# MALARIOLOGY

*A Comprehensive Survey of All Aspects of This Group of Diseases from a Global Standpoint*

By

SIXTY-FIVE CONTRIBUTORS

Edited by

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VOLUME II

1949

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VOLUME II

SECTION IV. INTERMEDIATE HOST (*Continued*)

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# CONSPECTUS OF MALARIA INCIDENCE IN NORTHERN EUROPE, THE MEDITERRANEAN REGION AND THE NEAR EAST

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## THE MACULIPENNIS COMPLEX

The distribution of malaria in Europe and its extraordinary variations in intensity from one region to another were a complete enigma to malariologists before 1930. Celli had pointed out as early as 1910 that the geographic distribution of *Anopheles maculipennis* in Italy could not be made to coincide with the map of malaria. In 1920–21 Roubaud in France and Wesenberg-Lund in Denmark discovered almost simultaneously that *A. maculipennis* often continued to breed in undiminished numbers in districts from which malaria had completely and spontaneously disappeared. James, an international observer, wrote in 1929 that "it was seldom or never possible anywhere to correlate the numerical abundance of *Anopheles* with the amount of malaria." It was discovered that in the areas of so-called "anophelism without malaria," *A. maculipennis* rarely bit human beings, and this led observers to postulate the existence of races or strains of this mosquito which fed by instinct on certain domestic animals rather than on man. There were no distinguishing marks by which such "races" could be recognized, and the problem continued to agitate European epidemiologists for a decade. (For an extended account of the whole discussion, see Hackett, 1937.)

The epidemiologic confusion was cleared up in 1931 when evidence was brought forward by Martini, Missiroli and Hackett (1931) to show that *A. maculipennis* is not a homogeneous species, but is a group or complex of several independent species which, in spite of their almost complete morphologic similarity, differ widely in physiology, behavior and adaptation to environmental conditions, and hence in their relationship to malaria transmission. The various species could be differentiated by the characters of their eggs, and thus their separate ranges could be geographically defined and their ecology and feeding habits studied (Hackett and Missiroli, 1935). It has been shown that each member of the *maculipennis* group lays its eggs in a certain characteristic type of breeding place to which its larvae are adapted, so that in any area within its climatic range its presence and density depend on the amount of available water surface of the required type. Its effectiveness as a vector of malaria on the other hand depends on the frequency and regularity with which it resorts to human beings as a source of food. The distribution and intensity of malaria throughout the range of the *maculipennis* group, which covers the major portion of the palearctic region, are thus in general satisfactorily explained by the ecology and biting habits of its component members, although, as will be shown, anomalous situations exist which are difficult to interpret on the basis of our present knowledge. Other vectors intrude only on the fringes of this vast territory, and with the exception of *A. superpictus*, a Near Eastern form, do not complicate the present analysis.

Seven more or less independent populations of the *maculipennis* complex are found in Europe, western Asia, the Near and Middle East and North Africa, and are responsible for practically all the malaria. Of these, two and very probably a third can be immediately dismissed from consideration since they have never been incriminated as vectors. The Mediterranean forms, *A. melanoon melanoon* and *A. melanoon subalpinus*, have so little contact with man that they are never concerned in malaria transmission under the present conditions of rural life in Europe, and, with only a slight reservation, we may say the same of the ubiquitous *A. maculipennis* (the type form, usually referred to as *typicus*) which throughout its accepted range confines itself to feeding on domestic or wild animals. The mild endemic malaria of Caucasia, north and south of the mountains, has been attributed to this form, since it is reported to be the only anopheline present, but, in a brief survey carried out in 1934, Hackett and Barber were struck by characters appearing in many egg batches which indicated the possibility of the existence of new varieties of this species in the southeastern corner of Europe. Our knowledge of these and of the Asiatic forms in general is too incomplete to warrant any conclusions. It should be emphasized, however, that there is no insuperable barrier, under all conditions, which prevents even these three species from occasionally biting man. When we speak of natural effective restriction to animal hosts, we do not mean that this is absolute for any species, but only that it is ordinarily sufficient under local circumstances to prevent accomplishment of malaria transmission.

The remaining four species of the *maculipennis* group are all vectors in different degrees and determine among them the pattern of malaria in the region under consideration. In general, *A. messeae* and *A. atroparvus* are powerfully attracted to stabled animals, almost to the exclusion of man, but may overflow into human habitations in search of food under various circumstances, among which are a disproportionate density of anophelines, a scarcity of animals or for other reasons connected possibly with temperature, humidity or odor, the exact nature of which is still largely conjectural. On the other hand, the two other species, *A. labranchiae* and *A. sacharovi*, are continually penetrating into houses in relatively large numbers wherever they are found, and they are not known anywhere to be effectively deviated from man by domestic animals; their presence is always a sign of severe malaria. No two of these species, however, react alike to environmental stimuli, either in feeding, oviposition or other behavior patterns which have a bearing on transmission, and this explains their separate roles in the spread of malaria.

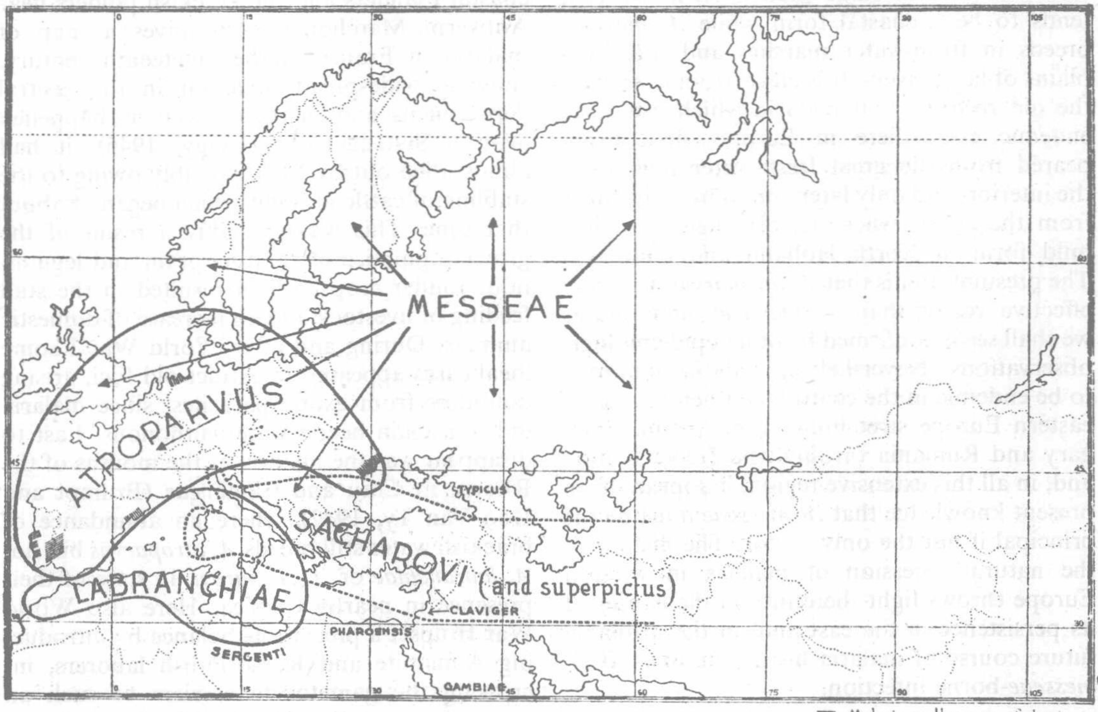


Fig. 238. Distribution of the malaria vectors of the western palearctic region: four members of the *malculipennis* complex, and secondary vectors of other species.

As can be seen from the accompanying map (Fig. 238), *A. labranchiae* and *A. sacharovi* are confined to the Mediterranean countries and the Near East, and all the malaria in Europe north of the Alps and the Caucasus is attributable to *A. atroparvus* and *A. messeae*. Both of these forms are such poor vectors under modern conditions of agriculture and the stabling of domestic animals that the infection has died out spontaneously over most of western Europe during the last fifty years.

Since *A. atroparvus* is much more tolerant of salt in the larval stage than is *A. messeae*, it tends to be a coastal form while *A. messeae* breeds in fresh-water marshes and the flood plains of large rivers. It is clear, from a study of the old records, that malaria which was once endemic everywhere in Europe, first disappeared from the great fresh-water regions of the interior, and only later and more reluctantly from the coast, where it still lingers on in a mild form in North Holland and Germany. The presumption is that *A. atroparvus* is a more effective vector than *A. messeae*, and this as we shall see is confirmed by other epidemiologic observations. Nevertheless, malaria continues to be endemic in the central continental area of eastern Europe stretching from Poland, Hungary and Rumania through the Soviet Union, and, in all this extensive region, it appears from present knowledge that *A. messeae* must be the principal if not the only vector. The history of the natural recession of malaria in western Europe throws light therefore on the causes of its persistence in the east and on the probable future course of malaria history in areas of *A. messeae*-borne infection.

## THE MALARIA OF NORTHERN EUROPE

During the last century no part of Europe was exempt from malaria. Ekblom (1935) says that while indigenous malaria is now probably extinct in SWEDEN, this is in striking contrast to the great epidemics of the past. Up to about 1880, when the decline began, there were from 4000 to 8000 cases a year. Since 1910 the number of cases has been negligible, although as late as 1927 there were a few sporadic cases around Stockholm. This in general is the story of malaria in the rest of SCANDINAVIA, FINLAND and the BALTIC STATES. Renkonen (1944) says that the last considerable epidemic in Finland occurred in 1902, with 3300 registered cases. In 1920–21, during the tremendous Russian epidemic, there were about 500 cases each year, since when the infection has completely died out. World War II caused epidemic resurgences of malaria here and there, which have not, however, reestablished permanent foci.

In BELGIUM and FRANCE there are many records of malaria in the last century, the infection tending to persist along the coast after it had disappeared in the interior. In Belgium, for example, Rodhain and van Hoof (1942) connect the last expiring traces with the intense breeding of *A. atroparvus* in the marshes of coastal Flanders and the brackish polders near Antwerp. Marchoux (1926) gives a map of malaria in France in the nineteenth century, showing widespread infection in the central departments and in Alsace, but as happened also in SWITZERLAND (Geigy, 1945), it had almost died out by 1875, possibly owing to the stabling of cattle at night which began at about that time. This was probably a result of the growing practice of rotating grain and leguminous fodder crops, which resulted in the stall feeding of livestock and an increase of domestic animals. During and after World War I some local cases appeared in extinct old foci, arising doubtless from exotic parasites, since malaria did not again become autochthonous. Last to disappear was the malaria at the mouths of the Rhone, in Crau and Camargue (Brumpt and Dao Van Ty, 1942), where an abundance of brackish water still breeds *A. atroparvus* but not *A. labranchiae* or *A. sacharovi*, in spite of their presence in nearby Corsica. Here also World War II upset a precarious balance by introducing Annamite and Russo-Polish laborers, increasing the gametocyte carriers to such an extent that a small epidemic of local cases broke out in 1943. Camargue is cattle country, and it is evident that, under normal conditions, malaria can no longer maintain itself there even in the presence of great numbers of *A. atroparvus*.

In the BRITISH ISLES we have the same picture of a malaria widespread under more primitive conditions of animal husbandry, but disappearing after 1870, first in the interior where *A. messeae* is the only anopheline vector, and much later along the coast where *A. atroparvus* prevails. Marshall (1938) states that the last recorded cases of true autocthonous malaria (i.e., from native strains) occurred in Sheerness at the mouth of the Thames as late as 1887, but that in 1918, soldiers invalided home with malaria, were often sent to convalesce in coastal districts of Kent and Essex with the result that large numbers of local inhabitants contracted the disease. Although sporadic cases of malaria are not infrequently recorded in England now, the author says "it is difficult to believe that malaria is still indigenous in Britain." Parasites are continually imported from abroad, but, while local secondary cases may occur, the strains apparently do not maintain themselves. James (1929) contrasts Whitley's map of malaria in England in 1860 with the situation in 1929 when the number of locally contracted cases had for several years "varied between 2 and 6."

There was a great deal of discussion among malariologists before 1930 as to the causes of the dying out of malaria infection in England, and it was attributed to "progressive improvements of a social, economic, educational, medical and public health character." This is doubtless vague enough to be true in general, but the specific causes must have been connected with the increasing diversion of the two ineffective vectors from man to his domestic animals. It is now clear that the association of *A. messeae* with man, here as on the Continent, was always tenuous, maintained just above the critical level necessary for malaria transmission by the primitive conditions of rural life a century ago, when the cattle went unstabled and the marshes undrained. *A. atroparvus*, on the other hand, is a more domestic mosquito, performing most of its functions under shelter, as might be expected of a coastal species exposed to the weather of northern Europe. Martini thought that it sought principally certain microclimatic conditions of temperature and moisture to which it was adapted when resting or feeding, rather than the blood of any particular kind of animal, and was thus led by instinct into warm, humid stables more often than into human bedrooms. It is evident, however, that contact with man occurs more frequently than in the case of *A. messeae*, especially where *A. atroparvus* is produced in great quantities. Even so, this degree of association is insufficient under present circumstances to keep malaria alive in coastal England, Belgium or France.

In all of western Europe north of the Alps, there is in fact only one small region on the coast of the North Sea belonging in part to the NETHERLANDS and in part to GERMANY where malaria can still be said to be endemic. This lies between Amsterdam and Wilhelmshaven, and comprises the Dutch provinces of North Holland, Friesland and Zeeland, and German East Friesland. *Vivax* malaria occurs here annually, with epidemic waves every twenty years or so, and is transmitted by *A. atroparvus* which breeds in tremendous numbers in the slightly brackish waters. The incidence of malaria in North Holland, Friesland and Zeeland rose with World War II, and doubled between 1941 and 1945 owing to flooding with seawater. But the most dangerous period is possibly yet to come when the salinity is reduced to 0.8 per cent or below, affording ideal breeding conditions for *A. atroparvus*.

Swellengrebel and de Buck (1938) brought out two new factors to account for the persistence of malaria in this prosperous, highly developed, cattle-raising area. They discovered that while *A. messeae* goes into immobile hibernation in untenanted, cold shelters during the winter months, *A. atroparvus* retreats indoors into warm stables where there is plenty of food. If, as often happens, it overwinters in a house, it lives upon the family; and if some member should be a carrier, in a short time most of the family will have contracted malaria.

The Dutch malariologists also noticed that malaria was not evenly distributed, but that infected anophelines were most numerous in certain houses, where cases appeared year after year. These belonged to the families with many children, who are always the most persistent carriers. The continuity of the infection was dependent on carriers, since the overwintering mosquitoes did not remain infective until spring. Birth rate therefore seems to be a factor in *A. atroparvus*-borne malaria, and the Dutch birth rate is the highest in Europe. Overwintering anopheles also occur on the English coast, and in former days produced a similar focal type of infection which gave a bad name to certain so-called "malaria houses" described by James in 1916. The declining birth rate in England may have been a factor in the gradual decrease of indigenous malaria.

*A. atroparvus* undoubtedly enters houses in midsummer as well as fall, as Weyer (1934) has shown in Germany, but the focal or family type of malaria would indicate that they rarely become infected at that season. This is ascribed to a combination of low summer temperatures (always near the critical level necessary for the development of the parasite in the insect host).

and the relatively short life of the female mosquito exposed by reproductive activity at this season to the multiple hazards of an inclement climate.

Nevertheless, Martini (1934) believes that most of the malaria in Germany is contracted in summer and not in winter (as in Holland), but that it escapes recognition, owing to a curious characteristic of *vivax* malaria in northern Europe, first noticed in 1902 by Korteweg (1921) and abundantly confirmed in England, Germany, Sweden, Finland and Russia. Most of the infections acquired in late summer and autumn are not followed by any clinical manifestations for seven or eight months. They remain latent all winter, and the protracted incubation is not terminated until spring when the first frank attack occurs, ordinarily in April or May. The annual peak of malaria thus occurs before the anophelines begin to breed, and is produced by the mosquitoes of the year before. There is often no further increase in cases during the rest of the year and the late summer peak which is the most striking characteristic of southern European malaria is completely suppressed. This is well shown by Russian dispensary statistics (Hackett, 1937, p. 78) and can therefore have no connection with the overwintering habits of *A. atroparvus*, since that species does not occur in northern Russia. Initial latency of this sort seems to be a character of certain strains of *P. vivax*.

The extensive range of *A. atroparvus* brings it also into SPAIN and PORTUGAL where, except in one small area on the east coast, it is the only vector and causes a serious amount of malaria. It is widely distributed over the Iberian Peninsula since it breeds in all suitable waters, salt or fresh, wherever there is lack of competition from fresh-water forms. In Valencia the rice fields are occupied by *A. melanoon* in great numbers, and no *A. atroparvus* or malaria occurs.

Pittaluga says that before 1900 there were 5000 deaths a year from malaria in Spain, but that by 1930 these had fallen to 500 or less. This reduction of 90 per cent in thirty years can only in part be ascribed to antimalaria measures; it is another example of the effect on a poor vector of gradual changes in the conditions affecting rural life. Much of this was undone by the Civil War. In 1937–38, according to Dr. Carlos Zozaya, malariologist of the Republican Army, malaria appeared in Madrid and throughout the valley of the Tagus, the infection extending south to the Mediterranean and north to the Pyrenees, along the battle front. All this was due to *A. atroparvus*, which became a vector again owing to inundations, the disappearance of cattle and other unbalancing effects of war. Malaria at present is again losing ground; it is mildly endemic in the Tagus, Guadiana and Guadalquivir valleys in western Spain, but more tenacious in the north than in the south; it is receding in the Ebro Delta owing to agricultural development and it persists in a small southeastern area on the Mediterranean Coast between Alicante and Murcia, where *A. labranchiae* has established its only bridge-head in Spain. Malaria is not likely to disappear spontaneously in the presence of *A. labranchiae*. The CANARY ISLANDS, which are provinces of Spain, are reputed to be malarious, although no statistics are available. The vectors are said to be *A. sergenti* and *A. hispaniola*.

In PORTUGAL (Cambournac and Hill, 1938) malaria is a serious problem in the alluvial plains of the Sado, Tagus and Mondego Rivers where rice is extensively grown; it is sporadic in two or three other valleys but elsewhere, in spite of the presence of *A. atroparvus*, no malaria occurs. Malaria is present only in rice-growing regions, where there is a tremendous production of anophelines, and where there is also a dearth of large domestic animals. It is clear that endemic malaria in Portugal is due to the high density of *A. atroparvus*, which is a vector largely by force of numbers. Neither malaria nor anophelines are reported from the island of MADEIRA, or the AZORES.

*A. atroparvus* is not known to be a vector elsewhere except in southwestern Russia on the Black Sea littoral between the Bug and Danube Rivers. It was formerly the cause of a mild endemic malaria on the Istrian Peninsula south of Trieste, a region of multiple small lime-sinks, but was brought below the critical density by the introduction of *Gambusia*.

The malaria of western Europe is thus of small moment, but of great historical and epidemiologic interest. Once practically universal, the great recession began about 1870, first over the wide interior range of *A. messeae* where not a trace of malaria now remains west of Hungary and Poland, and somewhat more slowly in the haunts of *A. atroparvus*, which is found breeding almost everywhere in European coastal waters. Even in prodigious numbers it is only a moderately effective vector, for the quantitative relationship between *A. atroparvus* densities and malaria transmission is greatly modified by the methods and extent of animal husbandry, by low summer temperatures and possibly by the age composition of the human population.

As we go east and southeast in Europe, *A. messeae* gradually becomes important as a vector. In POLAND the last great outbreak of malaria coincided with the Russian epidemic of 1921–22, with over 50,000 cases on the Ukrainian border, but there are still endemic foci along the Vistula, including both Krakow and Warsaw, which cause several hundred cases a year. World War II destroyed horses and cattle and created new breeding places; there was a great recrudescence of malaria in the Ukraine, and doubtless in Poland also. Southward in SLOVAKIA and RUTHENIA (Subcarpathian Ukraine) the disease has always been endemic especially along the southern border adjacent to a malarious area in Hungary (Drbohlav, 1936). Here the picturesque gypsy villages on the edges of larger towns are a factor in the maintenance of malaria and in this resemble the Negro villages in the southern United States. There is no malaria in the rest of CZECHOSLOVAKIA or in AUSTRIA, but in HUNGARY, it constitutes a problem of public health importance. A survey by Lörincz (1937) showed that 80 per cent of the malaria occurs in two endemic areas: in the northeast along the Ruthenian frontier where large flood plains and cut-off bends of the rivers breed *A. messeae* in great numbers, and in the southwest next to Yugoslavia in a region of extensive marshes and artificial fishponds. In the great central plain, part of which is below sea level, the water is stagnant and highly alkaline; it breeds *A. atroparvus*, but not in sufficient numbers to cause more than a sporadic malaria.

The bulk of the malaria transmitted by *A. messeae* occurs over the wide expanse of the SOVIET UNION, in the great river basins extending from the Black and Caspian Seas almost to the Arctic Ocean. Much has been published on malaria by Russian authors working in various sectors of this vast domain, but no general review of the whole situation is yet available. We know that malaria is widespread and on the whole not very severe, although it is subject to annual epidemic peaks. In the north these tend to occur, as in western Europe, in early spring before the hibernating anophelines have produced a summer generation, and are probably due to infections contracted in the previous year which have undergone a protracted latency. In years when heavy rainfall producing extensive flooding coincides with a long, hot summer, notable epidemics may occur such as the great pandemic of 1921–22 in which famine and disorganization also played a role. Malaria reaches the highest latitude in the world in Russia, and, during the above epidemic, cases occurred as far north as 64 degrees, on the Dvina River not far from Archangel (see under Latitude).

Hackett and Barber (1935) made a brief malaria survey in July 1934 in the Volga Basin and the Caucasus region, and found only *A. messeae* and "typicus" (*A. maculipennis* in the strict sense), findings which are recorded in English in Hackett and Missiroli (1935, p. 62). *A. messeae* greatly predominated in the Volga Basin and occurred almost in pure culture in peat bogs east of Moscow, on the steppes east of Saratov, along the Volga River and on its delta. The results of the precipitin test on freshly ingested blood from a number of specimens showed that *A. messeae* feeds on man to a varying degree depending on local conditions. It was not plentiful in houses, and many bedrooms had to be searched to obtain a sufficient number with fresh blood for the test. In a large majority of the places visited there were fewer stables than dwellings and fewer pigs, cows or horses than human beings. This was only a year after the famine of 1933, and the amount of livestock was probably below normal.

It would seem that *A. messeae* is a vector here, but not in western Europe, because of a less developed agriculture and animal husbandry. The only comparable area where a widespread infection is due to *A. messeae* is in that part of the Danube Basin which lies in the Balkan Peninsula above the delta. Here the conditions of rural life are not dissimilar to those in Russia, and it is significant that neither on the Danube Delta with its great herds of cattle, nor along the upper reaches of the river in Austria and Germany, is there any malaria, although the anopheline species is the same. Considering the evident attraction exerted by stabled animals where these are present, and the scarcity of engorged specimens in human bedrooms under all conditions, it seems probable that malaria transmission over the extensive range of *A. messeae* occurs only where centers of population, insufficiently protected by stabled domestic animals and antilarval measures, lie close to large and very productive breeding places. The future outlook is one of gradually disappearing malaria as the conditions of rural life improve.

### THE MEDITERRANEAN REGION AND THE NEAR EAST

When we turn to the Mediterranean Basin and the lands of the Near East (which are taken here to include the Balkans and southwestern Asia from Turkey to Iran), we find malaria persisting as a serious endemic disease wherever the anopheline vectors *A. labranchiae* and *A. sacharovi* can breed. As the map indicates, they divide this region between them. *A. labranchiae* occurs in the western Mediterranean, and seems centered geographically in Sicily, spreading to Spain, Corsica, the northern coast of Africa and the rest of southern Italy; it does not anywhere invade the southern coast of France. *A. sacharovi* (referred to in the earlier literature as *elutus*), an even more dangerous vector owing to its habitual association with man, overlaps *A. labranchiae* in Italy, and occupies the whole of the Near East except Arabia. It extends eastward in a broad band lying roughly between the 30th and the 44th parallel as far as Sinkiang in western China and the Outer Mongolian Republic. Only in SPAIN and ITALY is *A. labranchiae* exclusively a brackish-water, coastal form. In the former country it is restricted to a short stretch of Mediterranean Coast in the provinces of Alicante and Murcia, but in Italy it is a coastal form breeding on all the shores south of the 43rd parallel, which is the latitude of the northern tip of Corsica. Where antilarval measures have not reduced it to impotence, it produces an endemic malaria which varies in intensity with the rainfall, but which is always severe. *A. sacharovi* also occurs sparsely on both coasts of Italy and on the islands of Corsica and Sardinia, but is greatly outnumbered by *A. labranchiae;* it is evidently not at home in this western region but, being such an effective vector, cannot be ignored. It is the cause of the malaria on the Po delta and northward along the Adriatic Coast as far as the River Tagliamento, an area beyond the range of *A. labranchiae.* World War II did great damage to drainage works in Italy and produced a recrudescence of malaria such as had not been experienced in forty years and which is only slowly being brought under control.

On the islands of CORSICA, SARDINIA and SICILY, and along the BARBARY COAST of North Africa from Tripolitania to Morocco, where it has no fresh-water competitors such as *A. messeae* or *A. melanoon, A. labranchiae* breeds in fresh and saline waters alike, and in both rivers and marshes. This is a deadly combination, since it is favored by either rain or drought, and hence malaria is always hyperendemic where the streams are perennial, as on the large Mediterranean islands already referred to. In North Africa, however, west of Egypt, malaria depends on rainfall, which is highly irregular from year to year. *Anopheles* breed wherever there is water, and malaria can occur in every inhabited part, but the rainfall is cyclical so that epidemic years, when precipitation is above the average, alternate with dry periods of low transmission when the rivers dry up and the marshy areas are greatly reduced. North African malaria is therefore typically epidemic in character; transmission may be very intense throughout the coastal zone, or it may fail altogether.

MOROCCO, ALGERIA and TUNIS are much alike in physical geography and malaria incidence. They are characterized by ranges of hills running parallel to the coast, providing a succession of climates from the sea to the desert. Malaria is more severe on the coastal belt, but Langeron found it also in the high valleys of the Atlas Mountains up to 8000 feet, where the vector was probably *A. hispaniola.* The desert oases have a permanent endemic malaria due mainly to *A. sergenti*, a more important vector than *A. multicolor*, which, though occasionally incriminated on epidemiologic evidence, has not yet been found infected. The desert nomads are always heavily parasitized and provide a constant reservoir of infection. With the above exceptions, *A. labranchiae* is responsible for all the malaria in these countries, but its range ends somewhere in Libya, and both rainfall and malaria diminish rapidly east of Tunis. Tripolitania is irrigated in part, and the coastal strip has marshes, *Anopheles* and malaria. The remaining three provinces are desert, and so is Egypt except for the widely spaced oases, the delta and the narrow valley of the Nile.

Some sixteen million people live in a restricted area in EGYPT under conditions of climate, irrigation and housing very favorable to the spread of malaria. It is surprising therefore to find so little infection although the disease is mildly endemic everywhere. Parasite indexes are only 1 to 2 per cent in the upper delta and 3 to 7 per cent near the coast; splenomegaly is useless as a guide owing to almost universal schistosomiasis. Towns practically malaria-free will show spleen indexes of 30 to 50 per cent. Egypt is surrounded by regions of intense malaria, but neither the *Anopheles* of the western Mediterranean (*A. atroparvus* and *A. labranchiae*), nor those of the Near East (*A. sacharovi* and *A. superpictus*), nor the dangerous African pair, *A. gambiae* and *A. funestus*, have reached the Nile Delta. *A. pharoensis* breeds there in enormous numbers, especially in rice fields, and is responsible for the amount of transmission which takes place (Barber and Rice, 1937), but like *A. messeae* it becomes a vector only under very favorable conditions, where the human population is dense and unprotected and the breeding places are many and close at hand. A curious characteristic of Egyptian malaria is the predominance of quartan infections in the oases, and their absence on the delta, a phenomenon attributed to the supposed short life of *A. pharoensis* under conditions of heat and saturation deficiency, which is in contrast with the adaptation of *A. sergenti* (the oasis vector) to desert life. This does not explain the complete absence of *P. vivax* in most of the Egyptian oases (Siwa, Baharia, etc.). *A. gambiae* invaded Egypt from the Sudan in 1942–44, possibly by plane, since hitherto this mosquito has not contrived to pass the barrier formed by a straight stretch of the Nile, 58 kilometers long below the second cataract, where it flows between steep banks down to the Egyptian frontier. *A. gambiae* was exterminated in Egypt in 1945 by intensive antilarval measures, and steps have been taken to prevent its reintroduction.

Turning to the BALKANS, we come now upon the last and most dangerous member of the *maculipennis* group, *A. sacharovi*. The habitat of this very effective vector is the Near East, and it is accompanied almost everywhere by a second vector *A. superpictus*, which is complementary in many of its habits. *A. sacharovi* is a mosquito of early and midsummer, breeding in marshes; *A. superpictus* appears somewhat later and continues into the autumn, breeding in foothill streams. The combination of these two species intensifies the malaria, diversifies its distribution and prolongs the transmission season. Adapted as they are in the larval stage to different types of water surface, one may thrive under conditions unfavorable to the other, so that, with few exceptions throughout their common and extensive range, only the highest mountains and uninhabited deserts are free from malaria.

*A. superpictus* has been generally considered a secondary vector, that is, unable by itself to maintain a high degree of endemic malaria without the presence of a more efficient vector like *A. sacharovi*. In Greece the intensity of malaria seems to be more sensitive to variations in the production of *A. sacharovi* than to that of *A. superpictus*. Nevertheless, Barber's (1936) survey of Cyprus revealed what *A. superpictus* can do under ideal conditions. *A. sacharovi* had only a spotty distribution in coastal marshes and 80 per cent of the malaria, hyperendemic over most of the island, was due to *A. superpictus*. The amount seemed quite out of proportion to the small quantity of water available for anopheline breeding in the rainless summers. In Albania too, while *A. sacharovi* assumes a much greater importance, it does not breed far from the sea, and the piedmont malaria due to *A. superpictus* can be exceedingly severe, like that of southern Bulgaria. Hence we should not underestimate the role of *A. superpictus* in maintaining the malaria situation of the Near East.

In the Balkans, as in Cyprus, *A. sacharovi* breeds only in brackish lagoons and marshes of the coastal belt while *A. superpictus* uses the broad, gravelly beds of the torrential hill streams which become greatly reduced in volume toward the end of summer. Neither apparently can breed in the great river basins tributary to the Danube and the Vardar, which produce only *A. messeae*, a vector of importance, however, where rural life is primitive, animal husbandry undeveloped and anopheline density high. YUGOSLAVIA is therefore malarious throughout and Rankov thought that the wide distribution of severe malaria in southern Serbia, which constitutes the Vardar Basin, was probably due to the fact that cattle are relatively scarce in the villages, and are kept in the fields in summer. The flood plain of the Danube is agriculturally more progressive and has less malaria, but the Dalmatian Coast, with its combination of *A. sacharovi* and *A. superpictus*, is hyperendemic throughout. One peculiarity of malaria in Yugoslavia is that the peak of *vivax* infections is said to come later than in Italy, and overlaps that of *P. falciparum* in September. This is called by Simic the "Balkan type" of malaria curve.

Both RUMANIA and BULGARIA, like Yugoslavia, are characterized by having two types of malaria—that of the great river valleys (the Pruth, Danube, and Maritsa), which is relatively mild and geographically discontinuous, because it is carried by *A. messeae*, and that of the Black Sea Coast which becomes progressively more severe from north to south as the range of *A. atroparvus* gives way to that of *A. sacharovi* near Constantsa. It is noteworthy that the delta of the Danube is practically malaria-free, in spite of the remarkable production of *A. messeae* everywhere, although the flood plains above the delta are malarious. This has not been satisfactorily explained although Zotta (1932) refers in this connection to the great amount of cattle on the delta (which however is unstabled) and to the fact that many specimens of *A. messeae* proved to have avian blood in their stomachs. When the delta was occupied in 1917–18 by Bulgarian and Turkish troops, it became a hotbed of malaria, an infection which has since spontaneously disappeared. There is also a great contrast between the almost nonmalarious highlands of Transylvania in the north, which are beyond the range of *A. superpictus*, and the hyperendemic Struma Valley in the mountains of south Bulgaria where *A. superpictus* alone is the vector (Drensky, 1939–40). The characteristic anopheline of the Rumanian highlands is "typicus," which Martini and Zotta (1933) thought must be the vector of the low-grade transmission found in some areas (Sokola, Ploeni, etc.). This commonly innocuous form has not been incriminated elsewhere except, as already noted, in the Caucasus region.

GREECE deserves special mention as possibly the most heavily infected country outside of the tropics (see Balfour, 1936; Pampana 1941). Malaria here causes the maximum injury and loss, since it is everywhere hyperendemic, but because of the winter pause and the variable climate, is unable to reach that intensity of transmission which establishes adult immunity in parts of tropical Africa. Macedonia and Epirus are the most heavily infected regions, and the barren Greek islands the least. Ciuca calculated that of the six and a half million inhabitants of Greece before World War II, two millions were infected, and Balfour gives the death rate from malaria as 80 per 100,000 for the whole country over the five-year period 1930–34, as compared with 1.7 in Italy in 1938. According to Barber, Mandekos and Rice (1937), 69 per cent of the infants in Macedonian villages under observation in 1936 became infected during the course of the summer. Foy stated that blackwater fever was more prevalent in Greece than in any other country in the world. This situation is due to the deadly efficiency of the *sacharovi-superpictus* combination, to the long transmission season from April to November, and to the partial loss of immunity suffered periodically by the population because of the cyclical nature of the climate, in which several years of excessive rainfall are succeeded by a period of drought during which transmission almost fails. This is the "endemic-epidemic" malaria described by Balfour, which bears a great similarity to that of North Africa described above. Malaria was greatly increased over a long period by both World Wars. Mass exchanges of population after World War I led to the settlement in 1922 of more than a million nonimmune immigrants in some 1400 new villages in Macedonia; while after World War II, the general destruction, displacement of people, undue rainfall and insufficient food and drugs produced epidemics in places such as Athens where malaria had almost disappeared.

In the MIDDLE EAST, from Constantinople to Iran, the same pair of anophelines, *A. sacharovi* and *A. superpictus* are the cause of all the widespread malaria except for the ARABIAN PENINSULA, where the anopheline fauna is derived from Africa on the west, and from India on the east. We owe to Buxton (1944) the collection of the little knowledge we have of the malaria of this relatively uninvestigated region. Travellers are always impressed with the prevalence of this disease in a country which is mainly desert; but wherever man can live there must be water, and wherever there is water in Arabia there is malaria. On the coast of the Red Sea *A. gambiae* is the vector, producing much malaria at Mokha and Mecca, but apparently less at Medina. Yemen has a relatively dense population and is highly malarious. On the south coast, malaria is rare and epidemic at Aden, but severe in the oases where it is probably due to *A. culicifacies*, although *A. gambiae* is widespread in the Aden Protectorate. Central Arabia is notorious for "oasis fever" which has wiped out colonies of settlers; it resembles the desert malaria of western Egypt and may be caused by *A. sergenti* or possibly *A. multicolor*. On the northeast coast, Muscat is malarious all the year, owing to *A. culicifacies* or *A. stephensi*. Malaria is very common also on the BAHREIN ISLANDS, important because of their oil wells, and accounts for a quarter of all the patients who are hospitalized. While the average rainfall is but 3.25 inches, with three to six rainy days a year, the climate is hot and humid and the date plantations have copious springs of warm, slightly brackish water. According to Afridi and Majid (1938), *A. stephensi* is the vector, and Manama the largest city, with a population of 50,000, had a spleen index of 39 and a parasite rate of 22. It is interesting that under these oasis-like conditions, the infections are divided almost equally among *P. falciparum*, *P. vivax* and *P. malariae*.

None of the authors mentions the presence of either *A. sacharovi* or *A. superpictus* in Arabia, but both are the principal vectors in all the other regions of the Middle East. Here *A. sacharovi* for some unexplained reason shifts its breeding places from brackish marshes and lagoons to fresh water, and invades the interior of all these countries. In TURKEY it breeds on the coast and on the Anatolian plain, occupying all suitable water, fresh or salt; all the provinces of economic importance are malarious. Martini suggested that this species is now relieved at last, by heat and dryness, from competition with the other *maculipennis* forms. Further east, *A. sacharovi* abandons salt marshes entirely. Sautet could not find it in a coastal marsh near Alexandretta nor in brackish waters in Lebanon or Syria, and Kligler (1930) refers to it as a fresh-water form in Palestine. In Iraq it seeks the flood waters of rivers, and in Iran it has become a rice-field breeder. Thus its breeding habits become diversified in its eastern range and the distribution of malaria is modified and extended.

LEBANON, SYRIA, PALESTINE, and TRANSJORDAN are described by Macdonald and Leeson (1946) as a single geographic unit, and consist essentially of a very narrow coastal plain, a coastal range of mountains rising in places to 9000 feet, a rift valley which varies in altitude from +3000 to −1300 feet, an inland range of mountains and east of this a vast expanse of desert. Rainfall decreases from west to east. *A. sacharovi* breeds typically in marshes, and is present almost throughout the coastal plain and rift valley; *A. superpictus* breeds in the streams scattered through the two mountain ranges; *A. sergenti* is a desert form present only in the east, breeding in minute seepages and the edges of channeled water as in Egypt. There is a fourth vector, *A. claviger*, which presents surprising anomalies in several respects: it breeds during the hot summer in water stored underground and it enters houses freely, biting the human occupants. These habits, which are foreign to it in every other part of its vast range, cause it to invade cities where cisterns are numerous (Jerusalem has more than 60,000) and convert it into a vector of urban malaria. All four of these anophelines infest houses, stables and tents, and make malaria the most prevalent and important disease. It is relatively light in LATAKIA and LEBANON where there are practically no streams or marshes, and large rivers like the Tigris are not dangerous in their upper courses, but elsewhere malaria prevails on the coast, in the rift valley, in the hills, and in the oases of the eastern desert, the largest of which, Damascus, lies in a well-watered plain draining eastward into a marshy depression without an outlet. Palestine differs from Syria and Lebanon in maintaining effective control of the disease, so that although malaria is still endemic in every region of the country, the spleen rates in such important areas as Jerusalem, Safad, Haifa and Jaffa have been reduced practically to zero.

IRAQ is an extension eastward of the Syrian Desert, and is remarkable for the two great rivers, the Tigris and Euphrates, which enclose the ancient inhabited land of Mesopotamia. Neither of these rivers is a dangerous source of anophelines, and what little malaria there is at Baghdad or Mosul is *vivax* in type. Where the rivers meet near Basra the infection becomes endemic and severe owing to great lakes and marshes. There *P. falciparum* predominates, and epidemics follow the flooding of the rivers which occurs every three or four years and gives a tremendous impulse to the breeding of *A. sacharovi*.

IRAN, with which we complete the synopsis of malaria in the western palearctic region, presents features with which we are already familiar in the Middle East. The infection is endemic wherever altitude or waterless desert does not preclude transmission. *A. sacharovi*,