped as "malarial diseases" in the classification in use from 1847 to 1900; (2) "remittent fever," in the early years of the statement, signified, as a rule, relapsing fever, and in later years enteric fever; (3) throughout the period a large proportion of the deaths correctly ascribed to malaria were those of soldiers, sailors and others, who contracted the disease abroad; (4) from inquiries made into the deaths registered as due to malaria since the war it appears that, even at the present day, there is a large error in the figures of mortality attributed to malaria.

Notwithstanding the corrections which these points necessitate, I think that during perhaps fifty years of the period, an appreciable number of the cases of indigenous malaria occurring in England were fatal. There are two reasons for this conclusion: (1) That among over 500 cases of indigenous malaria into which we have inquired during the last twelve years, some would certainly have terminated fatally if quinine were now so difficult to obtain as it must have been for the poor in England before about the last quarter of the nineteenth century; (2) that Dr. Stevenson, Advising Medical Officer in the Registrar-General's Department [5], has shown clearly, by analysis of the malaria deaths of both sexes, that up to about 1890 there were fatal cases of indigenous malaria in the endemic areas of the disease in Kent and Essex.

Summary of Part I.

(1) General belief that indigenous malaria was formerly prevalent in England, and has almost entirely disappeared, is justified, but requires modification. Distribution of the disease has always been peculiarly limited, and no material change in this distribution has occurred at any rate within the last seventy or more years. (2) The disease was more prevalent and probably more severe and protracted than it is to-day and an appreciable number of cases were fatal, but it is doubtful if we are entitled (in order to explain the greater severity and fatality) to assume the endemic existence and spread of the malignant tertian parasite. (3) In great part, the change that has occurred is of the nature of a "clinical disappearance" rather than of a disappearance of the causes of endemicity. Except in London and other large towns, we cannot find in England any locality which, having been "malarious" in former times, has entirely lost its malarious "potentiality." What has happened is that, although the malarious character of the area has not been changed, the sickness and mortality caused by malaria in it have been effectively reduced, and (except in circumstances such as occurred from 1916 to 1918) kept in check by various factors which are continuously in operation. Thus the disease has come finally to be of little or no importance as a cause of sickness and death.

Part II.

Agreeing with the general belief that there has been a reduction, amounting almost to "disappearance," of malaria from England, our next task is to endeavour to ascertain the circumstances or factors to which this change was due. When Sir Ronald Ross discovered the mosquito-cycle of the malaria parasite, it was believed that this provided a complete explanation of the disappearance of malaria from England and some other European countries. It had always been thought that "residence in marshy districts" caused malaria, and that "drainage of the marshes" reduced it. As a result of the discovery it was at once assumed that the explanation was now clear; the marshes were breeding-places of anopheles mosquitoes, and by draining them one eradicated these breeding-grounds and so caused the mosquitoes (and therefore the malaria) to disappear. Unfortunately it was soon found that, whatever drainage may have been done in the endemic areas within historical times, the particular species of anopheles which carries malaria in England (*maculipennis*) was still prevalent there, as well as in many other rural districts in which no spread of malaria occurred. Indeed, it was found that the abundance of these insects in nearly every rural district of the country is greater than in many exceedingly malarious places in the tropics. Therefore it had to be admitted that any disappearance or reduction of malaria which may have occurred in rural districts in England was not due to a disappearance or reduction of the anopheles mosquito which carries the disease. For the same reason we had

to admit that if the steady decline of malarial diseases in marshy districts in England was due to improved drainage (as was often affirmed), this drainage must have acted in some other manner than by reducing the prevalence of anopheles mosquitoes. Evidently the problem was much more complex than had been anticipated; research into other factors than anopheles was necessary, and we were not able to take our stand outside the maze of debatable problems on their relative influence. That was more than thirty years ago, and the position is not greatly changed to-day; we are still in the stage of studying, as intensively as possible, each of many factors and of trying to estimate their relative shares in bringing about the diminution of the disease.

I propose now to summarize, briefly, the experience in England relative to each of the factors which from time to time has been thought to have some influence in this matter.

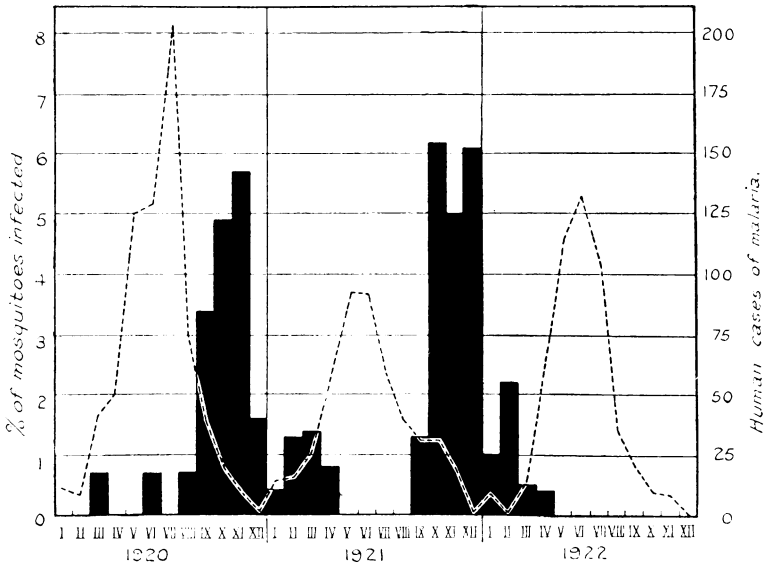


FIG. 3 (after Swellengrebel).—Dotted line equals seasonal incidence of malaria in man (clinical cases). Black shading equals seasonal incidence of malaria in anopheles (maculipennis). (Professor Swellengrebel's figures for villages near Amsterdam.)

(1) *Factors Relating to the Parasite.*—An outstanding problem connected with the malaria parasite in its human host is whether or not the malignant tertian parasite (*P. falciparum*) and the quartan parasite (*P. malariæ*) ever existed and spread indigenously in this country but are now unable to do so. Neither of these species has been found among more than 500 indigenous cases of malaria contracted from the bites of mosquitoes, which were inquired into during and since the Great War, and at the present time local malaria in England seems to be due entirely to the benign tertian parasite (*P. vivax*). I have already mentioned that the absence of *P. falciparum* is not due to a lack of importation. In this connection it has been suggested that climate may have an influence on the malaria parasite during its life in the human host, in addition to its known influence on the parasite in the insect host. It has been said that when persons infected with the malignant tertian

parasite (*P. falciparum*) pass a winter in England or other cold climate, this species quickly dies out and they become free from the infection. The chief epidemiological evidence in favour of the view that climate influences the parasite in its human host is the finding that the seasonal incidence of clinical malaria differs for each species of parasite and cannot be correlated with the seasonal incidence of the infection in anopheles mosquitoes. In Northern Europe the seasonal incidence of malaria in mosquitoes is a phenomenon of autumn and winter, while the seasonal incidence of clinical malaria in man is a phenomenon of spring and early summer. This is shown in the diagram of Professor Swellengrebel's [6] findings in villages near Amsterdam (fig. 3, p. 6).

In England, in the old days, malaria was always a phenomenon of the early months of the year, as is evidenced by the common form of greeting in the nineteenth century: " Have you had your ague this spring ? " The spring in England is a period when the first brood of anopheles mosquitoes has not yet appeared. For

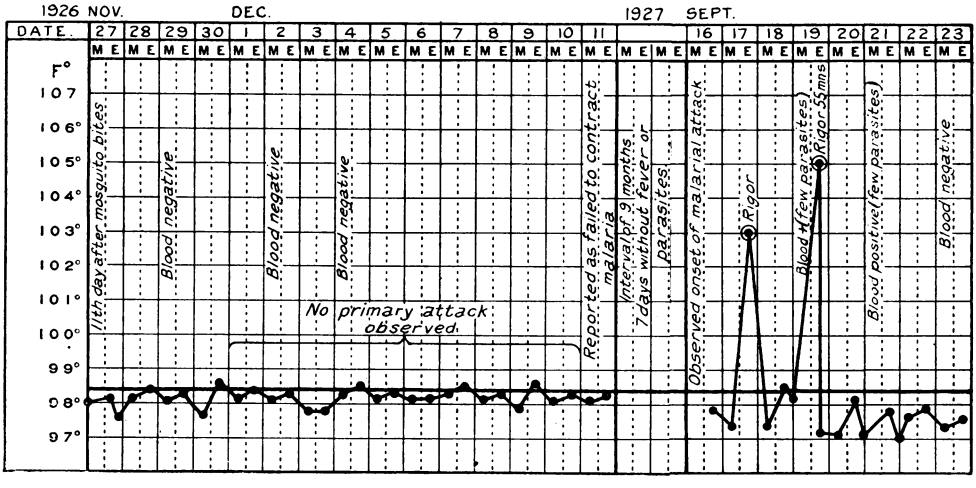


FIG. 4.—Temperature chart of case of latent malaria ; the patient was infected by mosquito bites on November 16, 1926.

this reason until quite recently it has been difficult to make the spring rise of malaria fit in with our knowledge of the mosquito-malaria cycle. The explanation has been provided by laboratory work in connection with the malaria treatment of patients suffering from general paralysis in England. In this work it has been found that, in many patients who are intentionally infected with malaria by mosquito bites, the infection remains latent for a period which is very commonly between seven and ten months. The above chart illustrates this curious phenomenon (fig. 4).

Apparently the same phenomenon occurs in nature, with the result that in England, Holland, and countries of northern Europe, where nearly all new infections are contracted between July and September, many observed clinical attacks happen in April or May—that is, about eight months later. The cause of this latency is unknown, but this and the other points I have mentioned indicate that it is not sufficient to study the life history of the parasite in the mosquito, if we wish to arrive at a satisfactory explanation of the cause of the disappearance of malaria from England and at a rational means of dealing with this disease.

Intimately connected with a study of the parasite in its human host is the problem of the "enhancement" or "deterioration" of virulence in different strains, but as yet our knowledge of this subject is not sufficient to enable it to be dealt with profitably.

(2) *Factors Relating to the Sources of Infection.*—At present local malaria in England is maintained chiefly by spread from imported cases of the benign tertian parasite, but partly by spread from a true indigenous strain of this parasite which, as we believe, has never entirely disappeared from certain areas of the country. The occasional occurrence of a sufficient prevalence to constitute an "epidemic" (as happened notably in 1917, and probably in 1859 and some other years) has always been due essentially to an unusually large importation of cases and carriers from abroad.

(3) *Factors Relating to the Carrier of Infection.*—There are three species of anopheles mosquitoes in England, namely, *maculipennis* Meigen, *bifurcatus* Linnaeus, and *plumbeus* Stephens. In the laboratory, under suitable conditions of temperature and humidity, each of the species can act as an efficient host of malaria parasites,[1] but in natural conditions in England at present, *maculipennis* is the only one that has been definitely incriminated, the reason being that this is the only species which, at present, spends its life in close association with man. It is possible that in olden times, when man had different habits, one or both of the other species may have been concerned in spreading the parasites of the disease.

I have already mentioned the distribution of *maculipennis* in relation to malaria in England. When it was found that the distribution of these insects and of malaria could not be correlated qualitatively, an endeavour was made to correlate them quantitatively, to show, in fact, that "drainage of the marshes," although it had not caused the anopheles mosquitoes to disappear, had reduced their numbers very greatly, so much that not enough were left to ensure the spread of malaria.[2] This view had to be abandoned when it was found that, in a number of districts in which malaria did not spread, the prevalence of anopheles was greater than in the endemic areas, and that, in fact, it was seldom or never possible anywhere to correlate the numerical abundance of anopheles with the amount of malaria; there may be much malaria with exceedingly few anopheles, and no malaria (or very little) with a great abundance of those insects. The latter condition is now called "anophelism without malaria," and is the present condition in parts of England, Denmark, Holland, Italy and many other countries. This is one of the reasons why it is surprising that a section of the older school of malariologists still pin their faith to "anopheles reduction" as the best method of controlling malaria.

The most important habit of *maculipennis* in relation to malarial transmission in England is that it is essentially a "domestic" mosquito which, instead of living and biting in the open air, as most mosquitoes do, habitually frequents dwelling houses, cowsheds, stables, pigsties, and other buildings in which it can obtain shelter from wind, sun and rain, and easy access to people or animals on whose blood it feeds. Except in unusual circumstances, it has never been detected in the act of biting in the open air. This means that malaria in this country cannot be contracted except in houses or other buildings; it must be entirely a "house disease." The result of inquiries into the origin of locally contracted cases in England entirely supports this conclusion. Thus it is important to ascertain in what types of houses, cowsheds, stables and other buildings *maculipennis* is most commonly present, and why it

[1] In a series of experiments in our laboratory at Horton, *plumbeus* seemed to be the most efficient of the three species as a host of *P. vivax*.

[2] See the *Journal of Hygiene*, vol. i, 1901, p. 44: "It is not a matter of the geographical distribution of anopheles so much as of their *numerical* distribution."

is more abundant in some types of shelter than in others. So far as is known at present, the following are the determining factors in this matter: (1) The daily or nightly presence, in the building, of human beings or animals to serve as food supply; (2) absence of draughts, particularly near the roof; (3) relative darkness and particularly the existence of dark, cobweb-laden corners, rafters, straw thatch, or cracks and crevices into which the insect can crawl until it is almost hidden from view; (4) dampness; (5) a relatively warmer temperature than the open air. The common observation that in England, Holland, Denmark, etc., *maculipennis* is more abundant in cowsheds and stables than in dwelling houses is a consequence of the operation of these factors; in all probability it is not due in any way to a selective preference for the blood of cows or other animals rather than of man, as has been suggested by Roubaud and others. The preference of *maculipennis* for resting in buildings which fulfil the conditions above noted has a great influence on the incidence and spread of malaria, for it is obvious that when the inhabitants of a place live in houses which fulfil those conditions, the disease is more likely to spread among them than if they live in houses which are less attractive to the malaria-carrying insects. Thus the type of housing in rural districts where malaria is endemic becomes an all-important factor in connection with the transmission and persistence of the disease.

Closely related to this factor is the problem of the duration of stay of *maculipennis* in dwellings in which it has settled. Do individual anopheles which have flown into a house remain there for a number of days, or do they fly out again after having bitten a member of the household and obtained a meal of blood? It is not easy to answer this question briefly, for it may be that the habits of *maculipennis* in this respect vary at different seasons of the year. We may suppose that when individual specimens of this species find themselves in a house which complies with all their needs of food supply, warmth, shelter and safety, there is no reason why they should leave it until the ripening of their eggs necessitates a search for water on which to lay them. If growth and maturation of the eggs take a week, that would be the usual duration of stay in the house. But *maculipennis* is a species in which egg development ceases completely at the end of August or early in September. At this period the process of growth and deposition of eggs is replaced by accumulation and enlargement of the "fat body" preparatory to the winter season when the insect (if the climate is cold enough) will go into "hibernation." Thus, from the time when egg development ceases, there is no reason why the insect should leave the house at all. That this is what often happens in nature seems to be proved by epidemiological observations in so-called "malarious houses." It has been found in England that in these houses, if one member of the family happens to be a malaria-carrier, cases continue to occur at intervals in that family or house for several weeks, but the disease does not spread to neighbouring houses. This can only be explained on the assumption that the mosquito which bites the malaria-carrier remains in the house sufficiently long to become infective and to infect other members of the family. The following is a simple example among many that are available:—

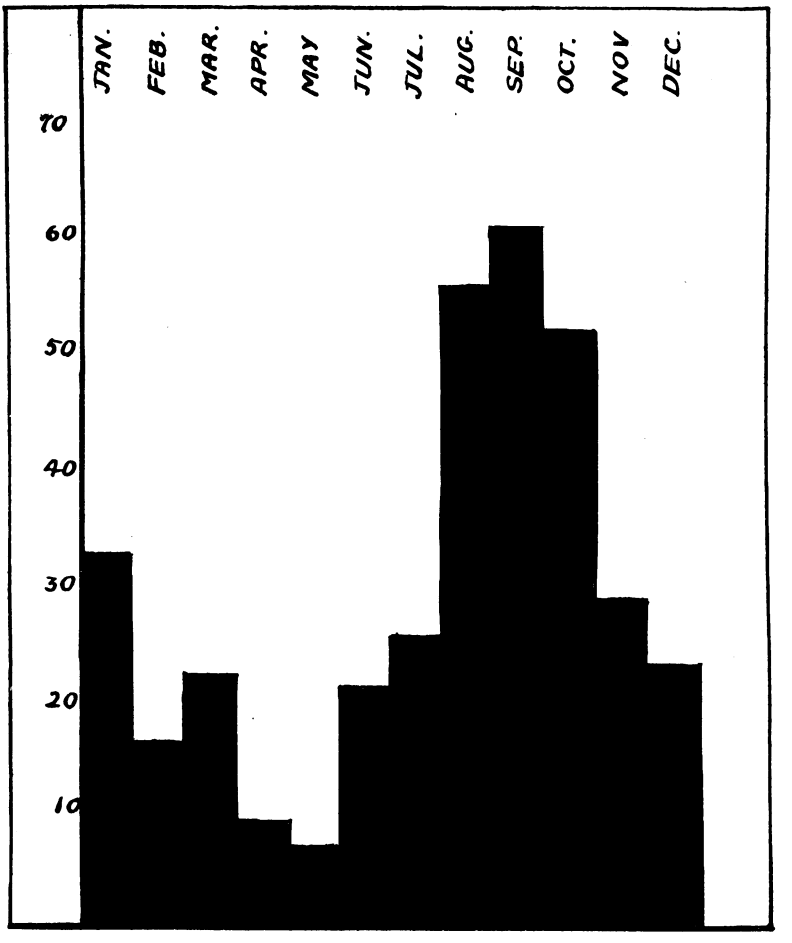
W—— Cottage, Essex.

Date	Malarial events
September 1, 1919	J. B. aged 22, invalided with malaria from Macedonia, had a relapse (*P. vivax* found)
October 4, 1919	R. B., his young brother, aged 9, who shared his bed started a primary attack (*P. vivax* found)

In this instance the mosquito which infected the brother (R. B.) must have remained in the house—probably in the bedroom—at least fifteen days. It is to be noted that epidemiological histories of this kind can only be related of certain kinds of houses and certain types of people who live in them. I shall refer to this again

when speaking of the habits and customs of the inhabitants of endemic areas. Here I will only say that the fact that infective mosquitoes are those which have remained a long time in the same house is of great importance as indicating a simple method of preventing transmission of the disease.

I shall mention only one other habit of *maculipennis* which has an important bearing on the incidence and spread of malaria, namely, its length of life at different



MONTHLY PERCENTAGE OF MOSQUITOES WHICH LIVED LONG ENOUGH TO BECOME TRANSMITTERS OF MALARIA.

FIG. 5.

seasons of the year in relation to malarial infection. I have already mentioned that in northern Europe malarial infection of anopheles caught in houses does not begin to rise appreciably until September, and that it increases remarkably in October and November. This is surprising in view of the fact that growth of the malarial parasite in the mosquito's body is known to depend greatly on temperature and that

the hottest months of the year in northern Europe are July and August. I think that the paradoxical finding is explained by a knowledge of the length of life of the insect in different months of the year. Under natural conditions in England an anopheles must live at least fifteen days after biting the infecting patient in order to become infective. In our laboratory work on infecting anopheles for transmitting malaria, as a therapeutic measure, to patients with general paralysis, we find that very few anopheles live that length of time during May and June, but that a large number live a long time during August, September and October. Therefore those are the months in which we find it easier to provide a sufficient supply of infective insects. This is illustrated in the chart on page 10 which represents the figures for five years during which 14,400 anopheles were used (fig. 5).

Interesting results of inquiry into various other habits of anopheles in relation to malarial transmission are available, but are omitted from the present paper as not seeming to bear directly on the problem under consideration.

(4) *Factors Relating to the Recipient of Infection.*—Under this heading, knowing that local malaria in England is at present maintained chiefly by importation of relapsing cases, the problem of the "susceptibility" or "resistance" of the local inhabitants is of chief interest for the purposes of our subject. In our laboratory work we have proved that persons can be easily "immunized" against a strain of the benign tertian parasite, but that this resistance breaks down if they are inoculated with another species (quartan) or even with another strain of the same species. For this reason, in an isolated village where benign tertian malaria was endemic, the inhabitants would quickly become "immune" or "tolerant" to their own strain of parasite and (clinically at any rate) the disease would seem to disappear. This is what has happened in several isolated country villages near the south-east coast of England. But when one of the inhabitants who has gone abroad returns infected with a foreign strain of the parasite, cases of clinical malaria begin to crop up in the village even among people who have previously claimed that they were "immune." Thus there is a good deal to be said for the view that the peculiar distribution of malaria in England, and the rise and fall of incidence in endemic centres, is defined and decided essentially by the importation of new cases of the disease and new strains of the parasite. On this subject we must take our stand on the proved influence of the factor of importation during and since the European war. We do not know to what extent similar conditions of importation existed formerly, but it is certainly worthy of consideration whether, by an examination of the overseas traffic of England with malarious countries from the earliest historical times to the present day, combined with a knowledge of the localities from which the seafaring population of Great Britain has always been drawn, the introduction of cases and carriers might not be found to be more closely correlated with the peculiar malarial distribution in this country than is any other factor. Whether this would be the finding or not, we know from recent experience that when the importation of new cases into an endemic locality ceases, or when the imported cases are quickly discovered and treated by quinine, the disease soon becomes negligible as a cause of sickness in the locality. This is one of the reasons which justify the view that the influence of the human source of infection in maintaining a condition of malarial endemicity in England is greater than is the influence of the insect-carrier or any environmental condition.

(5) *Factors Relating to the Environment, Climate, Temperature and Humidity.*—Several workers in recent years, notably Dr. A. MacDonald [7] and Colonel C. A. Gill [3], I.M.S., have attributed an important rôle to temperature and humidity in determining the distribution of locally contracted malaria in England and in explaining its "disappearance." Some workers, particularly Dr. Hansen in Denmark, have even thought that progressive changes in the climate of the country as a whole might be an important factor in bringing about the disappearance. It is understood

that, in England at any rate, there has been no appreciable secular change of climate within historical times. As regards humidity, it appears that at all the seasons of the year the relative humidity of the atmosphere in every part of England is favourable to the development of the malaria parasite (benign tertian) in the mosquito ; therefore this factor does not play a part in determining the seasonal incidence of infections. It is otherwise, however, with the temperature factor, for it has been ascertained that if a mean monthly temperature of not less than 61° F. (16° C.) is regarded as being the lower " critical " limit of temperature necessary for development of the parasite in the mosquito, the period during which mosquitoes can ordinarily become infective in England is limited to the months of July and August. But it must be remembered that this would be correct only if the mosquito (*maculipennis*) were to live entirely in the open air while the parasite was developing within it. This it does not do. From what we know of the epidemiology of the disease, the only figures of temperature and humidity which are useful in discussing this subject are those of the interior of houses, rooms, stables, cowsheds, pigsties and other buildings in which *maculipennis* passes so great a portion of its adult life.

(6) *Factors Relating to the Association between the Source, the Carrier and the Recipient of Infection.*—The spread of malaria depends not only on many factors which influence respectively the source, the carrier and the recipient of infection, but also on other factors which bring the source, the carrier and the recipient into the necessary close association with one another. In a cottage where the whole family sleeps in the same room this association is much closer than in a modern house containing several separate bedrooms, and it is obvious that infection among the family is much more likely to spread in the former than in the latter. This is probably the chief reason why the incidence of malaria is always higher among the poor than among those who can afford to live in better houses. If malaria were not so definitely a " house disease," as it is, this difference of incidence would not be so universally recorded. Many details on this subject are available for various localities and houses, but as they do not lend themselves to brief summary I must omit them from this paper.

(7) *Factors Relating to Quinine.*—England has always been a chief centre for the distribution of quinine to other countries, and it is not possible to ascertain, for different years, the amount consumed locally, as distinct from the amount manufactured, imported and exported. Cinchona bark was in common use in the endemic areas of malaria in Kent as long ago as 1780, but quinine was not introduced there until about 1840, and at first it cost £1 per drachm. Between 1875 and 1887, the average wholesale price was about 8s. 6d. per ounce, and in 1892 it cost less than 10d. per ounce.

It is difficult to avoid the conclusion that the introduction of quinine into general practice in this country and its progressive cheapening until it could be bought directly from chemists by the poorer classes, was one of the most important factors in causing the observed reduction in the fatality and incidence of malaria. The chief reasons for this conclusion are :—

(1) Clinical study of cases of indigenous malaria occurring in England in recent years, as well as study of the disease in persons intentionally given an attack for therapeutic purposes, has revealed that benign tertian malaria, when untreated by quinine, is often a serious disease which, in persons who are enfeebled from any cause, not infrequently results fatally. In villages in England I have seen several locally contracted cases in children which, not having been correctly diagnosed for a week or more, were so serious that a fatal issue might have resulted if diagnosis and quinine treatment had been delayed much longer. Among patients suffering from general paralysis who undergo an attack of benign tertian malaria in the hope of curing their mental disease, the fatality attributable primarily to the malarial attack is between 10 and 12 per cent. [9].

(2) Dr. Stevenson's analysis of the change in the relative numbers of malarial deaths in England among males and females respectively, from 1880 onwards, cannot be explained on any other hypothesis than that it was due to the more general use of quinine in this country. I have summarized his analysis elsewhere [8] and need not reproduce it here.

(3) The fact that in the epidemic of 1917 in Kent a surprisingly large number of locally contracted cases occurred, was due chiefly to failure, for more than two months, to diagnose the disease correctly. As soon as the disease was recognized to be malaria, the discovery and quinine treatment of cases and carriers stopped the epidemic very quickly. There have been several occurrences which might have led to a similar epidemic since then (the most recent was in June this year), but the prompt discovery and treatment of the person or persons capable of infecting the local anopheles quickly eliminated the risk.

Summary of Part II.

From consideration of the evidence bearing on the influence of each factor which has been described in this part of my paper, I have come to the conclusion that the diminution of local malaria in England was due neither to natural causes[1] nor to the intentional application of any particular preventive method reputed to be specific, but to progressive improvements of a social, economic, educational, medical and public health character. At first sight, some of these improvements may seem to bear little or no relation to our knowledge of the evolutionary cycle of the malaria parasite in mosquitoes, but, when they are examined in detail they accord well with it. For example, on the subject of "social improvement" we can say at once, from our knowledge of the habits of the malaria-carrying mosquito (*maculipennis*), that this insect is parasitic on man in proportion as human habits and mode of life are primitive and like those of the indigenous inhabitants of undeveloped countries. In those countries all the members of a family live huddled together in a single cave or hut, made of straw or stones or mud bricks, without windows or other means of introducing light and ventilation. These huts are invariably infested with anopheles mosquitoes as well as with ticks, fleas, bugs and other vermin. In England the "civilizing" social influences of several hundred years have gradually removed the bulk of the people from the necessity of living in that manner, and, particularly during the last seventy years or more, there have been great changes for the better in social and economic respects and in general welfare. Houses are better lighted and ventilated; they have windows and they are less damp; they have floors and are provided with ceilings shutting off the bedrooms from the rafters of the roof, they are more open and less crowded, and are more frequently painted or whitewashed inside than they used to be. These changes, as well as more cleanly conditions in the home generally, have made the houses much less liable to harbour anopheles mosquitoes and have broken, to a considerable extent, the close association between those mosquitoes and man which existed when living conditions were primitive. Undoubtedly this dissociation has contributed materially towards the reduction of malaria. Other advantages accompany social and economic improvements: roads are made; scattered houses become easy of access; there is co-operation between various households; villages spring up; a school and church are built; educated people come into contact with the inhabitants and it becomes possible for a doctor to make a living in the locality; sick-clubs may be formed, or the Poor Law may come into action to bring medical assistance to those unable to pay for it, and there are arrangements for dealing with infectious diseases and epidemic outbreaks; later there may be arrangements for lighting, for water-supply and for the disposal of

[1] The view is quite common that the downward trend of malaria in some countries is a natural phenomenon independent of human action and unexplainable.

night soil and refuse. It is not contended that all these arrangements have a direct influence in reducing the incidence of malaria; what is meant is that they are signs of progress towards a higher and more cleanly standard of living; people who are willing to adopt and utilize them have arrived at the stage of civilized social life in which they are not so indifferent to the advantages of health and comfort as more backward populations are; they have become less willing to live in constant close association with lice, fleas, bugs, mosquitoes, rats and other vermin, and when they are ill they take pains to get proper medical attention and proper treatment with quinine. Even in England it is easy to see that malaria persists as an endemic disease only in a few isolated rural areas which are notoriously backward in medical and hygenic arrangements and in the common amenities of modern civilized life. In these localities the level of wages is low, work is scarce, a whole family may live in one room of a dilapidated wooden shack, and no doctor is available within eight or ten miles. Proceeding from west to east across Europe this correlation between the incidence of malaria and a low standard of living becomes very plain. If we get as far as Africa and India it is, of course, the outstanding epidemiological fact, which has struck even those who still believe that malaria can be controlled by some "new method" or "short cut" which will save the responsible authorities from taking measures to raise the people from their present backward economic condition and low, insanitary state of social life and culture.

There are other countries than England in which a similar "natural decline of malaria" has occurred, and I think the cause of the decline is the same in them, though the realization of this has been delayed by endeavours to show that it was due to factors or measures thought to be more in accord with the knowledge of the mosquito cycle of the malaria parasite. If there is anything new or useful in the ideas that I have attempted to bring forward in this paper, I shall be glad if what I have said helps to justify and to encourage public health workers who (having realized that among the many million native inhabitants of endemic and hyperendemic areas in the world generally, malaria, like tuberculosis and syphilis, is a "social disease") are attempting to control it with those ideas in view.

Concluding Remarks.

In order to prevent misunderstanding, I should like to add that my paper is not concerned at all with plans for dealing with malaria among particular groups of people who live in places or under conditions where accepted standards of living, and the medical and sanitary arrangements, make it practicable and desirable to supplement existing work by a direct attack aimed either at the insect host and carrier or at the parasite in man. Fortunately that kind of work needs no encouragement, for an increasingly large number of entomologists and specially trained medical men are already engaged in it. Moreover, although this work is of great local interest and importance, it is clearly a "side-line" in a different category from, and having little or no connection with, the malaria problem among the bulk of the population of malarious countries. The latter, of course, is the problem that must be solved before we can begin to speak of "winning a victory over malaria" or of "ridding the world from the menace of this scourge." The populations referred to are the indigenous peasantry—the inhabitants whose malarious condition is usually represented on a map of the world by marking about half of the whole map in red. In general these people are poor, illiterate, uncultured and almost entirely without the common household and personal equipment usually believed to be necessary, or at any rate desirable, for a healthy and comfortable life. In most countries their dwellings are little better than those of primitive man, and so many of them are chronically under-nourished and infected with worms and other

parasites and pathogenic bacteria that it has often been said that they do not know what "health" means. Among such people, malaria cannot be dealt with as an isolated problem separate from other social, medical and public health affairs, or without the aid of educational arrangements designed to get the people to understand, and be willing to take advantage of, medical and sanitary measures established for their benefit. In every malarious country, too, the low economic status of the bulk of the people who suffer so greatly from the disease must be raised before they can be in a position to put the educational teachings into practice. Therefore this economic improvement is the matter to which attention must first be directed. In broad outline this is the line of reasoning which justifies the modern view that the correct way of beginning to combat malaria in its endemic areas is to introduce agricultural schemes which aim primarily at improving the economic prosperity of the people, but are accompanied by progressive arrangements for adequate medical attention in sickness, for technical and elementary school education and for simple sanitary measures of housing, water-supply, conservancy and general welfare. These schemes, for which the name "bonifications" is gradually coming into general use, include a system of irrigation or other arrangement, by which a very large area of land can be made to yield an abundant return. Their advantages are that, while being profitable to the Governments responsible for them, they are of immense benefit to the indigenous population by changing completely their material conditions so that instead of being poor, sparse, semi-nomadic and uncivilized, they become settled and well-to-do and able and willing to assist actively in combating malaria, tuberculosis, syphilis, and other "social diseases." The sources of malaria are not eradicated by these schemes, but as the people live in better houses, have more and better food, and are within easy reach of medical aid, they are not infected so frequently, and the disease, when it occurs, is quickly and effectively treated and overcome. Thus severe and fatal cases become rare and, after a time, the disease ceases to be of great importance as a cause of sickness and death.

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Discussion.—Sir MALCOLM WATSON said he understood Colonel James' argument to be as follows: (1) Malaria has practically disappeared from England. (2) Anopheles have not disappeared. They are perhaps commoner than previously. (3) Social improvement and proper housing have been the real cause for the disappearance of malaria. (4) If the social condition of the people in the tropics is improved, malaria will decrease so much in severity that it will be possible to forget all about anopheles and malaria.

He (Sir Malcolm) could not accept Colonel James's statement that the type of house was an "all-important" factor in malaria in the tropics, whatever it might be in Europe. Nor did he believe that however beneficial good houses, good food, good sanitation and doctors and schools might be, they would themselves reduce malaria to the extent that Colonel James hoped for.

He had seen all the good things included in the word "bonificatio" in the tropics but they had entirely failed to control malaria. In Kuala Lumpur the highest Government officials, living in the best houses in the town, with better food and better sanitation than the ordinary inhabitants, had suffered more severely from malaria than the town people, who were farther away from the breeding places of the anopheles.

In Singapore, troops in Tanglin barracks and in the barracks on Blakan Mati suffered from malaria, although they were under ideal conditions from an ordinary sanitary standpoint, and not until the anopheles' breeding places had been dealt with did they become free from malaria.

Turning to estate labour in Malaya: good food, good houses, hospitals and medical attention were provided on a scale unlikely to obtain in any indigenous rural population in Asia or Africa, yet the death-rate had been appallingly high—often reaching 200 or 300 per mille per annum—until the anopheles danger was removed. He (Sir Malcolm) could not agree with Colonel James's suggestion that it was seldom, if ever, possible anywhere to correlate the numerical abundance of anopheles with malaria. In his experience, the spleen-rates had a very definite relationship to the breeding-places of the species of anopheles which carried malaria.

There was a vital distinction between the malaria of Europe where the disease had a precarious existence, and that in the tropics where the rate of infection might lead to an admission-rate of 3,000 per mille per annum.

He made these remarks lest Colonel James's paper should be put forward as an excuse for neglectiug work on anopheles in the tropics. He did not believe that ordinary sanitation was sufficient by itself to produce a figure of immunity of much value either to the individual or to the community of which he was a member.

[Sir Malcolm then showed cinematograph pictures illustrating the "Malaria Problems of Ceylon and Bengal," the most striking features of which were the splendid houses which had been abandoned on account of the disease.]

Dr. Bentley had at one time regarded malaria in Bengal as an economic question, but his view nowadays was that it was entirely due to certain species of mosquitoes and would be controlled only by controlling these mosquitoes.

There were certainly many anopheles breeding-places in London 250 years ago which had entirely disappeared in modern London, where all streams were underground and all streets were paved.

From his experience in the tropics, he found it difficult to believe that the drainage of the country districts, including the fens, had not led to a material reduction in the number of anopheles.

Dr. MANSON-BAHR said: Personally, I have had little experience of indigenous malaria contracted in England, and do not wish to be considered hypercritical if I criticize the graphs of mortality from malaria in England during the last fifty years which Colonel James has set before us. I am sure that he himself would acknowledge that they are only approximately accurate. When, as at present, the art of diagnosis has reached a higher pitch than was formerly the case, other causes of pyrexia, such as phthisis, endocarditis, septic infections of the urinary tract, syphilis, and malignant disease are frequently mistaken for malaria, and, in the absence of a properly conducted post-mortem examination, death would be attributed to it. I have met with cases in which an enlarged septic kidney was for several years regarded as a spleen, and the pyrexial attacks were attributed, even by medical boards, to attacks of malaria. This does not mean that I disbelieve in the existence of indigenous malaria in England, or that it has greatly diminished in recent years. I am wondering to what extent the provision of glass windows in houses has assisted in the diminution. And may it not be by the provision of cattle sheds in the vicinity of houses that the anopheles, e.g. in Romney Marsh, have come to prefer bovine to human blood? The question of the "soil" also comes into operation. Is it not a fact that when people are better housed, nourished, and clad, malaria, especially the benign tertian variety, takes on a much milder form? In my experience, benign tertian infections contracted in Europe are much less severe and much more easily cured by quinine than those contracted in the tropics. Colonel James is unquestionably right in stating that, in Europe at any rate, the malaria infection is contracted in the interior of houses when the victim is asleep. At the same time, Sir Malcolm Watson is also correct. Other things being equal, the amount of malaria is proportional to the prevalence of an appropriate species of anopheline mosquito; but everyone will acknowledge that many factors are concerned.

Sir WILLIAM HAMER said he agreed that the official mortality statistics showed three epidemic prevalences of "malarial diseases" in this country. It should, however, be noted that the first prevalence was in the year of the great influenza (1847), the second was coincident with the "trailer" of 1855, and the third with the pandemic influenza of 1857-58, which (as Hirsch has pointed out) practically escaped being recorded as such in England and Wales. So that influenza presumably accounted for the three English prevalences of "malarial disease" of registration times. With regard to earlier centuries, Creighton carefully scrutinized the evidence, in his "History" and in contributions to "Traill's Social England," and he noted that: "While Sydenham and his learned colleagues were not ignorant of the endemic agues of marshy localities, they made little account of them, in comparison with the aguish or intermittent fevers that came in epidemics all over England." Moreover, Creighton might be said to have securely laid the ghost of epidemic malaria in England by his demonstration of the remarkable time-relationships between these epidemics of "ague" (so-called) and epidemics of influenza.

Sir MALCOLM WATSON said it was impossible that Sydenham could have written as he had done without having had an extensive clinical experience of malaria. [The speaker read an extract from Sydenham's work illustrating his point.]

Dr. H. S. STANNUS said that his own experience in Africa had convinced him that most Europeans became infected with malaria by mosquitoes in the house—in which term he included the verandah, outside closet, etc. In this respect Colonel James had established a most valuable fact. Sir Malcolm Watson had drawn a disparison between the primitive dwellings shown by Colonel James and the large mansions now derelict in Bengal, but he (the speaker) suggested that these large mansions afforded the same favourable conditions for mosquitoes as did the hovels mentioned by Colonel James.

COLONEL JAMES (in reply) said that Sir Malcolm Watson was evidently under the misapprehension that the paper was concerned with malaria in the tropics. But there was nowhere a "statement that the type of house was an all-important factor in malaria in the tropics"; indeed the word "tropics" did not appear in the paper. Moreover, if Sir Malcolm was correct in thinking that there was a vital distinction between the malaria of Europe and that of the tropics, it seemed inappropriate of him to quote experience in the latter countries as refuting experience in the former.

The lantern-slide demonstration of houses in England and on the Continent seemed to have led some speakers to think that housing was the only factor brought forward as being concerned in the disappearance of malaria from England. This was not so. The paper dealt at length with many other factors, and it was surprising that no speaker had discussed, for example, the reference to the introduction and progressive cheapening of quinine which was described in the paper as having been one of the most important factors in causing the observed reduction in fatality and incidence.

Again, no one had discussed the paragraphs relating to the influence of imported cases of the disease, although it was well known that, even at the present day, malaria began to spread in certain parts of England whenever imported relapsing cases remained undiscovered. These occurrences prove, of course, that in those places the numerical prevalence of anopheles had not been reduced below the limit at which the disease would spread.